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SECTION 1

Information regarding Project / Project Personnel

i	Grant Number	57445
ii	Title of the Project	Investigation and Evaluation of Chronic Kidney Disease of Uncertain Aetiology in Sri Lanka
iii	Principal Investigators	Ministry of Health Dr Nihal Jayathilake Dr Palitha Mahipala World Health Organization Dr Shanthi Mendis Dr Firdosi Rustom Mehta Dr Lanka Jayasuriya Dissanayake Dr Navaratnasingam Janakan
iv	Co-investigators	Details attached below
v	Institute(s) where research was being carried out	Ministry of Health (MoH) in collaboration with World Health Organization (WHO)
vi	Date of award	22 November 2010
vii	Date of completion of Project	31 December 2012
viii	Total allocation of funds (SLR)	70,000,000
ix	Total spent (SLR)	Financial report attached
x	Number of Research Students employed	Hospital registry - 02 (pre-intern doctors) Literature repository - 02 (pre-intern doctors)
xi	Post graduate degree completed with dates	Nil
xii	Number of Technical Assistants and/ or laborers employed and period of service	45 Field Assistants worked for population prevalence study, environmental studies and analytical studies for a period of two years Two coordinators were appointed for coordination of field activities and administrative & secretarial work for the clinical trial for a period of one year
xiii	Publications/Communications arising from the project during the	A paper entitled 'Chronic kidney disease of uncertain aetiology (CKDu) in Sri Lanka; prevalence and

SECTION 2

Executive Summary of the Project

An apparently new form of chronic kidney disease which cannot be attributed to diabetes mellitus, hypertension, primary glomerular nephritis or other known etiologies has emerged in certain parts of Sri Lanka. This Chronic Kidney Disease of uncertain etiology (CKDu) is slowly progressive, probably starting in the second decade of life, and asymptomatic until very advanced. In these areas, CKDu has become a major public health problem causing devastating social, economic and health impacts.

The total number of affected individuals with CKDu is unknown; large numbers however are currently undergoing treatment for this condition. The financial cost to the patients and the state is considerable. Prevention would be the most cost-effective and affordable approach.

To resolve this public health issue, the Ministry of Health requested the collaboration of World Health Organization to conduct a multisectoral and multidisciplinary research built on existing evidence. This coordinated series of research activities from varying disciplines was designed to generate evidence regarding aetiology and other aspects within a specified time period to make prevention an option.

An operational platform for the implementation of this research project was established with the formulation of three committees at different levels i.e. National Steering Committee, Management Committee & Scientific Committee, with clearly defined roles and responsibilities. In addition to these committees, there was a panel of International Experts providing technical inputs for the conduct of research. They also helped in ensuring quality and standards of research through peer review of protocols, reports and publications. Ethical clearances were obtained through relevant ethical review committees.

The whole research was divided into 4 main components as below:

- I. Prevalence and causative factors for CKDu in Sri Lanka
- II. Randomized Clinical trial to examine the renal effects of an Angiotensin Converting Enzyme Inhibitor (Enalapril) in adults with CKDu
- III. Socioeconomic and productivity impact of CKDu
- IV. Nephrotoxic herbal remedies used in Sri Lanka

I. Prevalence and causative factors for CKDu in Sri Lanka

The prevalence and causative factors for CKDu was a comprehensive study with many subcomponents as follows:

- Ia Population prevalence Study
- Ib Analytical & Environmental Study
- Ic Hospital Based CKDu registry
- Id Geographical mapping of identified variables
- Ie Establishment of a Literature repository for CKDu

Ia Population Prevalence Study:

A cross sectional study was conducted to determine the prevalence of CKDu. This study determined the age-standardized prevalence of CKDu as 12.9% (95% confidence interval [CI] = 11.5% to 14.4%) in males and 16.9% (95% CI = 15.5% to 18.3%) in females. Severe stages of CKDu were more frequent in males (stage3: males versus females = 23.2% versus 7.4%; stage 4: males versus females = 22.0% versus 7.3%; $P < 0.001$). The risk was increased in individuals aged >39 years and those who farmed (chena cultivation) (OR [odds ratio] = 1.926, 95% CI = 1.561 to 2.376 and OR = 1.195, 95% CI = 1.007 to 1.418 respectively, $P < 0.05$). The risk was reduced in individuals who were male or who engaged in paddy cultivation (OR = 0.745, 95% CI = 0.562 to 0.988 and OR = 0.732, 95% CI = 0.542 to 0.988 respectively, $P < 0.05$). The prevalence of CKDu found in this study was higher than that reported previously (2 – 3%).

Although the prevalence in females was higher, more severe stages of CKDu were seen more often in males. The reason for this discrepancy is not clear. Factors such as low iron stores in females in lower socioeconomic groups may have an influence on the excretion of heavy metals and oxidative stress on the kidney. This would make the kidneys more vulnerable to CKDu, resulting in a higher prevalence in females. On the other hand, male sex has been reported to be a risk factor for progression to end-stage renal disease, and this may partly explain the occurrence of more severe stages of CKDu in men.

Ib Analytical & Environmental Study

A cross sectional study was conducted, to determine the risk factors for CKDu. Arsenic, cadmium, lead, selenium, pesticides and other elements were analyzed in biological samples from individuals with CKDu and compared with age- and sex-matched controls in the endemic and non-endemic areas. Food, water, soil and agrochemicals from both areas were analyzed for heavy metals. The analytical & environmental study consisted of 4 different components as follows:

- Case-control studies comparing newly diagnosed cases of CKDu and matched controls to identify risk factors for CKDu
- Cross sectional comparison of potential environmental toxins in endemic and non endemic areas for CKDu
- Determination of pesticide residues
- Analytical Studies of Human post mortem tissues

The mean concentration of cadmium in urine was significantly higher in those with CKDu (1.039 $\mu\text{g/g}$) compared with controls in the endemic and non-endemic areas (0.646 $\mu\text{g/g}$, $P < 0.001$ and 0.345 $\mu\text{g/g}$, $P < 0.05$) respectively. Urine cadmium sensitivity and specificity were 70% and 68.3% respectively (area under the receiver operating characteristic curve = 0.682, 95% CI = 0.61 to 0.75, cut-off value ≥ 0.397 $\mu\text{g/g}$). A significant dose–effect relationship was seen between urine cadmium concentration and CKDu stage ($P < 0.05$). Urine cadmium and arsenic concentrations

in individuals with CKDu were at levels known to cause kidney damage. Food items from the endemic area contained cadmium and lead above reference levels. Serum selenium was $<90 \mu\text{g/l}$ in 63% of those with CKDu and pesticides residues were above reference levels in 31.6% of those with CKDu.

These results indicate chronic exposure of people in the endemic area to low levels of cadmium through the food chain and also to pesticides. Significantly higher urinary excretion of cadmium in individuals with CKDu, and the dose–effect relationship between urine cadmium concentration and CKDu stages suggest that cadmium exposure is a risk factor for the pathogenesis of CKDu. Deficiency of selenium and genetic susceptibility seen in individuals with CKDu suggest that they may be predisposing factors for the development of CKDu.

1c Hospital Based CKDu registry

In order to monitor the trends in the disease burden attributable to chronic kidney disease (CKD) in general and chronic kidney disease of uncertain aetiology (CKDu) in specific, efforts were taken to establish a computerized database. As an initial step to conversion to a national registry, hospital-based registries of patients attending renal clinics were established in selected hospitals in the North Central Province namely TH Anuradhapura, DGH Polonnaruwa, BH Medirigriya and BH Madawachchiya. Once the initial work was completed the datasets were handed over to Ministry of Health for conversion to a national level registry.

As per the preliminary analysis, out of the 1997 included in the registry 775 (39%) could be identified as CKDu. Others were due to hypertension 798 cases (40%), hypertension & diabetes 118 cases (6%), diabetes 90 (5%), snakebite 121 (6%), obstructive uropathy 32 (2%), glomerulonephritis 30 (2%), polycystic kidney disease 10 (1%) and other known causes 18 cases (1%).

Bivariate analysis found that compared to CKD of known aetiology patients, CKDu patients were more likely to be males (OR = 2.4, 95% CI: 1.9, 3.0), aged ≤ 50 years (OR = 1.6, 95% CI: 1.3, 2.0), residents of Anuradhapura district (OR = 1.26, 95% CI: 1.04, 1.5), less educated (OR = 1.3, 95% CI: 1.04, 1.7), past or current smokers (OR = 1.9, 95% CI: 1.6, 2.3), regular consumers of alcohol (OR = 1.9, 95% CI: 1.6, 2.4), consumers of illicit liquor (OR = 1.9, 95% CI: 1.6, 2.3) and exposed to agrochemicals (OR = 1.9, 95% CI: 1.6, 2.4).

Aetiology (known vs. unknown) was not related to ethnicity (OR = 1.1, 95% CI: 0.5, 2.2), income (OR = 1.1, 95% CI: 0.9, 1.4), occupation (OR = 0.9, 95% CI: 0.7, 1.2) and source of drinking water (OR = 1.3, 95% CI: 0.98, 1.6).

1d Geographical mapping of identified variables

This study was undertaken to map all sampling populations (Household level) in population prevalence study which was conducted to confirm or refute previously reported wide ranges in the prevalence of CKDu as well as mapping of sites of environmental samples including water, soil, weedicides and fertilizers obtained from endemic and non-endemic areas.

Ie Establishment of a literature repository for CKD

Establishing a literature repository on CKD especially CKDu was a long felt need. Since early 2000, CKDu has caught the attention of many clinicians, epidemiologists, policy makers and researchers. Many of them have conducted studies ranging from case studies to population based studies. In addition, Ministry of health, regional health authorities, universities, NGOs and international organizations have conducted several meetings and seminars and produced discussion papers and reports. Unfortunately, many of these documents remain as 'grey literature' and not accessible to those who are interested in this subject.

It is known that repositories facilitate a scholarly communication process. The dissemination and the wide use of the repository would facilitate, engender and encourage the ongoing collaborative and interdisciplinary research on CKDu.

In addition to the publication a CD was also produced which includes international publications, slide presentations and news paper articles were collected and compiled. A publication and a CD has been produced

II. Randomized Clinical trial to examine the renal effects of an Angiotensin Converting Enzyme Inhibitor (Enalapril) in adults with CKDu

The objective of this double blind controlled study was to investigate the effect of enalapril on the progression of CKDu by comparing and evaluating the effect of enalapril to a placebo on estimated GFR and albuminuria.

There was no significant difference in the baseline characteristics (age, sex distribution, albumin to creatinine ratio and eGFR) in the enalapril and placebo groups. The mean systolic and diastolic blood pressure levels declined significantly in both enalapril and placebo groups. The mean reduction in systolic blood pressure was 11.6 and 9.9 mmHg ($p=0.005$, 0.031), respectively. The mean reduction in diastolic blood pressure was 9.7 and 8.3 mmHg ($p<0.001$), respectively. There was no significant difference between the treatment and placebo groups in the reduction in systolic blood pressure and diastolic blood pressure.

There was a significant improvement in the albumin to creatinine ratio in the enalapril group compared to the placebo group ($p=0.005$). In the enalapril group, the mean albumin to creatinine ratio declined from 162.0 mg/g (SD 321.7) at baseline, to 55.4 mg/g (SD 122.4) at one year follow up. In the placebo group, the mean albumin to creatinine ratio increased from 197.9 mg/g (SD 461.6) at baseline to 253.2 mg/g (SD 558.7), at one year follow up.

In both groups, the eGFR declined significantly ($p<0.001$), during the 12 month followup. In the enalapril group the mean eGFR declined from 71.7 ml/min (SD 22.2) to 57.1 ml/min (SD 16.1). In the placebo group the mean eGFR declined from 73.8 ml/min

(SD 24.2) to 54.7 ml/min (SD 20.3). There was no significant difference in the rate of decline between the two groups.

These results indicate that enalapril was effective in reducing albuminuria in these patients with nephropathy due to exposure to environmental toxins.

III. Socioeconomic and productivity impact of CKDu

Only a few publications describe the psycho-socio and economic impact on the household and the coping strategies adapted by the households. There are also no published intervention studies on social support for the affected families. This socio-economic and productivity impact study was undertaken in this context as a part of the National Research programme for CKDu with the focus on understanding the disease burden at both local and national levels.

The socio-economic and productivity impact study has two research components, i.e., the community-based study and the hospital-based study. The community based study attempts to explore the socio-economic and psychological impacts of chronic kidney disease on affected individuals, households and communities with identified methods of mitigating it.

The focus of the hospital-based study is to estimate costs of care to the health system.

IIIa Community Based Study

The community-based study has gained comprehensive understanding of the impact of CKDu at individual, family and community levels from a phenomenological perspective. There is hardly any difference between the two communities in Medawachchiya and Padaviya DS Divisions in relation to the impact of CKDu even though there are some structural distinctions between the two locations where the greater majority of the population in Padaviya are migrants under the government resettlement programme initiated since late 1950s. Comparatively, the Medawachchiya DS Division is constituted with traditional villagers where the social integration is little higher than that of Padaviya. The main findings of the study are:

1. Community Discourse Developed on CKDu
2. Increasing Economic Burden on Families of CKDu Patients
3. The Farming Community Lacks a Proper Social Security Scheme
4. Importance of Regular Screening Programmes
5. Marginalization of Villagers in the Process of Discovering Etiology
6. Drinking Water as a Commercial Good in the Locality
7. Misuse of Fertilizers and Pesticides as a Risk Factor for CKDu.
8. High Demand for Government Hospital for Regular Treatment
9. Limitations in the Healthcare Delivery System

It is significant to note that the Public healthcare delivery system plays a dominant role in both identifying the CKDu patients and treating them for their ill-health. The

patients and their families were highly appreciative of the contribution made by the healthcare delivery systems as well as the role of the local healthcare providers in this regard. However, the healthcare delivery system has some limitation in implementing different interventions with regard to CKDu.

There are proposed social interventions to address the interrelated issues that are inherited with CKDu which needs to be reviewed and implemented at national and regional level.

IIIb Hospital Based Study

The studies were done in a range of facilities to estimate costs of care in the health system: Padaviya, Medawachchiya, (to represent Divisional Hospitals) and Anuradhapura Teaching Hospital and Renal Care and Renal Research Centre in Anuradhapura to provide information regarding care at the tertiary level.

Cost of hospitalization (including dialysis visits) to the household were estimated by interviewing patients or accompanying persons or carers regarding the cost of hospitalization in Anuradhapura hospital, Padaviya and Medawachchiya.

CKDu results in considerable costs to households, the health system and to the economy. Therefore there should be a concerted effort to mitigate these effects.

IV. Nephrotoxic herbal remedies used in Sri Lanka

Herbal / Ayurvedhic medicines, containing Aristolochic acid is implicated as a causative factor of renal disease. Herbal medicines made of *Aristolochia indica* (Sapsanda) which contain Aristolochic acid for treatment of various conditions are being used and this might be a contributory factor in the causation of CKDu. The major objectives of this study were to examine the species of *Aristolochia* that grow in Sri Lanka particularly and to list the species and remedies used in Sri Lanka that contain this product.

In Sri Lanka, about 66 Ayurvedic prescriptions which contain *Aristolochia* (Sapsanda/Sasanda) are available for the treatment of more than 20 diseases. *Aristolochia* species are mainly used in remedies to cure snakebites and other poison bites. *Aristolochia indica*, known as Sapsanda or Sasanda, is the major species used in remedies by Sri Lankan Ayurvedic practitioners. There are many remedies that contain *Aristolochia indica* in Ayurvedic literature, Further studies are required to objectively evaluate whether ayurvedic practitioners are currently using these remedies to treat patients and if so to ban/dissuade their use.

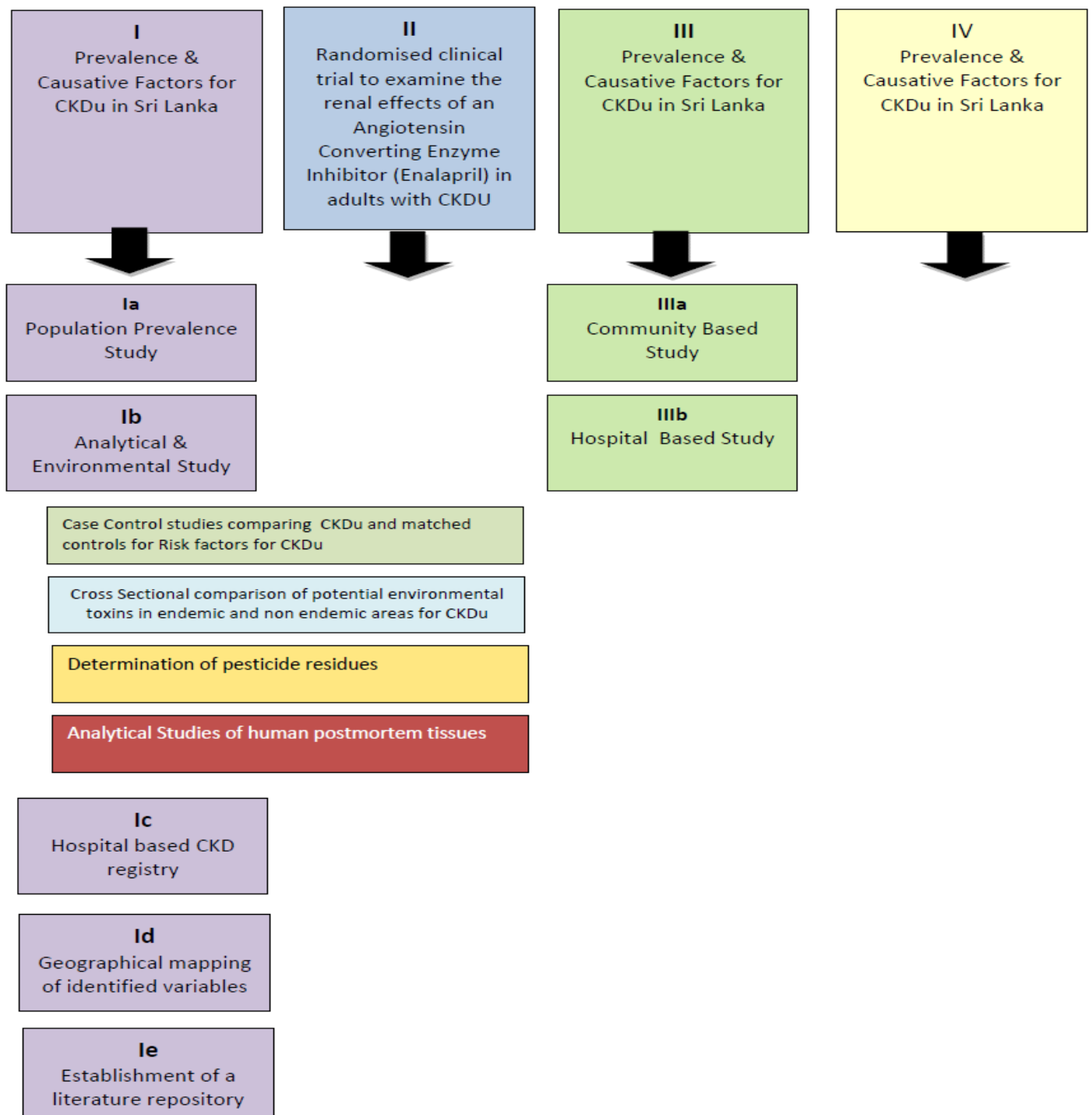
Conclusions

This coordinated research effort yielded valuable data which have already influenced much dialogue and action in the Country. This will also act as a base for further research and coordination in the future. The results have assisted in scientific advancement by dissemination of a research paper publication in the BMC

Nephrology, Compilation of a literature repository/CD and also creation of an extensive database with all variables and results of analyses.

The results have also influenced National and socio economic development through dialogue at the highest level and formulation of specialized ministerial committees which have resulted in submission of cabinet papers to influence implementation of the recommended action. Dissemination and application of the results is an ongoing process which will strengthen the research data in the processes of policy formulation and dialogue.

Summary of the work carried out under the National Research Effort for CKDu

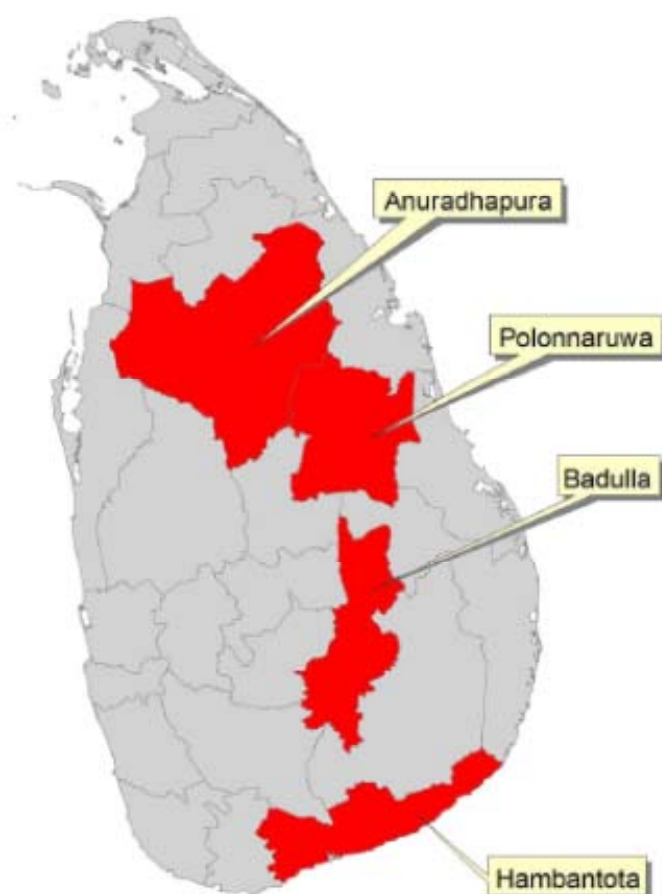


SECTION 3

Introduction & Background

An apparently new form of chronic kidney disease which cannot be attributed to diabetes mellitus, hypertension, primary glomerular nephritis or other known etiologies has emerged in the North Central Region of Sri Lanka. This Chronic Kidney Disease of uncertain etiology (CKDu) is slowly progressive, probably starting in the second decade of life, and asymptomatic until very advanced. The North Central Region includes North Central Province and parts of Eastern, North Western and Uva Provinces. In these areas, CKDu has become a major public health problem causing devastating social economic and health impacts.

Map of Sri Lanka showing the location of Anuradhapura, Polonnaruwa and Badulla districts in the endemic area and Hambantota district in the non-endemic area



The total number of affected individuals with CKDu is unknown; however hospital statistics suggest that in excess of 8,000 people are currently undergoing treatment for this condition. The financial cost for the management of these patients is considerable. Prevention would be the most cost-effective and affordable approach. However, currently it is not an option as the cause of the disease is uncertain.

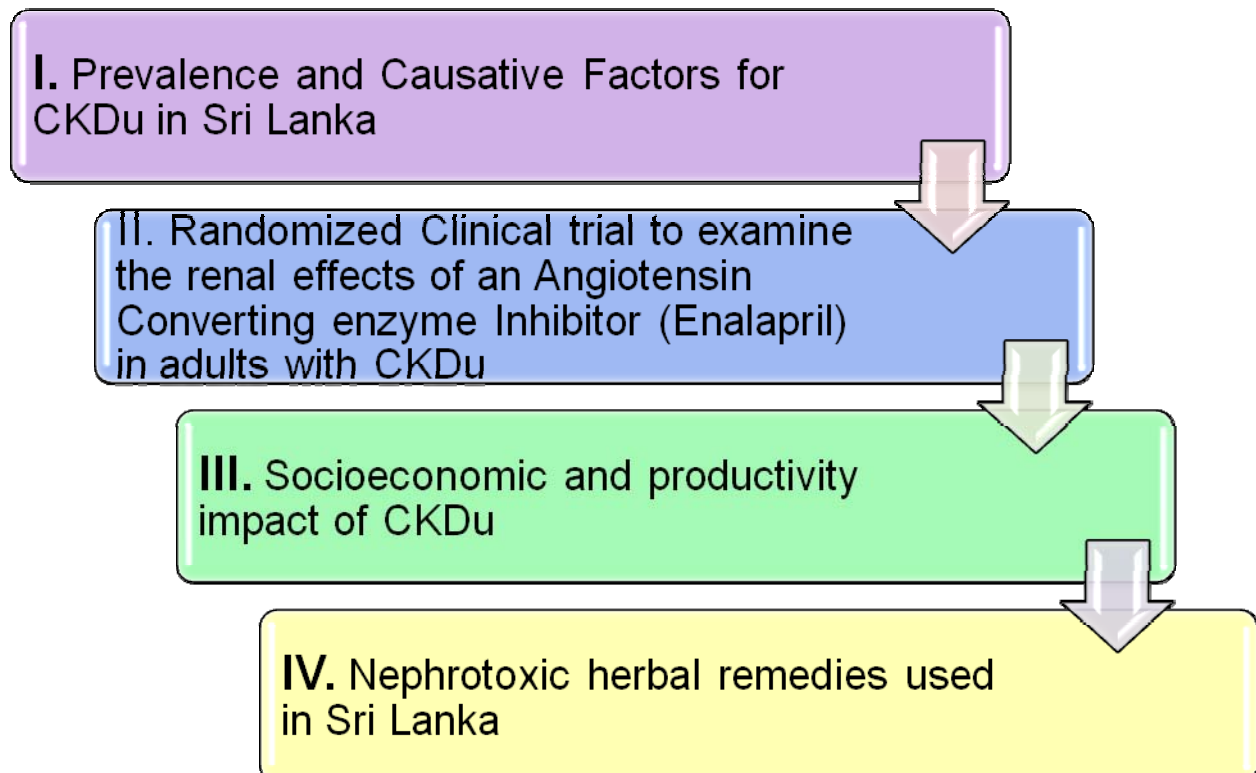
To resolve this public health issue, the Ministry of Health in collaboration with the World Health Organization conducted multisectoral and multidisciplinary research effort built on existing evidence. This coordinated series of research activities from varying disciplines was designed to generate conclusive evidence regarding the aetiology within a specified time period to make prevention an option.

The total budget for the comprehensive multidisciplinary research project was Rs. 100 million, of which Rs. 30 million was borne by the WHO. As this was of national importance, the National Science Foundation agreed to support this project, and submitted a research proposal to the Department of National Planning to secure the balance funds (Rs. 70 million) needed for the successful completion of the project.

The Studies conducted can be divided into 4 sub-projects as indicated below. A detailed report for each of the 4 subprojects will be submitted which highlights the following areas:

- Introduction / Background
- Scientific scope of the project (overall & specific objectives)
- Materials & Methods (including statistical methods)
- Results/Outputs
- Discussion
- Conclusions
- References
- Problems if any, encountered during the implementation of the project
- Major findings and follow up activities

Main Sub-Projects of the CKDu research



As can be seen from the main research sub projects listed above, there is a deviation from the studies agreed upon in the original proposal. As the research progressed over the study period (27 months) the priorities had to be re-aligned to the findings and evidence that was generated through the studies. In addition a few new studies were found imperative to be introduced in order to generate scientific evidence on the research subject. One of the main reasons for this was limited funds. As the studies progressed, expenditures for some components exceeded the amounts budgeted earlier. *It was clearly mentioned in the original proposal that the funding might not be sufficient for all studies listed and there may be need for priorities to be changed.* The following table briefly describes the deviations that occurred during the progression of the study and the names of the co-investigators.

Comparison of the Studies listed in the original proposal and changes made subsequently

No	Project Identified in Original proposal that is included in the subproject	Sub-project	Co-investigators
I.	<p>A survey of CKD of uncertain aetiology in the North Central Region (4.3)</p> <p>Cross sectional comparison of the high and low prevalence areas (4.4)</p> <p>Case – Control Studies comparing newly diagnosed cases of CKD of uncertain aetiology and matched controls (4.5)</p> <p>Analytical Studies of Human and animal tissues (4.6)</p> <p>Establish a national CKD Registry (4.7)</p>	<ul style="list-style-type: none"> - Population prevalence study - Analytical and environmental studies - Comprised of following components <ul style="list-style-type: none"> • Cross sectional comparison of potential environmental toxins in high and low prevalent areas for CKDu • Case-control studies comparing newly diagnosed cases of CKD of uncertain aetiology and matched controls to identify risk factors for CKDu • Determination of pesticide residues in urine of people with CKDu • Analytical studies of human post mortem tissue - Hospital based CKD registry - Geographical mapping of identified variables - Establishment of a literature 	<p>Dr Paba Palihawadana Dr Thilak Abeysekera Dr Meriyanthi Gunethilake Prof. J. M. R. S. Bandara Prof. Janitha Liyanage Prof. Rezvi Sheriff Prof. Oliver Ileperuma Prof. Ravindra Fernando Dr S. Ginige Dr Pathmalal Manage Dr L Rajapakse Dr P Bandara Dr U Karunaratne Dr D. L. Waidyaratne Dr R Alagiyawanna Dr A. V. Ranasinghe Dr A Bandaranayake Dr N. Seneviratne Dr N. M. Perera Dr A Kulasinghe Dr H Karunathilake Dr A. M. C. D. Abeysinghe Dr H. T. Wimalasena Mr. Dilip Hensman Mr. Sumudu Hewawasam Mr. Ruwan Bandara Mr. S. Sumanaweera</p>

		repository for CKD Not Done	
	Cohort Study (4.8)		
II.		Double blind randomized clinical trial to examine the renal effects of an Angiotensin Converting Enzyme Inhibitor (Enalapril) in adults with CKDu	Dr S. Mathu Prof. Rezvi Sheriff Prof. Saroj Jayasinghe Dr Thilak Abeysekera
III.		Socioeconomic and productivity impact of CKDu	Dr Chandani Liyanage Prof. Ramani Jayathilake Prof. Amala de Silva Prof. Saroj Jayasinghe Dr Anuradhani Kasthuriratne
IV.		Nephrotoxic herbal remedies used in Sri Lanka	Dr P. Hemachandra Dr P. Hewagamage Dr K. K. D. S. Ranaweera Dr D. N. Ethugala

The following table also briefly describes in detail why there was need for changes as the study progressed

Studies listed in the original proposal and changes made subsequently

	No.	Studies listed in the original proposal	Changes made & justification
I	1.	Systematic survey of selected households in North Central Region to find the prevalence of CKDu (4.3)	No changes made. A population prevalence study was conducted.
	2.	Cross sectional comparison of potential environmental toxins in high and low prevalent areas for CKDu (4.4)	No changes made
	3.	In-depth case control studies to identify risk factors for CKDu (4.5)	No changes made
	4.	Analytical Studies of Human and Animal tissues (4.6)	

		Human renal biopsy analysis	<p>The objective was to demonstrate the characteristic histological pattern and electron microscopic pattern of CKDu and subject the renal tissues for multiple element analysis.</p> <p>However, this study was not conducted due to reasons related to obtaining patient consent/ethical issues etc. In addition the cost for analysis of metals in human tissues, were far greater than originally anticipated and was considered not very cost effective</p>
		Human post mortem studies	No changes made
		Animal (slaughterhouse) studies	This study was not done due to low priority and logistic difficulties mainly the problem of identifying the exact location where the animal originated from etc
		Determination of pesticide residues in urine of people with CKDu	This was not originally included in the proposal. However subsequent to anecdotal evidence suggesting possible involvement of agrochemicals in the aetiology of CKDu, it was deemed essential to do this component as well.
	5.	National CKD Registry (4.7)	The original plan was to establish a national registry with inclusion of newly detected cases from the population prevalence study as well. However, due to logistic difficulties finally this activity was confined to four major hospitals in the endemic areas for CKDu. The activity was also re-named as “establishment of a hospital-based CKD registry”.
	6.	CKDu literature repository	This was not an identified activity under the original proposal however with the progression of the study and priority areas emerging this was found to be a useful document to from a

			<p>basis for scholarly communication and future research on the subject. An additional CD of relevant international publications, slide presentations and newspapers articles some following investigative journalism is also included</p>
		Cohort study (4.8)	<p>This follow-up study was to observe individuals with and without exposure of interest, prospectively, to compare the frequency of renal impairment and renal failure due to CKDu.</p> <p>Considering the long latent period for development of disease and the issues embedded in the cohort study design including financial commitment, it was decided to exclude this study from the research project.</p>
II		Double blind randomized clinical trial	<p>This study was not included in the original research proposal. Traditionally, CKDu patients are also treated with ACE inhibitors, despite lack of evidence on clinical efficacy and its effect in halting or reducing the progression of CKDu.</p> <p>In this scenario, it was found necessary to examine the renal effects of an ACE inhibitor (enalapril) in adults with CKDu.</p>
III		Socioeconomic and productivity impact of CKDu	<p>This study was not in the original proposal. The need to study the socioeconomic impact of the disease was felt during the conduct of the research project to elucidate the social impact of this condition amongst affected communities .</p>
IV		Nephrotoxic herbal remedies used in Sri Lanka	<p>This study too emerged as a priority with the progression of the research due to the widespread use of herbal medicine containing Aristolochic Acid. This was not highlighted as a separate study in the original proposal.</p>

Operational structure

An operational platform for the implementation of this research project was established with the formulation of three committees at different levels i.e. National steering Committee, Management Committee & Scientific Committee, with clearly defined roles and responsibilities . In addition to these committees, there was a panel of International Experts providing technical inputs for the conduct of research. They also helped in ensuring quality and ethical standards of research through peer review of protocols, reports and publications.

The following documents relating to the operational platform is attached overleaf.

- (a) Circular issued by the Ministry of Health
- (b) Functions & responsibilities of main stakeholders

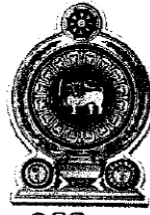
(a) Circular Issued by the Ministry of Health

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சுவசிரிபாய
SUWASIRIPAYA

எனது இல)
My No.) PA/ E&OH/ WE/ 7/2010

உமது இல)
Your No. :)

திகதி)
Date) 05/10/2010

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சுகாதார பராமரிப்பு மற்றும் போசணை அமைச்சு
Ministry of Healthcare & Nutrition

National Research Programme, Chronic Kidney Disease of Unknown Aetiology (CKDu)

The Ministry of Health in collaboration with the World Health Organization (WHO) had initiated a multisectoral and multidisciplinary research effort to generate conclusive evidence regarding the aetiology of a new form of chronic kidney disease (CKDu) prevalent in some areas of Sri Lanka. This research programme commenced using the funds provided by the WHO. As this is of national importance, the Treasury has agreed to provide further funding through National Science Foundation (NSF) and In this regard, an agreement has been finalized between the NSF and WHO. This fund will be made available by November 2010.

An operational platform for the implementation of this research programme has been established with the formulation of three committees at different levels (National Steering Committee, Managerial Committee and Scientific Committee) (annexure I). The research process is dynamic and currently nine components have been identified as of top priority. The details of these research components are given in annexure II.

Your kind cooperation and collaboration in moving this research effort of national importance is highly appreciated.

Dr. P. G. Maheepala
Additional Secretary (Medical Services)

Dr. P. G. Maheepala
Additional Secretary (Medical Services)
Ministry of Health
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Colombo 10

385, පූජා බද්දගම විමලවංශ හිමි මාවත, කොළඹ 10, 385, வணக்கத்துக்குரிய பத்தேகம விமலவங்க தேவரோ மாவத்தை, கொழும்பு 10.
385, Rev. Baddegama Wimalawansa Thero Mawatha, Colombo 10, Sri Lanka.

(b) Functions & responsibilities of main stakeholders

**National Research Programme for
Chronic Kidney Disease of Unknown Aetiology**

Functions & Responsibilities of Main Stakeholders

Ministry of Health

- Overall management of the research
- Provision of technical assistance and guidance
- Monitoring and evaluation at the field level
- Monitoring and evaluation at the central level
- Quality control
- Fund mobilization
- Fund management

World Health Organization

- Management and logistical assistance
- Technical assistance for research proposal development and data analysis
- Ensuring quality and ethical standards of research
- Fund mobilization
- Fund management
- Secretarial support
- Preparation of final report in collaboration with Ministry of Health

Terms of Reference

National Steering Committee

- Advice on policy issues in relation to the CKD problem in Sri Lanka
- Advice on technical, legal, scientific and administrative issues in relation to the CKD problem in Sri Lanka
- Ensure coordination amongst different stakeholders in the CKD research effort
- Liaise with donors and UN agencies for advocacy and resource mobilization
- Management of public relations

Management Committee

- Implement the decisions of the National Steering Committee
- Ensure multisectoral participation and support intersectoral action required
- Assist in resource mobilization for the CKD research effort
- Review of protocols, reports and publications produced by the Scientific Committee
- Identify priorities for CKD research and make recommendations on resource allocations
- Monitor and evaluate the implementation of CKD research

Scientific Committee

- Provide technical input for the development of the research proposal
- Preparation of the protocols for research
- Ensure the execution of studies according to the proposal and protocols
- Regular quality control of data generated
- Maintenance of database and analysis of data
- General management of funds available for the research
- Provide technical input for the preparation of periodical and final reports

International Advisory Committee

- Development and finalization of the research proposal
- Provide technical input for the development of protocols / reports & publication
- Give an international perspective to the research programme
- Ensuring international standards of research
- Ensuring quality and ethical standards of research
- Peer review of protocols, reports and publications

Committee Members

National Steering Committee

- Secretary, Ministry of Health (Chair)
- Secretary, Ministry of Disaster Management
- Secretary, Ministry of Agriculture
- Secretary, Ministry of Environment
- Secretary, Ministry of Technology & Research
- Secretary, Ministry of Social Services
- Secretary, Ministry of Indigenous Medicine
- Additional Secretary (Medical Services), Ministry of Health
- Director General of Health Services
- Deputy Director General, PHS I
- Country Representative, WHO
- Country Representative, UNDP
- Chief Epidemiologist, Epidemiology Unit

Management Committee

- Additional Secretary (Medical Services)
- Deputy Director General, PHS I
- Chief Epidemiologist, Epidemiology Unit
- Regional Director of Health Services, Anuradhapura
- Regional Director of Health Services, Polonnaruwa
- Regional Director of Health Services, Badulla
- NPO/NCD, WHO
- Head/ Representative, Central Environment Authority
- Head/ Representative, Department of Agriculture
- Head/ Representative, Disaster Management Centre
- Head/ Representative, National Science Foundation

- Head/ Representative, National Water Supply & Drainage Board
- Head/Representative, National Council for Persons with Disability
- Registrar of Pesticides

Scientific Committee

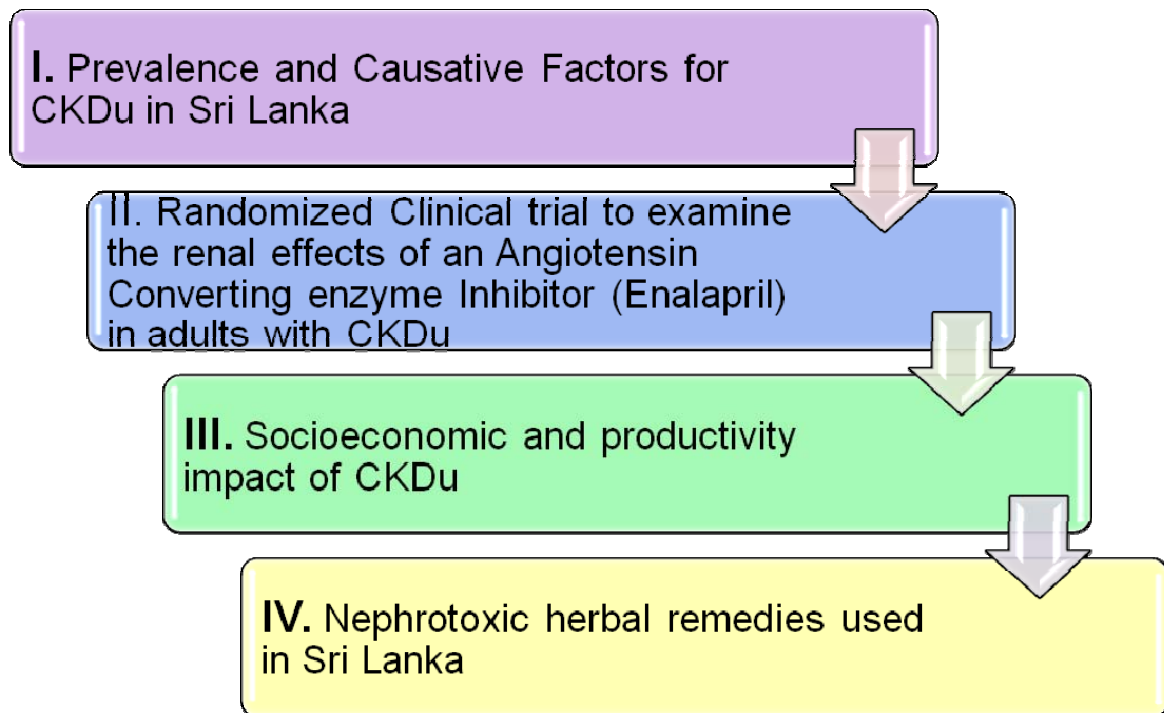
- Dr. P. G. Maheepala, Ministry of Health
- Dr. Firdosi Rustom Mehta, WR, World Health Organization
- Chief Epidemiologist, Epidemiology Unit , Ministry of Health
- Dr. Lanka Jayasuriya Dissanayake, World Health Organization
- Prof. Lalani Rajapakse, National Science Foundation
- Dr. Nirupa Pallegatte, Ministry of Health
- All the members of the study team listed in annexure II

International Advisory Committee

- Dr. Shanthi Mendis, Senior Adviser, WHO HQ, Geneva (Chair)
- Prof. Neil R. Poulter, Consultant Physician & Epidemiologist, Imperial College, London
- Dr. Kriang Tungsanga, Division of Nephrology, Department of Medicine, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
- Dr. Sandeep Mahajan, Associate Professor, Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India

As shown in below figure, the research on CKDu has been divided into main 4 sub- projects.

Main Sub-Projects of the CKDu research



For each sub-project the following is described in detail keeping in line with the requirement of National Science Foundation format of the final report.

- Introduction/Background
- Scientific scope of the project (Overall & specific objective)
- Materials and methods
- Results/outputs
- Discussion and conclusions including Major findings and follow up activities, Problems if any, encountered during implementation
- References

I. Prevalence and Causative Factors for CKDu in Sri Lanka

This sub-project comprised of following studies:

a) **Population Prevalence Study**

This study was conducted to ascertain the existence of CKDu in certain parts of the country

b) **Analytical and environmental studies:**

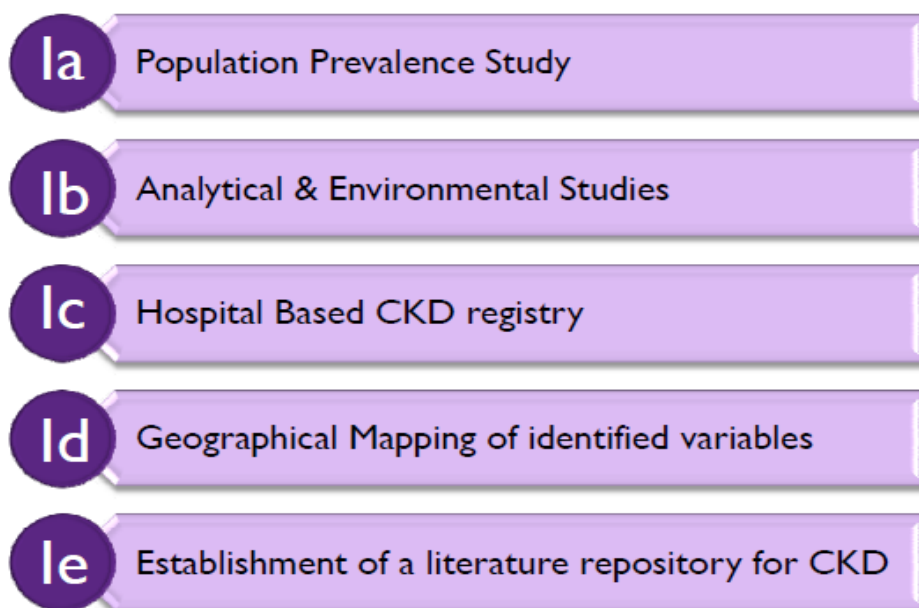
These studies were conducted to identify key determinant(s) of CKDu. This series of coordinated studies included the following components

- Cross sectional comparison of potential environmental toxins in high and low prevalent areas for CKDu
- Case-control studies comparing newly diagnosed cases of CKD of uncertain aetiology and matched controls to identify risk factors for CKDu
- Determination of pesticide residues in urine of people with CKDu
- Analytical studies of human post mortem tissue

c) **Hospital based CKD registry**

d) **Geographical mapping of identified variables**

e) **Establishment of a literature repository for CKD**





Introduction & Background

A population prevalence study was conducted under this research project during 2010-2012 in Selected Districts of Sri Lanka. This started with randomly selected households in selected GN divisions in three selected districts of Sri Lanka to identify CKDu cases, as per the case definition.

Scientific scope of the project

The prevalence of CKDu is not well known. Studies conducted up to now have either been hospital-based rather than population-based or have not used specific diagnostic criteria (1-13).

This study was therefore undertaken

- To confirm or refute previously reported wide ranges in the prevalence of CKDu
- To identify a case definition for CKDu

Materials and Methods

Ethical approval for the study was obtained from the Ethical Review Committee of the Sri Lanka Medical Association. Six divisional secretariat areas (administrative divisions) were selected randomly from three districts in the North Central and Uva provinces i.e. Anuradhapura, Polonnaruwa and Badulla. Twenty two villages (Grama Niladari areas) were selected randomly from these six divisions. Using the electoral lists of these villages, 100 households from each GN division were randomly selected for the study. Males and females between 15-70 years ($n = 6698$), were invited to participate. Out of this, only 6,132 (92%) were available for the survey. Out of the 6,132 available, 4,941 (74% of the eligible population) participated for sample collection which yielded a response rate of 80.6%. The remainder were either not available or did not give consent for sample collection. Written consent was given by the participants to join the study. Early morning urine samples of the respondents were initially tested. Those with $ACR \geq 30$ mg/g were invited for further biochemical studies - repeat urine ACR, HbA_{1C} and serum creatinine. 92% of people with $ACR \geq 30$ mg/g in the initial urine sample responded. Those who did not satisfy the CKDu definition (people with diabetes and/or hypertension and/or history of snake bite or glomerulonephritis or pyelonephritis or ureteric calculi) were excluded ($n = 310$) in calculating the prevalence rates of CKDu.

At the first visit, trained interviewers used a survey questionnaire to gather information on age, sex, marital status, education, occupation, smoking, alcohol consumption, current

residence, duration of residence in study area, source of drinking water, storage containers used for drinking water, exposure to agrochemicals, history of snake bite, glomerulonephritis, pyelonephritis and renal calculi. Height was measured to the nearest 0.1 centimeter. Weight measurements were taken using a calibrated weighing scale to the nearest 0.1 kg. A medical officer verified the medical information gathered and measured the blood pressure using a mercury sphygmomanometer after 15 minutes rest. The average of two readings taken 5 minutes apart was used.

Age structure of the surveyed population and the sampled population

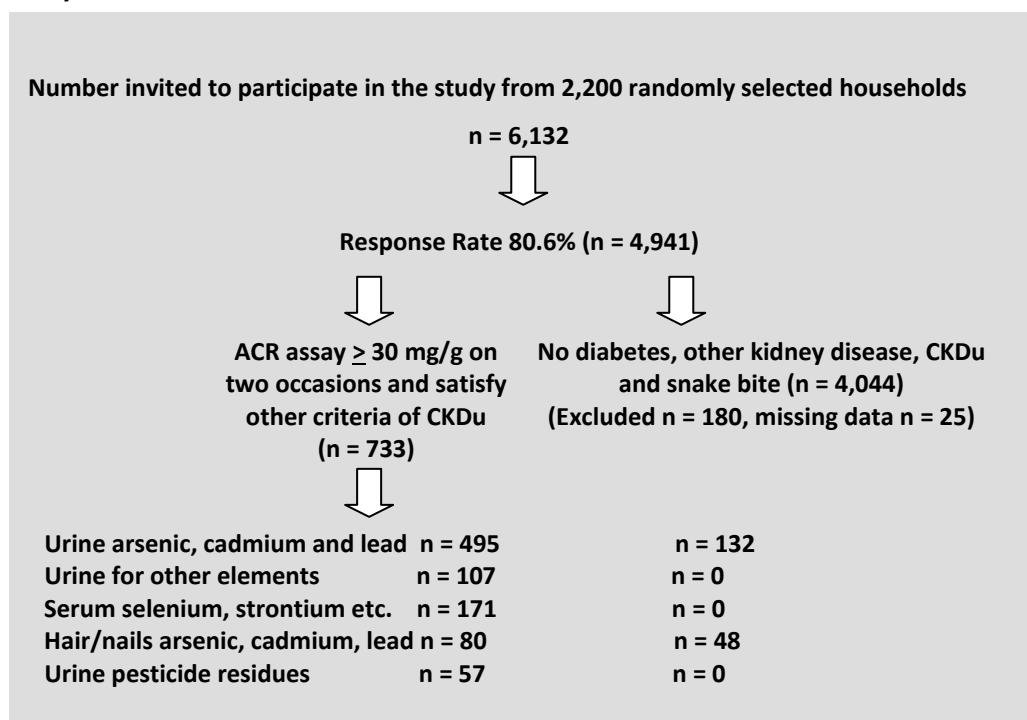
Age category	Surveyed Population	Sampled Population
15 - 20	13%	11%
21 - 30	22%	19%
31 - 40	22%	23%
41 - 50	20%	23%
51 - 60	16%	17%
61 - 70	7%	7%

Sex distribution of the surveyed population and the sampled population

	Male	Female
Surveyed Population	46%	54%
Sampled Population	42%	58%

This proposal has been reviewed and approved by the appropriate ethics committee, which is a committee whose task it is to make sure that research participants are protected from harm.

Flow chart of the study conducted in three districts (Anuradhapura, Polonnaruwa & Badulla) in the endemic area



Case definition of CKDu:

Participants who had persistent albuminuria i.e. albumin-creatinine ratio (ACR) $\geq 30\text{mg/g}$ in initial urine sample and in an urine sample obtained at a repeat visit were considered to have CKDu if they satisfied all the following criteria:

- No past history of ureteric calculi, glomerulonephritis, pyelonephritis or snake bite
- Not on treatment for diabetes.
- Normal HbA1c ($<6.5\%$)
- If on treatment for raised blood pressure, BP $< 140/90$ mm Hg and if not on treatment for blood pressure, BP $< 160/100$ mmHg

CKDu was graded as follow:

- **Grade 1:** Persistent albuminuria (i.e. ACR ≥ 30 mg/g in initial and repeat urine) equation > 90 ml/min/ 1.73m^2
- **Grade 2:** Persistent albuminuria and eGFR $60 - 89$ ml/min/ 1.73m^2
- **Grade 3:** Persistent albuminuria and eGFR $30-59$ ml/min/ 1.73m^2
- **Grade 4:** Persistent albuminuria and eGFR <30 ml/min/ 1.73m^2

Results/Output

The age-standardised prevalence of CKDu was higher in females 16.9% (95% confidence interval [CI] = 15.5% to 18.3%) than in males 12.9% (95% CI = 11.5% to 14.4%; $P = 0.001$). About 37% of those with CKDu were male. The distribution of CKDu stages 1 to 4 in males was 27.0%, 27.9%, 23.2% and 22.0% and in females 53.3%, 32.0%, 7.4% and 7.3%, respectively. More severe stages of CKDu were seen more frequently in males (stage 3: males versus females = 23.2% versus 7.4%; stage 4: males versus females = 22.0% versus 7.3%; $P < 0.001$). In both sexes, the prevalence increased with increasing age ($P < 0.001$).

The prevalences in the three districts were:

15.1% in Anuradhapura (17 GN divisions selected from 4 DS areas randomly)
20.6% in Polonnaruwa (3 GN divisions selected from 1 DS area randomly)
22.9% in Badulla (2 GN divisions selected from 1 DS area randomly)

The prevalences in the Gramaniladhari divisions were:

District	D.S. Division	G.N. Division	Prevalence
Anuradhapura	Kahatagasdigiya	Gonumeru Wewa	11%
		Mee-Kumbukwewa	11%
		Kokmaduwa	
	Galenbindunuwewa	Ellawewa	13%
		Getalawa	13%
		Hurulunikawewa	16%
		Hurulumeegahapattiya	11%
	Padaviya	Padaviya	19%
		Parakramapura	17%
		Elikimbulagala	16%
		Kumbukwewa	17%
		Bogahawewa	16%
	Medawachchiya	Katuwela	12%
		Kanadara Divulwewa	10%
		Kirigalwewa	12%
		Madawachchiya East	9%
		Poonewa	13%
Polonnaruwa	Medirigiriya	Thissapura	15%
		Ambagaswewa	17%
		Thalakolawewa	16%
Badulla	Mahiyangana	Belaganwewa	18%
		Girandurukotte	19%

There was a family history of kidney disease in parents or siblings in 20% of individuals with CKDu;

2.1% of individuals with CKDu had a history of ischaemic heart disease and/or cerebrovascular disease;

0.4% had a history of long-term use of herbal medicines for hypertension;

1.8% had a history of long-term use of aspirin; and

0.6% had a history of long-term use of analgesics.

Being male reduced the risk of CKDu (odds ratio [OR] = 0.745, 95% CI = 0.562 to 0.988, $P < 0.05$), and being older than 39 years increased the risk of CKDu (OR = 1.926, 95% CI = 1.561 to 2.376, $P < 0.001$).

When separate logistic regressions were run for each potential exposure, only occupation type (being a chena cultivation farmer increased the OR by 19.5%) and type of agriculture (engaging in paddy cultivation compared to cultivation of vegetables and other crops [chena cultivation] decreased the OR by 26.8%) were significant.

Demographic characteristics of CKDu cases in the endemic area and controls from the non-endemic area

Characteristic	Endemic area		Non-endemic area
	CKDu cases	Controls	Controls
Total number	733	4044	250
Males, %	37.1	42.5	56
Age (years), mean (SD)	39.1 (14.2)	43.7 (13.9)	35.5 (14.0)
Farmer, %	38	43.9	18.3
BMI, kg/m ² , mean (SD)	22.3 (4.6)	21.1 (4.1)	21.7 (4.4)
ACR ≥30 mg/g	733	0	0
ACR albumin–creatinine ratio, BMI body mass index, SD standard deviation.			

Chi square test was used to determine the differences in prevalence of CKDu in relation to age and sex. T-test of log-transformed values were used to test differences in quantitative variables. Results were also confirmed by non-parametric Wilcoxon rank-sum test.

A multiple logistic regression model was fitted for each of the two CKDu definitions. The models incorporated characteristics of interest including age, sex, education, smoking, illicit alcohol, occupation, type of agriculture, years of agriculture, drinking water source, drinking water from paddy, exposure to fertilizer, exposure to weedicides/pesticides, water container type, using protection against agrochemicals, and months living in the district. All were entered as categorical variables except months living in the district. These data analyses were performed using Stata 11 and p-values of less than 0.05 were considered statistically significant.

Summary Results of logistics regression analysis for exposure

Exposure	OR	95% CI		P value	n
		Lower	Upper		
Education					
No education	Reference				174
School grades 1–9	0.900	0.612	1.323	0.594	4374
Higher	1.201	0.588	2.452	0.614	74
Smoking					
Never	Reference				3480
Current/former	1.072	0.813	1.415	0.619	1126
Illicit alcohol consumption					
Never	Reference				3701
Occasional/frequent/past	1.184	0.905	1.548	0.216	874
Occupation					
Other	Reference				2816
Farmer	1.195	1.007	1.418	0.041	1780
Agriculture type					
Non-paddy	Reference				315
Paddy	0.732	0.542	0.988	0.042	2620
Years working in agriculture					
<10	Reference				660
10–19	0.834	0.603	1.152	0.271	777
20–49	1.092	0.777	1.535	0.611	1182
≥50	1.322	0.462	3.785	0.602	22
Source of drinking water					
Not well	Reference				798
Well	0.971	0.785	1.202	0.793	3819
Water storage container					
Others	Reference				1741
Aluminium	1.03	0.87	1.22	0.715	2879
Protection from agrochemicals					
Yes	Reference				191
No	1.011	0.661	1.546	0.959	4271

Separate logistic regressions have been run per exposure variable; OR < 1 means protective, and OR > 1 means that the exposure increases the odds of CKDu. The total number (n) of observations varies per exposure, owing to missing data. All results are adjusted for sex and age. For all analyses, male sex was found to be protective and the risk increased with age.

CI confidence interval, OR odds ratio.

Being male reduced the risk of CKDu (OR = 0.745, 95% CI = 0.562 to 0.988; *P* < 0.05), and being >39 years increased the risk of CKDu (OR = 1.926, 95% CI = 1.561 to 2.376, *P* < 0.001).

Discussion & Conclusions

The prevalence of CKDu found in this study (females 16.9%, males 12.9%) was higher than that reported previously (2% to 3%) [20]. Although the prevalence in females was higher, more severe stages of CKDu were seen more often in males. The reason for this discrepancy is not clear. Factors such as low iron stores in females in lower socioeconomic groups may have an influence on the excretion of heavy metals and oxidative stress on the kidney. This would make the kidneys more vulnerable to CKDu, resulting in a higher prevalence in females. On the other hand, male sex has been reported to be a risk factor for progression to end-stage renal disease [27], and this may partly explain the occurrence of more severe stages of CKDu in men. Further cohort studies need to be carried out to find the natural history of the disease in both sexes.

Previous studies have reported a family history of chronic kidney disease, ayurvedic treatment, and history of snake bite as significant predictors for CKDu [10,12,13].

In the present study, older age, being female and being a chena cultivation farmer increased the risk of CKDu. Family history was positive in one-fifth of those with CKDu, and a history of snake bite was one of the exclusion criteria.

Long-term use of herbal medicines or analgesics was reported in only a very small percentage of those with CKDu. Fanconi syndrome and other hereditary kidney diseases have not been reported in communities in this region.

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Formats used

Population Prevalance Study Consent Form

කැමැත්ත ප්‍රකාශ කිරීමේ සහතිකය
නිදන්ගත වකුගඩු රෝගය පිළිබඳව සිදුකෙරෙන පර්යේෂණය

මගේ සහභාගිත්වය බලාපොරොත්තුවන පර්යේෂණය සෞඛ්‍ය අමාත්‍යාංශයේ සහ ලෝක සෞඛ්‍ය සංවිධානයේ අනුග්‍රහය සහ සහභාගිත්වය මත සිදු කෙරෙන්නකි. මෙහි අරමුණ වන්නේ දැනට ශ්‍රී ලංකාවේ සමහර ප්‍රදේශවලින් බහුලව වාර්තා වී ඇති නිදන්ගත වකුගඩු රෝගය පිළිබඳව වැදගත් කරුණු (රෝගයේ පැතිරීම සහ හේතූන් ආදිය) හඳුනා ගැනීමයි.

මෙහිදී මා මුලින්ම සම්මුඛ සාකච්ඡාවකට සහභාගී කෙරෙනු ඇත. මෙම පර්යේෂණය සඳහා මාගේ මුත්‍රා සාම්පලයක් ලබා දීමට මම එකඟ වෙමි. සමහර විට පසු විපරම් සාකච්ඡාවක් සඳහාත් මා කැඳවීමට ඉඩ ඇත. එහිදී ශිරාවකින් ගනු ලබන රුධිරය ස්වල්පයක් (මි. ලී. 5ක්) දීමටත් මම එකඟ වෙමි. මෙම කටයුත්තට සහභාගිවීමෙන් මට පහත සඳහන් වාසි අත්වනු ඇත.

- මගේ වකුගඩුවල ක්‍රියාකාරිත්වය පරීක්ෂා කරනු ඇත (මේ සඳහා මුත්‍රාවල මයික්‍රො ඇල්බියුමින් සහ ඇල්බියුමින් ක්‍රියොටිනින් අනුපාතය යොදා ගැනේ)
- මගේ රුධිර පීඩනය මැන බැලෙනු ඇත. (අවශ්‍ය වුවහොත්)
- මගේ රුධිරයේ සීනි මට්ටම පරීක්ෂා කෙරෙනු ඇත. (අවශ්‍ය වුවහොත් මේ සඳහා ග්ලූසිකොසිලේටඩ් ගිමොග්ලොබින් පරීක්ෂණය යොදා ගැනේ)
- මගේ වකුගඩුවල ක්‍රියාකාරිත්වය තවදුරටත් පරීක්ෂා කෙරෙනු ඇත. (අවශ්‍ය වුවහොත් මේ සඳහා රුධිර මස්තු වල ක්‍රියොටිනින් මට්ටම පරීක්ෂා කෙරේ)

ඉහත පරීක්ෂණ වල ප්‍රතිඵල මත මට නැවත වරක් පරීක්ෂකවරුන්ව මුණගැසීමට සිදුවිය හැකි බවත්, එසේ වුවහොත් නැවත මුත්‍රා සාම්පලයක් සහ රුධිරය ස්වල්ප ප්‍රමාණයක් (මි. ලී. 5ක්) දීමට සිදුවේ. මෙම මුත්‍රා සහ රුධිර සාම්පල යොදා ගනිමින් සිදු කරන රසායනාගාර පරීක්ෂණ වල ප්‍රතිඵල මට ප්‍රතිකාර ගැනීමට අවශ්‍ය වුවහොත් ඒ සඳහා උපකාර වන බව දැනිමි.

ශ්‍රී ලංකාවේ සමහර ප්‍රදේශවල බහුලව දක්නට ඇති මෙම නිදන්ගත වකුගඩු රෝගය වළක්වා ගැනීම සඳහා අවශ්‍ය තොරතුරු සොයා ගැනීමට දායක වීමෙන් සමාජයටද වාසි රැසක් අත්වේ.

මෙම පර්යේෂණයට සහභාගී වීමෙන් මා අවම අවදානමකට හා සුළු අපහසුතාවයකට පත්වීමට සිදුවනු ඇත. මේ සඳහා මා සහභාගිවන්නේ මගේ කැමැත්තෙනි. මෙම කටයුත්තට සහභාගී වීම ප්‍රතික්ෂේප කිරීම නිසා මා සහ රෝහල්/සෞඛ්‍ය සේවාවන් අතර ඇති සබඳතාවට කිසිම හානියක් සිදු නොවේ.

රැස් කරගන්නා, සියළු තොරතුරුවල රහස්‍යභාවය දැඩි ලෙස සුරකින බව මා විසින් වටහා ගනිමි. ඉහත සඳහන් තොරතුරු පිළිබඳ මා හොඳින් දැනුවත් කොට ඇත. මා විසින් නගන ලද සියළු ප්‍රශ්නවලට ලැබූ පැහැදිලි සෘජු පිළිතුරු වලින් මම සෑහීමකට පත් වීමි.

මෙම සම්මුඛ සාකච්ඡාව ස්වකැමැත්තෙන්ම සහභාගී වීමට මම එකඟ වෙමි. එමෙන්ම සම්මුඛ සාකච්ඡා පැවැත්වෙන කාලසීමාව තුළ ඕනෑම විටෙක ඉන් ඉවත්වීමටද මා හට අයිතිය ඇති බව දැනිමි. එසේ කිරීමෙන් මාගේ ඉදිරි පරීක්ෂණ හෝ ප්‍රතිකාර සඳහා ද කිසිදු බලපෑමක් ඇති නොවන බවටද මා අවබෝධ කොට ඇත්තෙමි.

සහභාගිවන්නාගේ නම	දිනය (දි/මා/අවු)	සහභාගිවන්නාගේ අත්සන
අවුරුදු 15 සහ 16 වයස් කාණ්ඩ සඳහා දෙමාපිය/භාරකරු ගේ නම	දිනය (දි/මා/අවු)	දෙමාපිය/භාරකරු ගේ අත්සන
සහභාගිවන්නාට ලිවීමට/කියවීමට අපහසුනම් (සාක්ෂිකරු තෝරා ගැනීම සහභාගිවන්නා විසින් කළයුතු අතර පර්යේෂණ කණ්ඩායම සමග කිසිම සම්බන්ධතාවයක් නොතිබිය යුතුයි.		
ස්වාධීන සාක්ෂිකරුගේ නම	දිනය (දි/මා/අවු)	සාක්ෂිකරුගේ අත්සන
පර්යේෂකගේ නම	දිනය (දි/මා/අවු)	පර්යේෂකගේ අත්සන

නිදන්ගත වකුගඩු රෝගය පිළිබඳ පර්යේෂණය
ජනගහණය ආවරණ දත්ත පත්‍රිකාව

සහභාගිවන්නාගේ අනුක්‍රමික අංකය : ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

ජාතික හැඳුනුම්පත් අංකය (නොමැති නම් පමණක් වෙනත් හඳුනාගැනීමේ සහතිකයක අංකය) ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

මෙම පර්යේෂණය සඳහා තෝරාගැනුණු ලබා දෙන්නේ මගේ කැමැත්තෙනි
දිනය අත්සන

1. සහභාගිවන්නාගේ සම්පූර්ණ නම :

2. වර්තමාන ලිපිනයේ පදිංචි කාලය (අවුරුදු) ☐☐

ඉහත සඳහන් කළ ලිපිනයේ ඔබ පිටත් වන කාලය වසර 5 කට වඩා අඩු නම් පමණක් ඔබ වැඩි කාලයක් පිටත් වූ ලිපිනයට අදාළව පහත විස්තර සම්පූර්ණ කරන්න

3. දිස්ත්‍රික්කය :

4. ග්‍රාම නිලධාරී කොට්ඨාසය :

5. එම ලිපිනයේ පිටත් වූ කාලය : ☐☐

අදාළ කොටුවේ (✓) ලකුණු යොදන්න

6. උපන් දිනය : ☐☐ ☐☐ ☐☐ (දිදි / මාස / වච්චව)

7. උපන් දිනය හොඳින්ම නම්, ආසන්න වශයෙන් (අවුරුදු) : ☐☐

8. ස්ත්‍රී/පුරුෂ බව 1. පිරිමි ☐☐ 2. ස්ත්‍රී ☐☐

9. ජනවර්ගය

1. සිංහල ☐ 2. දමිළ ☐ 3. මුස්ලිම් ☐ 4. වෙනත් (සඳහන් කරන්න) ☐

10. අධ්‍යාපන තත්වය (සම්පූර්ණ කළ අවසාන පන්තිය)

1. පාසල් අධ්‍යාපනයක් ලබා නැත ☐ 2. නවවන පන්තිය දක්වා ☐ 3. අ.පො.ස. සා/පෙළ - උ/පෙළ දක්වා ☐

4. වඩා ඉහළ (පිස්සව විද්‍යාල, වෙනත්) ☐

11. ඔබ ජාතික කර්මාන්ත උරුමය රැකියාව කුමක්ද ?

1. රැකියාවක් නොකරයි ☐ 2. ගෘහණිය ☐ 3. ගොවිතැනට අදාළ ☐ 4. බිවර ☐

5. කම්කරු (කෘෂිකාර්මික නොවන) ☐ 6. හමුදා/පොලිස්/ග්‍රාමාරක්ෂක සේවය ☐ 7. කාර්මාලය ආශ්‍රිත සේවාවන් ☐

8. වෙනත් (සඳහන් කරන්න) ☐

ඔබ ජාතික ගොවිතැන් කටයුතු වල (ස්ථිර රැකියාවක් ලෙස හෝ අතිරේක ආදායම් මාර්ගයක් ලෙස හෝ) යෙදෙන්නේ නම් පමණක් ප්‍රශ්න අංක 12, 13 සහ 14 ට පිළිතුරු සපයන්න. එමෙන්ම ප්‍රශ්න අංක 15 සහ 16 ට පිළිතුරු සැපයීමෙන් වළකින්න.

12. ගොවිතැන් කටයුතු වලදී ඔබේ සහභාගිත්වය 1. ප්‍රධාන රැකියාව ලෙස ☐ 2. අමතර / අතිරේක රැකියාවක් ලෙස ☐

13. එම කටයුතු වල යෙදුණ කාලසීමාව (අවුරුදු) ☐☐

14. කුමන ආකාරයේ වගා කටයුත්තකද ?

1. වී වගාව ☐ 2. අතිරේක ගොවි ☐ 3. එළවළු ☐

15. ඔබ ජාතික කිසිම ආකාරයක ගොවිතැන් කටයුත්තක යෙදෙන්නේ නැතහොත්, මීට පෙර හෝ එම කටයුතු වල යෙදී තිබේද ?

1. නැත ☐ 2. ඔව් ☐

16. "ඔව්" නම් කාලසීමාව (අවුරුදු) ☐☐

17. ඔබ කෙදිනකවත් දුම් බී තිබේද ?

1. කවදාවත්ම නැත ☐ 2. මින් පෙර බිවත්, ජාතික දුම් නොබොම් ☐ 3. ජාතික දුම් බොම් ☐

18. ඔබ ජාතික දුම් බොන්නේ නම් කොපමණ වාර ගණනක්ද ?

1. ඉදහිට ☐ 2. හිතර (සතිකව තුන් වාරයකට වඩා වැඩියෙන්) ☐ 3. දිනපතා (5 වාරයකට අඩුවෙන්) ☐

4. දිනපතා (5 වාරයකට වඩා වැඩියෙන්) ☐

19. ඔබ කෙදිනකවත් හිඟ වියදම් මත්පැන් (උදා: කසිපු/වෙනත්) පානය කර තිබේද ?

1. කවදාවත්ම නැත ☐ 2. ඉදහිට ☐ 3. හිතර (සතිකව 3 වරකට වැඩියෙන්) ☐ 4. පෙර බිවත් ජාතික නොබොම් ☐

20. ඔබ පැනවීම් පදය ලබා ගන්නා ප්‍රධාන මූලාශ්‍රය කුමක්ද ?

1. පිළි ☐ 2. හල පිළි ☐ 3. පරිපා වතුර ☐ 4. වැව් වතුර ☐ 5. වෙනත් (සඳහන් කරන්න) ☐

21. ඉහත පල මූලාශ්‍රයන් ඔබ බිම්පිට පදය ලබා ගන්න

1. අඩු 5 ට අඩුවෙන් ☐ 2. අඩු 6-10 ☐ 3. අඩු 11-15 ☐ 4. අඩු 16-20 ☐ 5. අඩු 20 ට වැඩි ☐

22. ඔබ ඉහත සඳහන් කළ පල මූලාශ්‍රයට අමතරව පහත සඳහන් වෙනත් පල මූලාශ්‍රයකින් බිම්පිට/ආහාර පිසීමට වසර 5 කට වඩා වැඩි කාලයක් පදය ලබා ගෙන තිබේද ? (පිළිතුරු එකකට වඩා ලකුණු කළ හැක)

1. පිළි ☐ 2. හල පිළි ☐ 3. පරිපා වතුර ☐ 4. වැව් වතුර ☐ 5. වෙනත් (සඳහන් කරන්න) ☐

23. ඔබ කුඹුරේ වැඩ කරන විට කුඹුරේම ඇති පිළිකුන් හෝ ලියද්දකින් වතුර බොන්නවාද ?

1. ඔව් ☐ 2. නැත ☐

24. නිවසේදී ඔබ වතුර ගබඩා කර තබන්නේ කෙසේද ? (පිළිතුරු එකකට වඩා ලකුණු කළ හැක)

1. ඇලුමිනියම් හාපන වල ☐ 2. මැටි හාපන වල ☐
3. ප්ලාස්ටික් හාපන වල ☐ 4. වෙනත් (සඳහන් කරන්න) ☐

25, 26 සහ 27 හත ප්‍රශ්නවලට පිළිතුරු සැපයීමේදී "නිතරම නිරාවරණය වේ" හෝ රැකියාවක් ලෙස කෘෂිකාර්මය / වල් නාශක / කෘෂි රක්ෂක ඉසිමේ හෝ ඒකිනිමේ යෙදීම වේ.

25. ඔබ පැනවීම් පදය ලබා ගැනීම සඳහා භාවිත කරනු ලබන පොහොර වෙත කෙලෙසක හෝ නිරාවරණය වී තිබේද ?

1. නැත ☐ 2. ඉදහිට ☐ 3. නිතරම ☐

26. ඔබේ පිළිපිට කාලය තුළදී රක්ෂකයෙකු වෙත නිරාවරණය වී තිබේද ?

1. නැත ☐ 2. ඉදහිට ☐ 3. නිතරම ☐

27. ඔබේ පිළිපිට කාලය තුළදී රක්ෂකයෙකු වල් නාශක වෙත නිරාවරණය වී තිබේද ?

1. නැත ☐ 2. ඉදහිට ☐ 3. නිතරම ☐

28. කෘෂි රක්ෂක භාවිතයේදී ඔබ, ආරක්ෂිත ඇලුමි-පැලුමි (පැටු) මුඛ වැස්ම වැනි) භාවිතා කරන්නවාද ?

1. කෘෂි රක්ෂක භාවිතා කර නැත ☐ 2. ඔව් ☐ 3. නැත ☐

29. ඔබේ මුහුණ සහ පාද ඉදිමි තිබේද ? (විශේෂයෙන් ළමා කාලයේදී)

1. ඔව් ☐ 2. නැත ☐

30. ඔබේ මුහුණ සහ පාද රුධිරය පිටවී තිබේද ? (විශේෂයෙන් ළමා කාලයේදී)

1. ඔව් ☐ 2. නැත ☐

31. ඔබේ මුහුණ පිටවීමේ අඩුවක් පැති තිබේද ? (විශේෂයෙන් ළමා කාලයේදී)

1. ඔව් ☐ 2. නැත ☐

32. ඔබ පැනවීම් කුමන හෝ කල් පවතින / බරපතල රෝගයකට කලක් තිස්සේ ප්‍රතිකාර ගන්නවාද ?

1. ඔව් ☐ 2. නැත ☐

33. "ඔව්" නම් සහභාගිවන්නාගේ වෛද්‍ය චාරිකාව ප්‍රවේශයෙන් කියවා බලා අදාළ රෝගී තත්වය ඒ අනුවත්ම සටහන් කරන්න.

34. පැනවීම් ඔබට කවරාකාරයක හෝ වකුගඩු රෝගී තත්වයක් තිබේද ?

1. ඔව් ☐ 2. නැත ☐

35. "ඔව්" නම් ඔබ ප්‍රතිකාර ගන්නේ කුමන ස්ථානයකදී ? / රෝගලේන්ද ?

විමර්ශකගේ කේතය ☐☐

විමර්ශනය කළ දිනය ☐☐ . ☐☐ . ☐☐☐☐

කාර්යාලය ප්‍රයෝජනය සඳහා

Certificate of Consent

Evaluation and investigation of chronic kidney disease of unknown aetiology

The study that I am requested to participate is a study being conducted under the auspices of the Ministry of Health and World Health Organization. Its overall goal is to identify the prevalence and determinants of chronic kidney disease of unknown aetiology (CKDu) reportedly highly prevalent in certain parts of Sri Lanka.

My participation in this study involves an interview. In addition, I agree to give a sample of urine. I may be contacted in the future for a follow-up interview. During that time, I agree to give a small amount of blood (5 ml) which will be taken from a vein. I will access the following benefits:

- My kidney function will be checked (test to be used urine microalbumin & albumin creatinine ratio);
- My blood pressure will be measured (if needed);
- My blood sugar level will be measured (if needed & the test to be used glycosylated haemoglobin);
- My kidney function will be further checked (if needed & the test to be used serum creatinine).

I also may be contacted again depending on the results of above investigations. If called, I agree to give a sample of urine and small amount of blood (5 ml) again. I am aware these samples are for advanced biochemical tests (multi-element analysis), which may benefit me if I need any medical attention.

There are also benefits to society because the information obtained will be valuable in finding the cause/s of a type of kidney disease seen in some parts of Sri Lanka and in the prevention of this kidney disease.

There are minimal risks or discomforts associated with participating in this research project. My participation in this study is entirely voluntary. Refusal to participate will not affect my future relationship with any of the hospital/ health facility.

The information that is collected from this research project will be kept confidential. I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a subject in this study and understand that I have the right to withdraw from the study at any time without in any way affecting my medical care.

Print name of subject	Date	Signature of subject
<u>For subjects aged 15 and 16 years</u> Print name of parent/guardian	Date	Signature of subject
<i>If illiterate (The witness should be selected by the participant and should have no connection to the research team)</i>		
Print name of independent literate witness	Date	Signature of witness
Print Name of the investigator	Date	Signature of investigator

නිදන්ගත වකුගඩු රෝගය පිළිබඳ

පර්යේෂණ ව්‍යාපෘතිය සඳහා සහභාගී වන්නන්ට ලබාදෙන තොරතුරු පත්‍රිකාව

අරමුණ

අප ඔබගේ සහභාගීත්වය ඉල්ලා සිටින මෙම පර්යේෂණය සෞඛ්‍ය අමාත්‍යාංශයේත්, ලෝක සෞඛ්‍ය සංවිධානයේත් අනුග්‍රහයෙන් සිදු කරනු ලබන්නකි. මෙහි ප්‍රධාන අරමුණ වන්නේ දැනට ශ්‍රී ලංකාවේ සමහර ප්‍රදේශවලින් බහුලව වාර්තා වී ඇති නිදන්ගත වකුගඩු රෝගය පිළිබඳව වැදගත් කරුණු (රෝගයේ පැතිරීම සහ හේතුන් පිළිබඳ) හඳුනා ගැනීමයි.

සමීක්ෂණය සිදුකරන ක්‍රියා පිළිවෙල පිළිබඳ විස්තර

මෙම සමීක්ෂණය සඳහා සහභාගී වීමේදී ඔබ විසින් මිඩංගු කළ යුත්තේ පැයකට අඩු කාලයකි. මෙහිදී ඔබට සම්මුඛ සාකච්ඡාවකට භාජනය කරනු ඇත. එමෙන්ම ඔබගේ මුත්‍රා සාම්පලයක් ලබා දීමටත් සිදුවනු ඇත. සමහරවිට පසු විපරම් සාකච්ඡාවක් සඳහාත් ඔබට කැඳවීමට ඉඩ ඇත. එහිදී වෛද්‍යවරයෙකු විසින් ඔබේ රුධිර පීඩනය පරීක්ෂා කෙරෙන අතර රුධිරයේ සීනි හා වකුගඩු වල ක්‍රියාකාරීත්වය දැන ගැනීම සඳහා ඔබේ ශිරාවකින් ගනු ලබන රුධිරය ස්වල්පයක් ද ලබා ගනු ඇත. මෙම පරීක්ෂණයේදී යම් අසාමාන්‍යතා/රෝගී තත්වයන් හඳුනා ගන්නට ලැබුණහොත් ඔබට ප්‍රතිකාර සඳහා යොමු කරනු ඇත.

පර්යේෂණයට සහභාගී වීමෙන් ලැබිය හැකි වාසි

මෙම පර්යේෂණයට සහභාගී වීමෙන් ඔබට පහත සඳහන් වාසි අත්වෙනු ඇත.

- ඔබේ වකුගඩුවල ක්‍රියාකාරීත්වය පරීක්ෂා කරනු ඇත
- ඔබේ රුධිර පීඩනය මැන බැලෙනු ඇත. (අවශ්‍ය වුවහොත්)
- ඔබේ රුධිරයේ සීනි මට්ටම පරීක්ෂා කෙරෙනු ඇත. (අවශ්‍ය වුවහොත්)
- ඔබේ වකුගඩුවල ක්‍රියාකාරීත්වය තවදුරටත් පරීක්ෂා කෙරෙනු ඇත. (අවශ්‍ය වුවහොත්)

ශ්‍රී ලංකාවේ සමහර ප්‍රදේශ වල බහුලව දක්නට ඇති මෙම නිදන්ගත වකුගඩු රෝගය වලක්වා ගැනීම සඳහා අවශ්‍ය තොරතුරු සොයා ගැනීමට දායක වීමෙන් සමාජයටද වාසි රැසක් අත්වේ.

මුහුණ දීමට සිදුවිය හැකි අවදානම් සහ අසීරුතාවයන්

මෙම සමීක්ෂණයට සහභාගීවීම නිසා ඔබට කිසිදු අවදානම් තත්වයකට මුහුණ පෑමට සිදුනොවේ.

සහභාගීවීම සඳහා දීමනාවක් ලබා දීම

මෙම සමීක්ෂණයට සහභාගීවන්නන් හට කිසිදු මූල්‍යමය දීමනාවක් ලබා දීම සිදු නොකෙරේ.

තොරතුරුවල රහස්‍යභාවය

මෙම සමීක්ෂණයේදී පුද්ගලයන්ගෙන් ලබා ගන්නා තොරතුරුවල රහස්‍ය භාවය දැඩි ලෙස සුරකින අයුරින් කටයුතු සලස්වා ඇත. මෙම තොරතුරු අඩංගු ලිපි ලේඛන නම් සඳහන් නොකොට තබාගෙන ඒ වෙනුවට විශේෂ අංකයක් ඔබට ලබා දෙනු ඇත. නම් සහ අංක ඇතුලත් ලිපි ලේඛන පර්යේෂණ කණ්ඩායමේ සාමාජිකයෙකු හැර වෙනත් කිසිවෙකුට ලබා ගත නොහැකි ලෙස සුරක්ෂිතව තැබෙනු ඇත.

ප්‍රතික්ෂේප කිරීමට හෝ ඉවත් වීමට සහභාගිවන්නන් හට ඇති අයිතිය

මෙම පර්යේෂණය සඳහා සහභාගි වීමට ඔබ තුළ කැමැත්තක් නැති නම් සහභාගි නොවී සිටීමේ පූර්ණ අයිතිය ඔබ සතුව ඇත. එසේම අතරතුරදී ස්ව කැමැත්තෙන් ඉන් ඉවත්වීමටද ඔබට කිසිදු අවහිරයක් නොමැත. ඔබ දැනට ලබා ගන්නා සහ අනාගතයේ ගැනීමට නියමිත සෞඛ්‍ය සේවා ලබා ගැනීමේදී මෙම පර්යේෂණයට සහභාගි නොවීම කිසිදු බලපෑමක් හෝ ගැටළුවක් ඇති නොකරයි. පර්යේෂණයට සහභාගි වූ අයට හිමි වරප්‍රසාද ඔබටත් එලෙසම හිමිය. අවශ්‍ය ඕනෑම අවස්ථාවක මෙම පර්යේෂණයෙන් ඉවත් වීමට ඔබට අයිතියක් ඇත. එසේ ඉවත් වීමෙන් ඔබේ අයිතින් කිසිවක් ඔබට අහිමි නොවනු ඇත. එමෙන්ම ඔබට අවශ්‍ය සෞඛ්‍ය සේවා සැපයීමේදී කිසිදු ආකාරයක බාධාවක් ඇති නොවනු ඇත.

මෙම සමීක්ෂණය සම්බන්ධයෙන් අවශ්‍ය වෙනත් විස්තර දැන ගැනීම

වැඩිවිස්තර අවශ්‍ය නම් දැන් හෝ පසුව විමසිය හැකිය. පසුව අමතන්නේ නම් පහත ලිපිනයෙන් විමසන්න.

වෛද්‍ය පබා පළිහවඩන
ප්‍රධාන වසංගත රෝග විද්‍යාඥ
වසංගත රෝග විද්‍යා අංශය
ශ්‍රී ලංකා සෞඛ්‍ය අමාත්‍යාංශය
231, ද සේරම් පෙදෙස,
කොළඹ 10,
දුරකථනය : 0112 695112

මෙම යෝජිත ව්‍යාපෘතිය ආචාර ධර්ම පද්ධතීන්ට අනුකූල බව ඒ පිළිබඳ කමිටුව විසින් විශ්ලේෂණය කිරීමෙන් අනතුරුව ඒ සඳහා අනුමැතිය ලබා දී තිබේ. එම කමිටුවේ කාර්යභාරය වන්නේ පර්යේෂණයට සහභාගිවන්නන්ගේ අයිතිය සුරැකීම සහ පීඩාවන් වැළැක්වීමයි.

Information Sheet

Evaluation and Investigation of Chronic Kidney Disease of Unknown Aetiology in Sri Lanka

Purpose

The study that we are requesting you to participate in is a study being conducted under the auspices of the Ministry of Health and World Health Organization. Its overall goal is to identify the prevalence and determinants of chronic kidney disease of unknown aetiology (CKDu) reportedly highly prevalent in certain parts of Sri Lanka.

Procedures

Your participation in this study will take less than one hour. Procedures will include an interview. In addition, you will be asked to give a sample of urine. You may be contacted in the future for a follow-up interview. During that time, a medical doctor will examine your blood pressure and you will have a small amount of blood taken from a vein for investigations which include testing of your blood sugar and functioning of your kidneys. If, during the course of the study any thing is found abnormal, you will be referred to an appropriate health care facility.

Risks and discomforts

You are exposed to minimal risks as a result of participating in this study.

Benefits

If you participate in this research, you are likely to have the following benefits:

- Your kidney function will be checked;
- your blood pressure will be measured (if needed);
- your blood sugar level will be measured (if needed);
- Your kidney function will be further checked (if needed).

There are also benefits to society because the information obtained will be valuable in finding the cause/s of a type of kidney disease seen in some parts of Sri Lanka and in the prevention of this kidney disease.

Incentives

You will not be provided any incentive to take part in this research.

Confidentiality

The information that we collect from this research project will be kept confidential. Information about you that will be collected from the study will be stored in a file that will not have your name on it, but a number assigned to it instead. The name associated with the number assigned to each file will be kept under lock and key and will not be divulged to anyone except research team members.

Right to refuse or withdraw

You do not have to take part in this research if you do not wish to do so, and refusing to participate will not affect you in any way. If you have been already attending a health

facility or intend to attend or happen to attend any health facilities in future, you will still have all the benefits that you would otherwise have at these health facilities. You may stop participating in the research at any time that you wish without losing any of your rights. Your treatment at any of the health facilities will not be affected in any way.

Whom to contact

If you have any questions you may ask them now or later. If you wish to ask questions later, you may contact

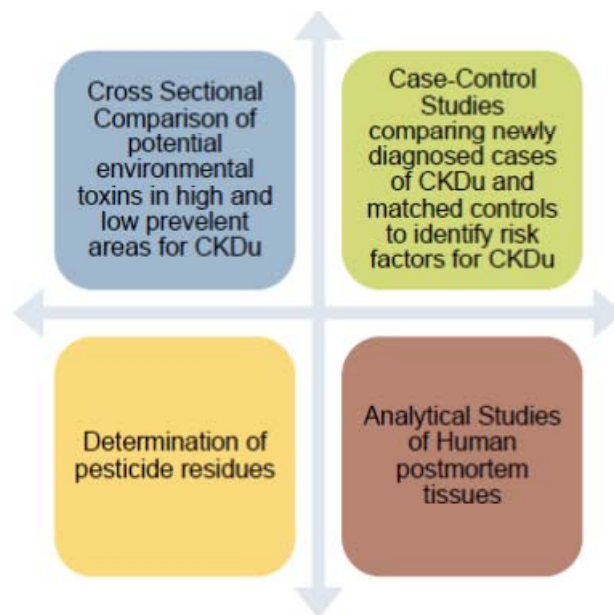
Dr Paba Palihawadana
Chief Epidemiologist
Epidemiology Unit, Ministry of Health
231, de Saram Place, Colombo 10.
Telephone: 0112695112



Introduction & Background

The work carried out under this well coordinated series of studies started with a systematic population-based survey of randomly selected households in selected GN divisions in North Central and Uva provinces of Sri Lanka to identify CKDu cases, as per the case definition. The data collected in the systematic survey allowed in-depth case-control studies analyzing blood and urine samples of cases and controls for potential environmental toxins including pesticide residues. Further, identification of high and low prevalent areas in the systematic survey helped to analyze wide range of environmental samples including soil, water, vegetables, rice, fish and agrochemicals obtained from those areas for toxins such as cadmium, fluoride, aluminium, lead, arsenic and selenium.

The components of the analytical & environmental studies can be categorized as follows:



i. Case-Control Studies comparing newly diagnosed cases of CKDu and matched controls to identify risk factors for CKDu

Scientific scope of the project

The role of known nephrotoxins such as arsenic (As), cadmium (Cd), lead (Pb) and certain pesticides (14-16), and other metals that could influence the natural history of kidney disease and the pathogenesis of CKDu such as aluminium, copper, chromium, sodium, potassium, calcium, magnesium, copper, zinc, selenium, titanium and strontium (17) have not been hitherto investigated comprehensively.

This study was therefore undertaken

- To identify the risk factors associated with CKDu
- To compare and contrast CKDu cases and controls in relation to exposure to heavy metals/ metalloids through analysis of biological samples (urine, hair, nails, blood and tissue)

Materials and Methods

For the analytical studies, cases were identified from the previously conducted population prevalence study. A case constituted a CKDu patient between 15-70 years who satisfied the selection criteria which had been stated earlier. A control constituted a person who was free of CKD and, age and sex matched to an individual case. Controls were identified from both endemic and non-endemic areas. Endemic areas refer to the 22 study GN divisions from Anuradhapura, Polonnaruwa and Badulla districts whereas non-endemic area refers to Hambantota district.

Samples of urine, blood, hair and nails were selected from cases and matched controls for analysis of different metals and metalloids.

Cd, As and Pb were analyzed in urine samples of a randomly selected subset of CKDu cases (n = 495) and randomly selected matched controls from the endemic area as well as from a non-endemic area (n = 250).

Sodium, potassium, calcium, magnesium, copper, zinc, and titanium were analyzed in the urine samples of a subset of people with CKDu (n=148). Their serum was also analyzed for selenium, aluminium, strontium, and chromium. Hair and nail samples were analyzed for Cd, As and Pb in a subset of CKDu cases (n = 80) and controls from the endemic area (n = 48).

Details of samples collected for case control studies (Refer Annexure II for more details)

Samples	No. of samples & details of investigation
Urine	Analysis for cadmium, arsenic and lead in samples from 496 CKDu cases
	Analysis for cadmium, arsenic and lead in samples from 132 controls residing in endemic area
	Analysis for cadmium, arsenic and lead in samples from 250 controls residing in non-endemic area (Hambantota)
Hair and nail	Analysis for arsenic in samples from 77 CKDu cases
	Analysis for arsenic in samples from 50 controls residing in endemic area
Serum	Analysis for heavy metals (strontium, aluminium, selenium & chromium) in samples from 171 CKDu patients recruited for clinical trial

Samples were collected in uncontaminated collection vials and stored frozen (-20°C) until transfer to the laboratory. All analyses were performed in an internationally acknowledged reference laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium) which also has a Trace Element External Quality Control Scheme. This expertise is not available in local laboratories and the decision to send samples to Antwerp was taken as per the advice from the international steering committee.

Measurements of arsenic (As), cadmium (Cd), lead (Pb) and other elements in urine, was performed by Inductively Coupled Plasma Mass Spectrometry.

Serum analyses were performed by electrothermal atomic absorption spectrometry. Limits of detection for aluminium, strontium, chromium and selenium were 0.1 µg/l, 0.5 µg/l, 0.01 µg/l and 1 µg/l respectively

Results / Output

As, Cd, Pb and other elements in urine:

In CKDu cases, the concentration of cadmium in urine was significantly higher compared to controls, in both the endemic and the non-endemic areas. Among CKDu cases, the concentration of cadmium in urine was positively correlated with lead ($r = 0.62$, $P < 0.001$) and arsenic concentrations in urine ($r = 0.28$, $P < 0.001$).

There was no significant difference in urine arsenic and lead concentrations in CKDu cases compared to controls.

The sensitivity and specificity for concentrations of cadmium in urine were 80% and 53.6% respectively (AUC = 0.682 95% CI = 0.61 to 0.75, cut-off value ≥ 0.23 $\mu\text{g/g}$). At a cut-off value of ≥ 0.397 $\mu\text{g/g}$, sensitivity was 70% and specificity 68.3%. The sensitivity and specificity for the concentration of arsenic in urine were 90% and 23.2% respectively (AUC = 0.64, 95% CI = 0.58 to 0.71, cut-off value ≥ 88.57 $\mu\text{g/g}$).

The concentration of lead in urine was a poor predictor of CKDu (AUC = 0.53, 95% CI 0.38 to 0.67).

Dose–response analysis showed that cadmium exposure is a risk factor for the development of CKDu: $P = 0.019$ for stage 3 and $P = 0.024$ for stage 4.

There was no significant dose–effect relationship between the concentration of arsenic, lead or selenium in urine and the stage of CKDu.

Urine concentrations of sodium, potassium, calcium, magnesium, copper, zinc, and titanium in CKDu cases were within normal limits

Urine concentration of arsenic, cadmium and lead for CKDu cases compared with controls from the endemic and non-endemic areas

	Mean, median (range) of concentration in urine ($\mu\text{g/g}$ creatinine)		
	Arsenic	Cadmium	Lead
CKDu cases ($n = 495$)	45.447, 26.3 (0.4 to 616.6)	1.039, 0.695 (0.005 to 8.93)	1.153, 0.95 (0.04 to 8.53)
Controls from endemic area ($n = 132$)	92.443, 6.99 (0.2 to 966.29)	0.646, 0.18, (0.005 to 5.13) ^a	1.254, 0.793 (1.21 to 6.64)
Controls from non-endemic area ($n = 250$)	56.572, 42.025 (5.38 to 350.28)	0.345, 0.265 (0.005 to 2.079) ^b	2.099, 1.434 (0.277 to 20.9)

^a Urine cadmium concentration of cases compared to controls from endemic area $P < 0.001$.
^b Urine cadmium concentration of cases compared to controls from non-endemic area $P < 0.05$.

Urine concentration of metals (sodium, potassium, calcium, magnesium, copper, zinc & titanium) in CKDu cases

	Metals in urine n = 107, (mg/g creatinine)			
	Mean	Median	Minimum	Maximum
Sodium	4105.50	3544.00	425.00	17458.00
Potassium	917.94	800.00	243.00	2469.00
Calcium	80.45	67.00	4.00	368.00
Magnesium	79.89	80.00	2.00	169.00
Copper	13.34	11.00	3.70	91.10
Zinc	229.99	235.99	31.00	510.00
Titanium	0.26	0.24	0.03	0.88

Serum aluminium, chromium, selenium and strontium in people with CKDu:

Serum aluminium and chromium levels were within normal limits. Serum selenium levels in subjects with CKDu ranged from 50.0 µg/l to 121.8 µg/l (reference range = 54 µg/l to 163 µg/l). A serum selenium concentration of 90 µg/l is required to reach the maximum level of glutathione peroxidase [26]. About two-thirds (63%) of subjects had selenium levels below this cut-off value. Serum strontium levels were above normal limits (mean = 83.17 µg/l, standard deviation [SD] = 32.15 µg/l; reference range = 14 µg/l to 84 µg/l). The sensitivity and specificity for serum selenium were 80% and 60% respectively (AUC = 0.789, cut = off value ≥94.3 µg/l;).

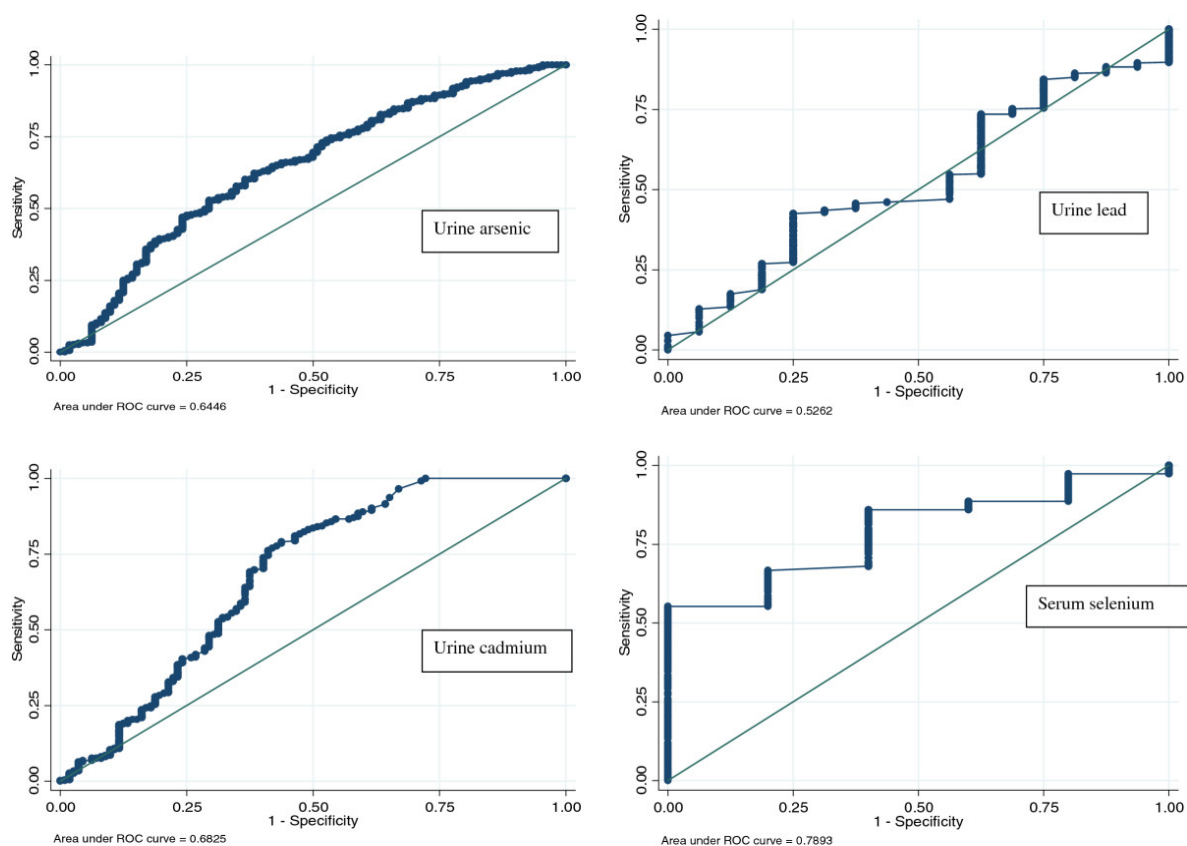
Serum concentration of aluminium, chromium, selenium and strontium in CKDu cases

	Serum concentration (µg/l), n = 171			
	Mean	Median	Minimum	Maximum
Aluminium	4.13	3.00	1.00	12.00
Chromium	0.118	0.06	0.01	1.15
Selenium ^a	88.27	84.5	50.0	121.8
Strontium ^b	83.17	82.00	29.00	198.00

^a Serum selenium reference range 54–163 µg/l.

^b Serum strontium reference range 14–84 µg/l.

ROC curves generated with arsenic, cadmium and lead and serum selenium concentrations



Cd and As in hair and nails:

A significantly higher cadmium concentration was also seen in the nails of CKDu cases ($n = 80$, mean = $0.017 \mu\text{g/g}$, median = $0.007 \mu\text{g/g}$, minimum = $0.001 \mu\text{g/g}$, maximum = $0.347 \mu\text{g/g}$) compared to controls ($n = 48$) from the endemic area (mean = $0.009 \mu\text{g/g}$, median = $0.001 \mu\text{g/g}$, minimum = $0.001 \mu\text{g/g}$, maximum = $0.091 \mu\text{g/g}$; $P < 0.05$).

Arsenic levels in hair were significantly higher in CKDu cases ($n = 80$; mean = $0.144 \mu\text{g/g}$, median = $0.139 \mu\text{g/g}$, minimum = $0.00 \mu\text{g/g}$, maximum = $0.452 \mu\text{g/g}$), compared to controls ($n = 48$) from the endemic area (mean = $0.125 \mu\text{g/g}$, median = $0.103 \mu\text{g/g}$, minimum = $0.006 \mu\text{g/g}$, maximum = $1.214 \mu\text{g/g}$; $P < 0.05$).

Discussion & Conclusions

Previous studies have reported divergent information on the role of cadmium in the causation of CKDu [14,15,19,20]. In the present study, individuals with CKDu excreted significantly higher levels of cadmium compared to those in the control group, in both the endemic and non-endemic areas.

Controls in the endemic area compared to those in the non-endemic area also had significantly higher urinary excretion of cadmium.

The sensitivity and specificity for urine cadmium were 80% and 53.6% respectively (AUC = 0.682, cut-off value $\geq 0.23 \mu\text{g/g}$). There was a dose–effect relationship between the concentration of cadmium in urine and the stage of CKDu.

A significantly higher cadmium concentration was also seen in the nails of those with CKDu compared to controls from the endemic area.

Cadmium is a known nephrotoxin and urinary excretion of cadmium is considered to be a reliable indicator of cumulative long-term exposure to cadmium [6]. The mean urine concentration of cadmium in CKDu cases was above the levels demonstrated in recent studies to cause oxidative stress and decreased glomerular filtration rate and creatinine clearance [28–33]. The results of this study indicate that cadmium exposure is a risk factor for CKDu.

The mean urine concentration of arsenic in CKDu cases was also above levels known to cause oxidative injury to the kidney [33]. In CKDu cases and controls from the endemic area, concentrations of arsenic in urine and in fingernails were higher than those reported in people living in low-exposure environments [34,35].

Urine is a major pathway for excretion of arsenic from the human body, so urine levels reflect exposure. In some studies, markers of oxidative stress have been demonstrated at urine arsenic concentrations as low as $3.95 \mu\text{g/g}$ [36]. The level of total arsenic in urine is associated with chronic kidney disease in a dose–response relationship, especially when the level is greater than $20.74 \mu\text{g/g}$ [36].

These findings support the contention that chronic exposure to low levels of cadmium may be a causative factor for CKDu in Sri Lanka. Co-exposure to cadmium and arsenic is known to produce additive effects on the kidney that are more pronounced than exposure to either metal alone [37,38].

Selenium has been shown to protect the kidney from oxidative stress [39]. A selenium concentration of $80\text{--}95 \mu\text{g/l}$ is needed to maximise the activity of the antioxidant enzyme glutathione peroxidase and selenoproteins in plasma [40,41]. In this context, it is significant that serum selenium was below $80 \mu\text{g/l}$ in 38% and below $90 \mu\text{g/l}$ in 63% of individuals with CKDu. Low selenium levels may have been a contributory factor increasing the vulnerability of the kidneys to oxidative damage caused by heavy metals and metalloids.

The association of raised serum strontium levels with raised serum cadmium levels has been reported previously [42]. Strontium levels were not analysed in food or water. The most likely explanation is an alteration of strontium handling and excretion, owing to the effect of cadmium on renal tubular function.

ii. Cross Sectional Comparison of potential environmental toxins in high and low prevalent areas for CKDu

Scientific scope of the project

The role of known nephrotoxins such as arsenic (As), cadmium (Cd), lead (Pb) and certain pesticides (14-16), and other metals that could influence the natural history of kidney disease and the pathogenesis of CKDu such as aluminium, copper, chromium, sodium, potassium, calcium, magnesium, copper, zinc, selenium, titanium and strontium (17) have not been hitherto investigated comprehensively.

This study was therefore undertaken

- To identify the risk factors associated with CKDu
- To estimate quantitatively the potential nephrotoxins in a wide range of environmental samples including water, soil, weedicides and fertilizers obtained from endemic and non-endemic areas
- To compare the presence of potential environmental toxins in post mortem tissues of deceased individuals due to CKDu with the similar data from post mortem tissues of controls

Materials and Methods

Arsenic, cadmium and lead were analysed in samples (n = 234) obtained from endemic and non-endemic areas. They comprised 99 sources of drinking water for individuals with CKDu (from ground wells, tube wells and natural springs), 123 other sources of water (from ground wells, tube wells, irrigation canals, reservoirs, natural springs) from the endemic area, and 12 from the non-endemic area.

Rice; pulses; vegetables, including leafy vegetables, coconut, yams and roots (e.g. kohila, lotus); freshwater fish; tobacco; pasture; and weeds obtained from endemic (n = 119) and non-endemic (n = 32) areas were analysed for arsenic, cadmium and lead. Soil, phosphate fertilizer, pesticides and weedicides were analysed for arsenic, cadmium and lead. Soil samples were obtained from paddy fields, other types of cultivations, and reservoirs in the endemic (n = 88) and non-endemic (n = 41) areas. Pesticides and weedicides commonly used in endemic and non-endemic areas were obtained from retailers while the commonly used fertilizers were obtained from the households.

Specimen handling and analysis Samples were collected in uncontaminated collection vials and stored frozen (−20°C) until transfer to the laboratory. All analyses were performed in a contract laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium), which has an external quality control scheme for analysis of trace elements.

Measurements of arsenic, cadmium, lead and other elements in urine, water, vegetables, agrochemicals and soil, was performed by inductively coupled plasma mass spectrometry (MS).

Details of environmental samples sent for analysis for cross sectional comparison of endemic and non-endemic areas for CKDu

Samples		Number of samples & details of investigation
Water	Drinking water	<ul style="list-style-type: none"> - Samples from 99 CKDu patients' (grade III & IV) drinking water sources - Reanalysis of selected samples from above which showed high arsenic level (n = 4) together with surface and deep water samples 2 each from vicinity (n = 16) - 13 drinking water samples (wells & directly piped from wells without treatment) from study areas - 5 control drinking water samples (well & water board supply) from Hambantota - Drinking water samples of 98 CKDu patients analysed for hardness at National Water Supply & Drainage Board, Anuradhapura - 12 natural spring water samples from Anuradhapura
	Irrigation water	<ul style="list-style-type: none"> - 6 from study areas - 2 from control area (Hambantota)
	Agro well water	<ul style="list-style-type: none"> - 6 from study areas - 2 from control area (Hambantota)
	Tube well water	<ul style="list-style-type: none"> - 10 from study areas - 3 from control area (Hambantota)
	Other water sources	<ul style="list-style-type: none"> - 35 samples from canals in study area - 53 samples from reservoirs in study area
Food	Rice samples	<ul style="list-style-type: none"> - 6 samples of rice from study area - 2 samples of rice from control area (Hambantota) - 10 rice samples from CKDu patients' households (Anuradhapura)
	Food samples	<ul style="list-style-type: none"> - 60 food samples from study area - 22 control food samples from Hambantota - 17 food samples (sesame & coconut) from study area
Tobacco, beetle & beedi		<ul style="list-style-type: none"> - 12 samples of tobacco & beedi from study area - 4 samples of from control area (Hambantota) - 15 samples from study area
Weeds		<ul style="list-style-type: none"> - 6 samples of weeds from study area - 2 samples of weeds from control area (Hambantota)

Soil	<ul style="list-style-type: none"> - 18 samples of soil & sediment of reservoirs from study area - 6 samples of soil & sediment of reservoirs from control area (Hambantota) - 88 soil (vegetable plot, chena, paddy field) samples from study area - 41 soil (vegetable plot, chena, paddy field) samples from control area (Hambantota)
Weedicides & pesticides	<ul style="list-style-type: none"> - 25 commonly used pesticides & weedicides from study area - 7 weedicides & pesticides from control area (Hambantota)
Fertilizers	<ul style="list-style-type: none"> - 13 fertilizer samples from study area - 6 fertilizer samples from control area (Hambantota)
Pesticide residues in urine	<ul style="list-style-type: none"> - Urine samples of 76 CKDu patients collected from Anuradhapura & Badulla Districts - 39 Control urine samples collected from Hambantota

Samples were collected in uncontaminated collection vials and stored frozen (-20°C) until transfer to the laboratory. All analyses were performed in an internationally acknowledged reference laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium) which also has a Trace Element External Quality Control Scheme. This expertise is not available in local laboratories and the decision to send samples to Antwerp was taken as per the advice from the international steering committee.

Measurements of arsenic (As), cadmium (Cd), lead (Pb) and other elements in water, vegetables, agrochemicals and soil was performed by Inductively Coupled Plasma Mass Spectrometry.

Results/Outputs

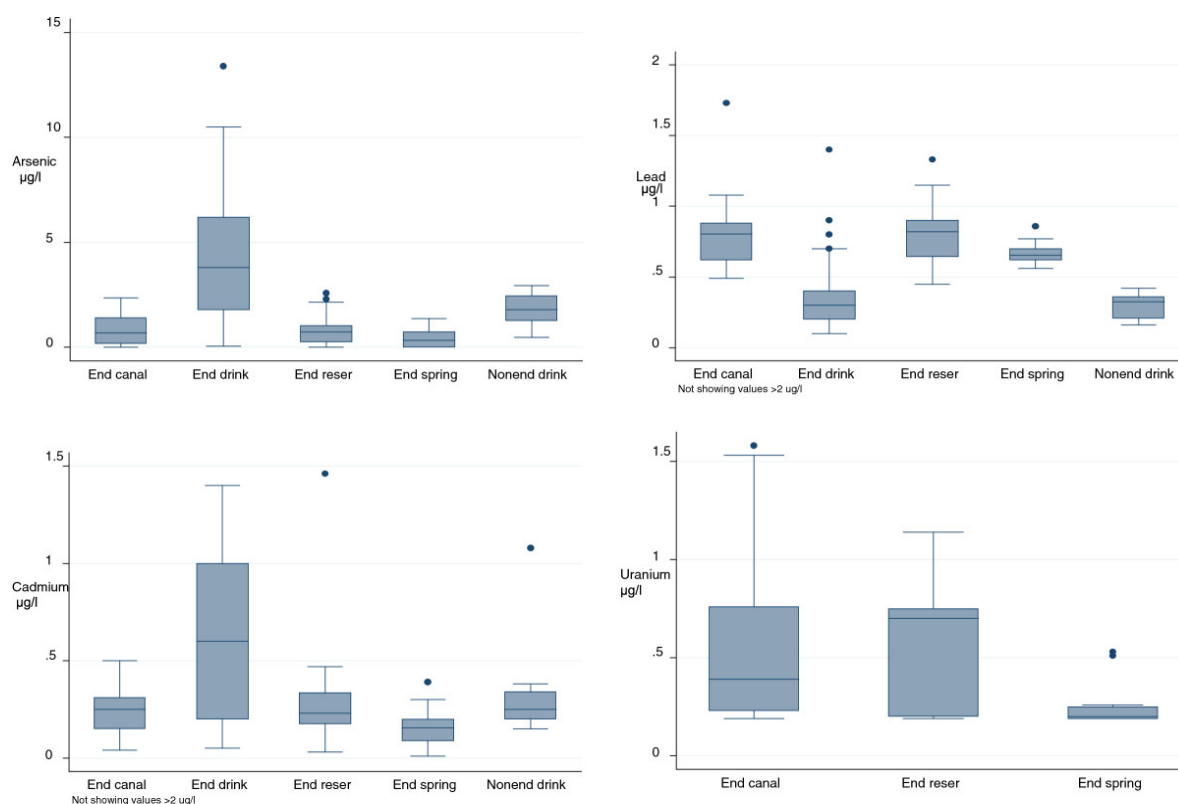
As, Cd, Pb and uranium in water (Endemic area $n=222$, non endemic area, $n=12$)

Levels of cadmium, lead and uranium in sources of drinking water used by individuals with CKDu ($n = 99$) were within normal limits.

Arsenic was borderline or raised in four samples (9.9 µg/l, 10.2 µg/l, 10.5 µg/l, 13.4 µg/l). Repeat analysis ($n = 32$) from the four sources showed normal arsenic levels.

In water samples from other sources, the arsenic concentration was 22.2 µg/l and 9.8 µg/l in two samples taken from a canal and a reservoir, the cadmium concentration was 3.46 µg/l in one sample from a reservoir and the lead concentration was 12.3 µg/l in one sample from a reservoir in the endemic area. All other samples from wells, tube wells, irrigation canals, pipe-borne water, reservoirs and natural springs, including those taken from the non-endemic area, had normal arsenic, cadmium and lead levels.

Concentration of arsenic, Cadmium, lead and Uranium in water in the endemic area (n=222) and non-endemic area (n=12)

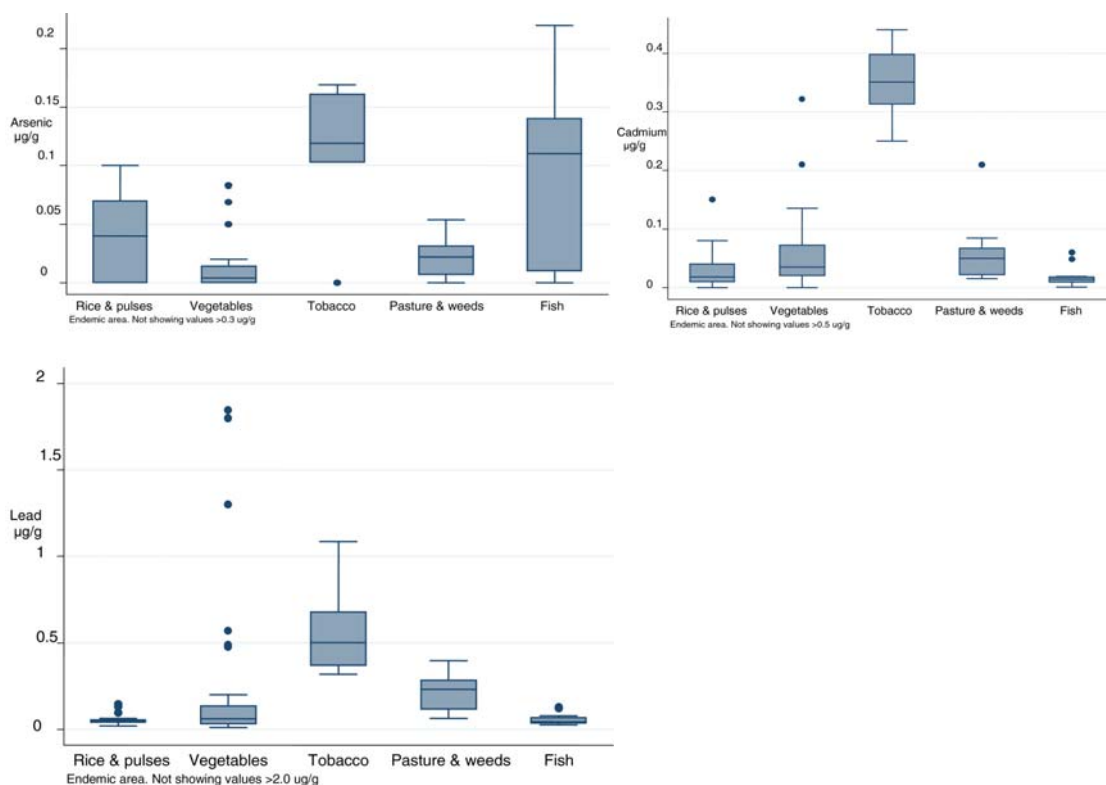


As, Cd and Pb in food, tobacco, betel leaves, pasture and weeds

Levels of cadmium in rice in both endemic and non-endemic areas were below the allowable limit (0.2 mg/kg;).

The maximum concentration of cadmium in vegetables in the endemic area and in the non-endemic areas was 0.322 mg/kg and 0.063 mg/kg respectively. Levels of cadmium in certain vegetables such as lotus root, and in tobacco, were high. Levels of cadmium in lotus and tobacco were higher in endemic than in non-endemic areas (lotus: mean = 0.413 mg/kg versus 0.023 mg/kg, median = 0.066 mg/kg versus 0.023 mg/kg, maximum = 1.50 mg/kg versus 0.03 mg/kg; tobacco: mean = 0.351 mg/kg versus 0.316 mg/kg, median = 0.351 mg/kg versus 0.316 mg/kg, maximum = 0.44 mg/kg versus 0.351 mg/kg in endemic versus non-endemic areas respectively).

Content of Arsenic, Cadmium and lead in food, tobacco leaves, pasture and weeds from the endemic area



As, Cd and Pb in soil and agrochemicals in the endemic and non-endemic areas

The level of cadmium in surface soil in the endemic area (n = 94, excluding samples from reservoirs), was $1.16 \mu\text{g/g}$ compared to $0.49 \mu\text{g/g}$ in the non-endemic area (n = 45, excluding samples from reservoirs)

Concentration of arsenic, cadmium and lead in surface soil and in phosphate fertilizer, pesticides and weedicides, in the endemic area compared with a non-endemic area. Samples of soil from vegetable plots from the endemic area were obtained from the vicinity of households with CKDu patients

Area and source	Arsenic µg/g	Cadmium µg/g	Lead µg/g
	Mean, median (minimum, maximum)		
Endemic area			
Soil from paddy cultivation <i>n</i> = 45	0.16, 0.11, (0.00, 0.85)	0.49, 0.43 (0.16, 0.56)	16.54, 15.75 (5.03, 34.54)
Soil from chena (shifting) cultivation <i>n</i> = 20	0.06, 0.04 (0.00, 0.22)	0.40, 0.36 (0.17, 1.27)	15.41, 13.82 (8.25, 28.33)
Soil from vegetable plot (home) <i>n</i> = 23	0.11, 0.07 (0.00, 0.46)	3.48, 0.37 (0.16, 70.00)	17.46, 16.76 (6.69, 41.02)
Soil from crop land <i>n</i> = 6	0.05, 0.06 (0.00, 0.01)	0.60, 0.5 (0.17, 1.47)	20.55, 20.29 (9.98, 32.1)
Soil from reservoirs <i>n</i> = 6	0.60, 0.5 (0.17, 0.43)	0.66, 0.52 (0.15, 1.36)	19.16, 17.16 (7.11, 33.49)
Phosphate fertilizer <i>n</i> = 13	0.06, 0.04 (0.00, 0.19)	2.98, 0.04 (0.01, 30.79)	94.23, 1.42 (0.17, 823.41)
Weedicides and/or pesticides <i>n</i> = 26	6.73, 1.68 (0.01, 94.93)	0.77, 0.31 (0.05, 9.34)	40.62, 1.79 (0.83, 930.81)
Non-endemic area			
Soil from paddy cultivation <i>n</i> = 21	0.17, 0.08 (0.01, 0.99)	0.45, 0.40 (0.01, 1.61)	14.49, 16.95 (0.02, 39.95)
Soil from chena (shifting) cultivation <i>n</i> = 10	0.40, 0.29 (0.09, 1.57)	0.59, 0.55 (0.34, 0.93)	14.84, 13.93 (5.42, 26.1)
Soil from vegetable plot (home) <i>n</i> = 10	0.27, 0.24 (0.08, 0.53)	0.47, 0.41 (0.29, 0.84)	18.01, 18.03 (5.57, 32.87)
Crop land <i>n</i> = 4	0.13, 0.13 (0.09, 0.18)	0.28, 0.28 (0.24, 0.33)	7.96, 7.96 (3.15, 12.77)
Phosphate fertilizer <i>n</i> = 5	0.43, 0.19 (0.00, 1.22)	0.49, 0.03 (0.01, 1.28)	20.29, 0.65 (0.09, 98.52)
Weedicides and pesticides <i>n</i> = 8	3.81, 1.38 (0.01, 13.15)	0.76, 0.3 (0.05, 2.0)	15.65, 1.89 (1.01, 56.39)

Discussion & Conclusions

Cd levels have previously been reported to be high in water sources in the domestic environment of people with CKDu and 10-20 fold the maximum stipulated level in reservoirs in the endemic area (8). Our results did not show this to be the case. On the contrary, Cd levels of all water samples analysed were within normal limits except in one sample from a reservoir which had a borderline Cd level (3.45 µg/l).

Drinking water is a major pathway for entry of inorganic As into the human body. The WHO guideline for As in drinking water is 10 µg/l (6). The U.S. Environmental Protection Authority has suggested that the concentration of As in drinking water should be no more than 5 µg/l (37).

Levels of Cd and Pb in vegetables and Cd in fresh water fish from the endemic area are above the maximum levels stipulated by certain Authorities (38). Since the Cd content of certain food items in the endemic area is above stipulated levels, the total weekly intake of Cd in people living in the endemic area could exceed these safe limits with detrimental effects on renal function particularly in vulnerable people (39, 40).

Reported mean dietary exposure to inorganic As in the US and various European and Asian countries range from 0.1 to 3.0 µg/kg bw per day (39). Recently the PTWI for As (0.015 mg/kg body weight per week) was withdrawn and environmental authorities are in the process of collecting more data for exposure assessment (40). The current recommendation is that every effort be made to keep concentrations of As as low as reasonably possible.

Previous studies have reported high Cd values in fertilizer (mean 47 µg/g) (8). The maximum Cd, Pb and As values in phosphate fertilizer from the endemic area in the present study were 30.8 µg/g, 823.4 µg/g and 0.19 µg/g respectively. The maximum acceptable level for As, Cd and Pb in phosphate fertilizer product at 1% of the nutrient level is 2, 4 and 20 parts per million (41). The mean Cd concentration of soil from the endemic area was 0.4 µg/g and is higher than the levels reported in agricultural soils in certain developed countries (42, 43).

The concentration of Cd, As and Pb in the soil and their impact on body burden and excretion is known to be influenced by many environmental factors such as the pH of soil, ability of soil to preserve and supply soil fertilizer, buffering capacity, content of soil organic matter and water quality, among others (43-46). The hardness and high content of fluoride in water in the endemic area may also influence the dynamics of Cd in soil (10, 47).

iii. Determination of pesticide residues

Scientific scope of the project

The role of known nephrotoxins such as arsenic (As), cadmium (Cd), lead (Pb) and certain pesticides (14-16), and other metals that could influence the natural history of kidney disease and the pathogenesis of CKDu such as aluminium, copper, chromium, sodium, potassium, calcium, magnesium, copper, zinc, selenium, titanium and strontium (17) have not been hitherto investigated comprehensively.

This study was therefore undertaken

- To identify the risk factors associated with CKDu
- To compare and contrast CKDu cases and controls in relation to exposure to pesticides through analysis of biological samples (urine)

Materials and Methods

Urine samples from CKDu cases (n = 57) and controls from the non-endemic area (n = 39) were analysed for pesticide residues (2,4-D, 2,4,5-T, 2,4,5-trichlorophenol, isopropoxyphenol, pentachlorophenol, 3,5,6-trichloropyridinol, p-nitrophenol, 1-naphthol, 2-naphthol, glyphosate, aminomethylphosphonic acid (AMPA)).

Urine samples were shipped on dry ice and were stored at -18 C until analysis. Analysis used validated liquid chromatography with tandem mass spectrometry (LC-MS/MS), Gas Chromatography-Mass Spectroscopy (GCMS) and Gas Chromatography with tandem mass spectrometry (GC-MS/MS) methods.

Results/Output

Pesticide residues were detected in the urine from individuals with CKDu (n = 57). The frequency of detection of 2,4-D, 3,5,6-trichloropyridinol, p-nitrophenol, 1-naphthol, 2-naphthol, glyphosate, AMPA was 33%, 70%, 58%, 100%, 100%, 65% and 28% respectively). Isopropoxyphenol, 2,4,5-trichlorophenol and pentachlorophenol were below detection limits. The proportions of CKDu cases with pesticide levels above reference values are shown in Table below.

Pesticide residues in urine of CKDu cases (n=57)

Parent compound	Biomarker	Reference limit (µg/l)	CKDu cases (µg/l), (minimum, maximum)	CKDu cases above reference limit (%)
2,4-D	2,4-D	<0.3	0.5, 0.62	3.5
Pentachlorophenol	Pentachlorophenol	<2	0.3, 2.2	1.7
Chlorpyrifos	3,5,6-trichloropyridinol	<11.3	0.5, 34.7	10.5
Parathion	p-nitrophenol	<25	0.5, 8.88	0
Carbaryl naphthalene	1-naphthol	<19.7	0.5, 45.1	10.5
Naphthalene	2-naphthol	<17.1	0.94, 47.88	10.5
Glyphosate	Glyphosate	<2	0.075, 3.36	3.5
Glyphosate	AMPA	<0.5	0.075, 2.65	14

Discussion & Conclusions

Certain pesticides residues were above reference levels in 31.6% of CKDu cases. Residues are demonstrative of the extent of the environmental distribution of pesticides and certain pesticides are nephrotoxic (4,5,53). Simultaneous exposure of people to heavy metals and nephrotoxic pesticides may be a contributory factor in the pathogenesis and progression of CKDu.

iv. Analytical Studies of Human postmortem tissues

Scientific scope of the project

The role of known nephrotoxins arsenic (As), cadmium (Cd) and lead (Pb) pesticides (14-16) and other metals and pesticides that could influence the natural history of kidney disease (aluminium, copper, chromium, sodium, potassium, calcium, magnesium, copper, zinc, selenium, titanium and strontium) (17), in the pathogenesis of CKDu have not been hitherto investigated comprehensively.

This study was therefore undertaken

- To identify the risk factors associated with CKDu
- To compare and contrast CKDu cases and controls in relation to exposure to heavy metals/ metalloids through analysis of biological samples (tissue)

Materials and Methods

Renal, hepatic and bone content of potential environmental toxins was evaluated in deceased individuals with CKDu and compared with the similar data from post-mortem tissues of those without CKDu.

Postmortem specimens (kidney cortex, liver and bone) were obtained from 26 CKDu patients and 14 accident victims aged between 40 - 60 years from the North Central Province and 2 from Western Province considered a non-endeic area. Written consent was obtained from the next of kin/ a close relative for obtaining postmortem tissues (kidney cortex, liver and bone) from the deceased who satisfied the selection criteria stated earlier. Powder free gloves were used during the procedure and a plastic knife was used for soft tissue handling and dissection. A piece of kidney was cut from middle third of left kidney (1cm x 1 cm x 1 cm, weighing more than 1 gm). A piece of liver was taken from the large lobe of the liver just beneath the lower surface, measuring 1cm x 1 cm x 1 cm and weighing more than 1 gm. Bone samples were obtained from anterior end of 2nd rib without cartilage. Tissues were stored at -20⁰C until quantitative analyses was done at an international reference laboratory (University of Antwerp).

Results/outputs

As, Cd and Pb in bone, kidney and liver (post mortem tissue):

The concentration of As, Cd and Pb (ug/l) in kidney, liver and bone were as follows-

- **Cadmium:** Kidney - mean 885.54, median 152.62, range 19.28-7458.54; Liver - mean 165.39, median 117.19, range 22.22-1471.41; Bone - mean 8.68, median 4.87, range 0.82-70.66
- **Arsenic:** Kidney - mean 4.04, median 2.34, range 0.0384-14.16; Liver - mean 5.38, median 2.42, range 0.13-26.16; Bone-mean 6.47, median 4.34, range 0.47-28.84
- **Lead:** Kidney - mean 0.89, median 0.6, range 0.01-2.54; Liver - mean 4.56, median 3.93, range 0.98-13.33; Bone - mean 64.04, median 47.13, range 2.11-233.92

Discussions & Conclusions

The mean cadmium and lead contents in bone were higher than the currently reported levels in healthy subjects.

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FORMATS USED

එකගත්වය පළකිරීමේ සහතිකයයි

හේතුවක් නොදන්නා නිදන්ගත වතුගඩු රෝගය පිළිබඳව විශ්ලේෂණය කිරීම සහ පර්යේෂණ පැවැත්වීම

පශ්චාත් මරණ පරීක්ෂණ අධ්‍යයනය

ඉහත අධ්‍යයනය සඳහා මෑත ශරීර අවයව සාම්පල ලබාගෙන පර්යේෂණ කරගෙන යනු ලබන්නේ සෞඛ්‍ය අමාත්‍යාංශය සහ ලෝක සෞඛ්‍ය සංවිධානය මගිනි. එහි මූලික ඉලක්කය වනුයේ, දැනට ශ්‍රී ලංකාවේ ඇතැම් ප්‍රදේශවල විශාල වශයෙන් වාර්තා වන හේතුව නොදන්නා නිදන්ගත වතුගඩු රෝගය සඳහා හේතුව සොයා බැලීමයි.

මියගිය තැනැත්තාගේ වතුගඩුවේ බාහිකයේ පටක අක්මාව, අස්ථි කොටස් මාගේ සහතික කිරීම සහ අනුදැනුම ඇතිව ලබා ගන්නා ලද බවත්, මියගිය තැනැත්තාගේ ඉහත පටක කොටස් ලබා ගැනීමට නිත්‍යානුකූලව කැමැත්ත දැක්වීමට මට අයිතියක් ඇති බවත් ප්‍රකාශ කරමි. මා විසින් මේ සඳහා එක්කෝණික ප්‍රකාශ කරනු ලබන්නේ සම්පූර්ණයෙන්ම ස්වේච්ඡාවෙන් බවත්, යම් තෙයකින් එක්කෝණික ප්‍රතික්ෂේප කිරීම නිසා, අනාගතයේදී මා රෝහල් හෝ සෞඛ්‍ය සේවාවන් සමග කටයුතු කිරීමේදී බලපෑමක් නොවන බව දන්නා බවත් ප්‍රකාශ කරමි.

තවද, මියගිය තැනැත්තාගේ සිරුරේ පටක කොටස් ගැනීමට, පර්යේෂකයන්ට ඉඩදීමෙන් මට හෝ මියගිය පුද්ගලයා දන්නා අයට කිසිදු කෙටිකාලීන ලාභ ප්‍රයෝජනයක් නොමැති බව දන්නා බව ප්‍රකාශ කරමි.

නමුත්, ඉහත පටක විශ්ලේෂණය කිරීමෙන් ලබාගන්නා දත්ත දැනට ශ්‍රී ලංකාවේ ඇතැම් ප්‍රදේශවල වාර්තාගත වන නිදන්ගත වතුගඩු රෝගයට හේතුව / හේතු සොයා ගැනීමට උපකාරී වන බවත් එමගින් වතුගඩු රෝගය වළක්වා ගැනීමෙන් සමාජයට යහපත් ප්‍රතිඵල උදාවන බවත් දනිමි.

මේ මගින් කිසිම කෙනෙකුට අපහසුතාවයක් හෝ තර්ජනයක් හෝ නොමැත. ලබාගනු ලබන එක් එක් සාම්පල කොටස් (වතුගඩු බාහිකය, අක්මාව, අස්ථි පටක) 100පට්ට වඩා කුඩා නොවන අතර 500පට්ට වඩා විශාල නොවනු ඇත. එමෙන්ම ඉහත සාම්පල ලබා ගැනීම නිසා දේහයේ බාහිර ස්වරූපය විකෘති නොවනු ඇත.

ඉහතින් දක්වන ලද තොරතුරු මා විසින් / මා වෙනුවෙන් කියවන ලදී. මා හට මේ පිළිබඳව ප්‍රශ්න කිරීමටත්, මා විසින් අයත ලද ඕනෑම ප්‍රශ්නයකට මා සැහීමට පත්විය හැකි පිළිතුරු ලබා ගැනීමටත් මට අවස්ථාව ලැබුණි. මම ස්වේච්ඡාවෙන් මියගිය තැනැත්තාගේ මෑත ශරීර අවයව කොටස් පර්යේෂකයන්ට ලබා දීමට ඉඩ දෙමි.

මියගිය තැනැත්තාගේ නම	දිනය (දි/මා/අවු)	එක්කෝණික පළකරන්නාගේ අත්සන
මියගිය තැනැත්තාගේ සහ එක්කෝණික පළකරන්නා අතර ඇති සම්බන්ධතාවය සඳහන් කරන්න		
එක්කෝණික පළකරන්නාට ලිවීමට/කියවීමට අපහසුනම් (සාක්ෂිකරු තෝරා ගැනීම එක්කෝණික පළකරන්නා විසින් කළයුතු අතර පර්යේෂණ කණ්ඩායම සමග කිසිම සම්බන්ධතාවයක් නොතිබිය යුතුයි).		
ස්වාධීන සාක්ෂිකරුගේ නම	දිනය (දි/මා/අවු)	සාක්ෂිකරුගේ අත්සන
පර්යේෂකගේ නම	දිනය (දි/මා/අවු)	පර්යේෂකගේ අත්සන

Certificate of Consent

Evaluation and investigation of chronic kidney disease of unknown aetiology

Post-mortem Study

The study for which the post-mortem specimens are requested is one being conducted under the auspices of the Ministry of Health and the World Health Organization. Its overall goal is to identify the determinants of chronic kidney disease of unknown aetiology (CKDu) reportedly highly prevalent in certain parts of Sri Lanka.

The deceased from whom the tissues of kidney cortex, liver and bone are to be taken was known to me and I confirm that I have the legal authority to give consent to take such tissues from the deceased. I am giving the consent entirely voluntarily and I am aware that refusal to give such consent will not affect my future relationship with any hospital/ health facility.

I am aware that there are no immediate benefits for me or any one else known to the deceased for allowing the investigators taking certain tissues from the deceased. However, I am aware that there are benefits to the society because the information obtained from the analysis of these tissues shall be helpful to find the cause/s of a type of kidney disease seen in some parts of Sri Lanka and hence in the prevention of this kidney disease.

There are no risks or discomforts to anyone. The weight of each specimen (kidney cortex, liver and bone biopsy) to be taken is not less than 100 mg and not more than 500 mg and taking these specimens will not distort the body or its external appearance.

.
I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to allow the investigators to take post-mortem specimens from the deceased.

Print name of the deceased State the relationship between the deceased & the person giving consent	Date	Signature of the person giving consent
<i>If the person giving consent is illiterate (The witness should be selected by the participant and should have no connection to the research team)</i>		
Print name of independent literate witness	Date	Signature of witness
Print Name of the investigator	Date	Signature of investigator

ஒப்புதல் சான்றிதழ்

இலங்கையில் காணப்படும் நோய் ஏது அறியப்படாத நீடித்த சிறுநீரக நோயை
மதிப்பிடுதலும் ஆய்வு செய்தலும்

பிரேதங்களில் நடாத்தப்படும் ஆய்வு

பிரேதங்களிலிருந்து பெறப்படும் மாதிரிகளை வேண்டிநிற்கும் இந்த ஆய்வானதுஇ சுகாதார அமைச்சினதும், உலக சுகாதார சுகாதார ஸ்தாபனத்தினத்தினதும் அனுசரணையுடன் நடாத்தப்படுகின்றது. இவ்வாய்வின் முழுமையான இலக்கானது இலங்கையின் சில பகுதிகளில் அதிகளவில் காணப்படுவதாக அறிவிக்கப்படும் நீடித்த சிறுநீரக நோயினை நிர்ணயம் செய்யும் காரணிகளையும் அடையாளம் கண்டு கொள்வதாகும்.

சிறுநீரகம், ஈரல் மற்றும் எலும்பு என்பவற்றிலிருந்து இழையங்கள் எடுக்கப்படவுள்ள இறந்த நபர் எனக்கு அறியப்பட்டவர். இறந்தவரிடமிருந்து இழையங்கள் எடுக்கப்படுவதற்கு ஒப்புதல் வழங்க எனக்கு சட்டரீதியான அதிகாரம் இருப்பதை உறுதி செய்கின்றேன். நான் எனது ஒப்புதலை வழங்குவதானது முற்றிலும் எனது சொந்த விருப்பிலாகும். ஒப்புதல் வழங்க மறுப்பதானது வைத்தியசாலையுடனோ அல்லது சுகாதார நிலையத்துடனோ எனக்குள்ள வருங்கால உறவைப் பாதிக்காது என்பதனை நான் அறிவேன்.

இறந்தவரிடமிருந்து இழையங்கள் ஆய்வாளர்களால் எடுக்கப்படுவதற்கு இடமளிப்பதானது எனக்கோ அல்லது இறந்தவரை அறிந்த வேறு யாருக்குமோ உடனடிப் பலன்களை வழங்காது என்பதை நான் அறிவேன். இருப்பினும், இந்த இழையங்களை ஆய்வு செய்வதனால் பெற்றுக் கொள்ளப்படும் தகவல்கள் இலங்கையின் சில பகுதிகளில் காணப்படும் ஒரு வகை சிறுநீரக நோய்க்கான காரணம் அல்லது காரணங்களை கண்டுபிடிக்கவும் அதன்மூலம் இச்சிறுநீரக நோயைத் தடுக்கவும் உதவுமாகையால், சமுதாயத்துக்கும் இதனால் பலனுண்டு என்பதனை நான் அறிவேன். .

எவருக்குமே எந்தவொரு அபாயமும், அசௌகரியமும் ஏற்படாது. எடுக்கப்படவுள்ள ஒவ்வொரு மாதிரியினதும் (சிறுநீரகம், ஈரல் மற்றும் எலும்பிலிருந்து) நிறையானது 100 கிராம்களுக்கு குறையாமலும் 500 கிராம்களுக்கு மேற்படாமலும் இருப்பதுடன், மாதிரிகளை எடுப்பதானது உடலையோ அதனது வெளித்தோற்றத்தையோ பாதிக்காது.

நான் முன்தரப்பட்ட தகவல்களை வாசித்தேன் அல்லது அவை எனக்கு வாசித்துக் காட்டப்பட்டது. இது பற்றி வினாக்கள் கேட்க எனக்கு சந்தர்ப்பம் தரப்பட்டதுடன்இ திருப்தியான முறையில் என்னால் கேட்கப்பட்ட வினாக்களுக்கு பதிலளிக்கப்பட்டது. எனது சுயவிருப்பில் இறந்தவரிலிருந்து மாதிரிகள் ஆய்வாளர்களால் எடுக்கப்படுவதற்கு ஒப்புதல் அளிக்கின்றேன்.

<p>இறந்தவரின் பெயர்</p> <p>இறந்தவருக்கும் ஒப்புதல் வழங்குபவருக்கும் இடையிலான உறவு முறையைக் கூறுக.</p>	<p>திகதி</p>	<p>ஒப்புதல் வழங்குபவரின் ஒப்பம்</p>
<p><i>ஒப்புதல் வழங்குபவர் படிப்பறிவு இல்லாதவர் எனின் (சாட்சியை பங்குபற்றுபவர் தெரிவு செய்ய வேண்டும்.. இந்நபருக்கு ஆய்வுக்குழுவுடன் தொடர்புகள் இருத்தலாகாது)</i></p>		
<p>படிப்பறிவுள்ள சுயாதீனமான சாட்சியின் பெயர்</p>	<p>திகதி</p>	<p>சாட்சியின் ஒப்பம்</p>
<p>ஆய்வாளரின் பெயர்</p>	<p>திகதி</p>	<p>ஆய்வாளரின் ஒப்பம்</p>

Introduction and Background

In order to monitor the trends in the disease burden attributable to chronic kidney disease (CKD) in general and chronic kidney disease of uncertain aetiology (CKDu) in specific, efforts were taken to establish a computerized database. As an initial step, hospital-based registries of patients attending renal clinics were established in selected hospitals in the North Central Province namely TH Anuradhapura, DGH Polonnaruwa, BH Medirigriya and BH Madawachchiya

Scientific scope and objectives

Hospital-based registries that were set up for patients attending renal clinics at TH Anuradhapura, DGH Polonnaruwa, BH Medirigriya and BH Madawachchiya detail in it. The database includes information on socio-demographics, lifestyle factors, environmental factors, information on co-morbidities and primary diagnosis that led to CKD, anthropometric measures and laboratory investigations.

This registry was established to

- identify CKDu cases for studies commissioned under the National Research Programme for CKDu, establishment of a National Registry
- characterize the CKD and CKDu cases with regard to socio-demographics, lifestyle and environmental factors and treatment modalities)

Materials and Methods

Prior approval for data collection was obtained from the Provincial and Regional Directors of Health Services. Permission to get access to hospital records was obtained from the Directors/ Medical Superintendents of the selected hospitals. The study involved no additional risks to patients and the objectives of the registry were explained to them before collecting data.

Appropriate administrative, technical, procedural, and physical safeguards have been established to protect the confidentiality of the data and to prevent unauthorized access to it. Data from the registry will be provided to researchers those who conduct legitimate research and the researchers should not use the data for purposes that are not related to research. The data will not be published or disclosed to any person unless the data have been aggregated (i.e. combined into groupings of data such that the data are no longer specific to any individual). A copy of any aggregation of data intended for publication should be submitted to the Scientific Committee, National Research Programme for CKDu

and relevant health authorities for review, and written approval should be obtained prior to publication.

The hospital-based registries have been established only in selected hospitals. The data collection sheet used for the registry is given in the appendix. The database currently contains information on approximately 2,000 CKD patients and it has been operational since 2009. Two pre-intern medical officers under the supervision of Epidemiology Unit, Ministry of Health involved in the data collection. Data collection was mainly by interviewing the patients during clinic sessions and by reviewing the clinic records. If necessary, clarification on clinical records was obtained from the medical officers serving at the clinics. Basic socio-demographics and clinical data of CKD patients attending renal clinics at TH Anuradhapura, DGH Polonnaruwa, BH Medirigiriya & BH Medawachchiya entered into a database.

The relevant categorical variables were dichotomized and bivariate analysis (preliminary analysis) was done. For all these variables, odds ratios (OR) and 95% confidence intervals (CI) were calculated to identify risk factors for CKDu. The software package SPSS 10 was used for data entry, analysis and editing. To identify the factors that were independently associated with CKDu, multiple logistic regression analysis was done.

The data collection tool used for the hospital registry is shown at the end of this section.

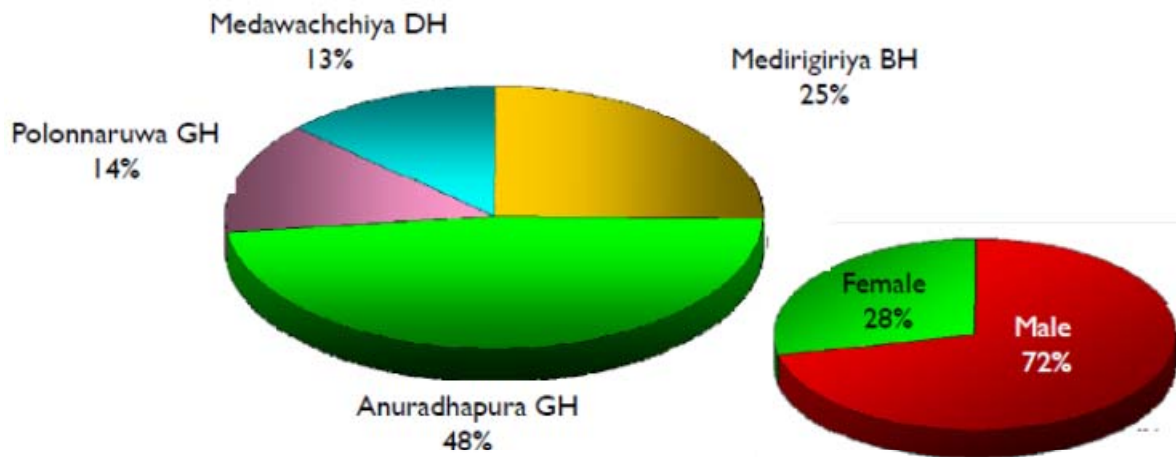
Results/outputs

As per the preliminary analysis, out of the 1997 included in the registry 775 (39%) could be identified as CKDu. Others were due to hypertension 798 cases (40%), hypertension & diabetes 118 cases (6%), diabetes 90 (5%), snakebite 121 (6%), obstructive uropathy 32 (2%), glomerulonephritis 30 (2%), polycystic kidney disease 10 (1%) and other known causes 18 cases (1%).

Bivariate analysis found that compared to CKD of known aetiology patients, CKDu patients were more likely to be males (OR = 2.4, 95% CI: 1.9, 3.0), aged ≤ 50 years (OR = 1.6, 95% CI: 1.3, 2.0), residents of Anuradhapura district (OR = 1.26, 95% CI: 1.04, 1.5), less educated (OR = 1.3, 95% CI: 1.04, 1.7), past or current smokers (OR = 1.9, 95% CI: 1.6, 2.3), regular consumers of alcohol (OR = 1.9, 95% CI: 1.6, 2.4), consumers of illicit liquor (OR = 1.9, 95% CI: 1.6, 2.3) and exposed to agrochemicals (OR = 1.9, 95% CI: 1.6, 2.4).

Aetiology (known vs. unknown) was not related to ethnicity (OR = 1.1, 95% CI: 0.5, 2.2), income (OR = 1.1, 95% CI: 0.9, 1.4), occupation (OR = 0.9, 95% CI: 0.7, 1.2) and source of drinking water (OR = 1.3, 95% CI: 0.98, 1.6).

Cases Registered in the hospital registry – 1997
True CKDu cases - 775 (39%)



Discussion & Conclusions

As the classification of aetiology of CKD was based on secondary data, it was not possible to confirm the sequence of events especially that of hypertension i.e. whether hypertension was primary (led to CKD) or secondary (due to CKD) diagnosis. Therefore, all the patients with hypertension were classified as “CKD cases due to hypertension”. Considering these facts, it could be stated that the proportion of CKDu cases derived from the registries was an underestimate. Even for other known causes of CKD, secondary data analysis would not suffice to attribute CKD totally to that particular cause/s.

The registry was intended to be the initial step towards a national registry. Steps were to be taken to expand this activity in a stepwise manner to all renal centres/ clinics in both public and private hospitals in Sri Lanka. In addition to the objectives listed earlier, it could also be used to evaluate renal replacement therapy programmes e.g. outcomes and factors influencing renal replacement therapy, information on patients waiting for renal transplant etc. There were also plans to introduce electronic data capture via the internet. Periodic reports containing descriptive and analytic epidemiologic data on CKD patients were expected to be published in future and this registry was to serve as a resource to the academic and clinical medicine communities to facilitate investigator-initiated research.

The database was shared with the Epidemiology Unit of the Ministry of Health and Provincial Health Authorities in 2011. However, due to lack of sustainable funding and failure to incorporate this into the national health information system, the national and provincial health authorities could not continue with this. The recently established CKD Unit of the North Central Provincial Directorate of Health Services is currently attempting to restart the hospital-based CKD registry work. They are also currently involved in geographical mapping of CKD cases with the support from WHO.

Formats used

CHRONIC KIDNEY DISEASE REGISTRY

Data Sheet

Necessary data should be obtained by reference to the Bed Head Ticket / Clinic Notes / Diagnosis Card or from the Treating Physician

Hospital:			
Mode of access:	Screening <input type="checkbox"/>	Referral <input type="checkbox"/>	Self referral <input type="checkbox"/>
NIC No: <input type="text"/>	Serial No:	Please write the number given in the clinic book/ BHT	
Name of the patient:			
Present Address:			
If above address was different from the address at the time of clinic registration, what was your previous address?			
1. Name of RDHS Division:		<input type="checkbox"/>	<input type="checkbox"/>
3. Name of PHI Area:		<input type="checkbox"/>	<input type="checkbox"/>
2. Name of MOH Area:		<input type="checkbox"/>	<input type="checkbox"/>
4. Name of GN Division:		<input type="checkbox"/>	<input type="checkbox"/>

Please tick the appropriate box where applicable

SOCIO - DEMOGRAPHIC CHARACTERISTICS

5. Age: (in years on the last birthday)		<input type="checkbox"/>	<input type="checkbox"/>	6. Sex:		1 Male <input type="checkbox"/>	2 Female <input type="checkbox"/>
7. Ethnicity:							
1 Sinhalese <input type="checkbox"/>	2 Tamil <input type="checkbox"/>	3 Moor <input type="checkbox"/>	4 Others	<input type="checkbox"/>			
8. Education: (last grade completed)							
1 No schooling <input type="checkbox"/>	2 Up to Grade 1-9 <input type="checkbox"/>	3 Up to GCE O/L-A/L <input type="checkbox"/>	4 Higher (university etc.) <input type="checkbox"/>				
9 Current Occupation:							
1 Unemployed <input type="checkbox"/>	2 Agriculture related <input type="checkbox"/>	3 Fishing <input type="checkbox"/>					
4 Manual worker (other than agriculture) <input type="checkbox"/>	5 Office work <input type="checkbox"/>	6 Others	<input type="checkbox"/>				
10 If you are involved in agriculture		10.1 Duration of your involvement (in years):		<input type="checkbox"/>	<input type="checkbox"/>		
10.2 Type of agriculture:	1 Paddy <input type="checkbox"/>	2 Crops <input type="checkbox"/>	3 Vegetables <input type="checkbox"/>				
10.3 Nature of your involvement:	1 Part time <input type="checkbox"/>	2 Full time <input type="checkbox"/>					
11 What is the occupation you have done for the longest part of your life?							
1 Never employed <input type="checkbox"/>	3 Manual worker (other than agriculture) <input type="checkbox"/>	5 Office work <input type="checkbox"/>					
2 Agriculture related <input type="checkbox"/>	4 Fishing <input type="checkbox"/>	6 Others	<input type="checkbox"/>				
12 Monthly income of the household (total income in rupees):							
< 5000 <input type="checkbox"/>	-10,000 <input type="checkbox"/>	-15,000 <input type="checkbox"/>	-20,000 <input type="checkbox"/>	>20,000 <input type="checkbox"/>			

LIFESTYLE FACTORS

13 Have you ever smoked?		1 Never <input type="checkbox"/>	2 Former <input type="checkbox"/>	3 Current <input type="checkbox"/>
14 If you smoke currently, how frequent?				
1 Occasionally <input type="checkbox"/>	2 Frequently <input type="checkbox"/>	3 Daily (less than 5) <input type="checkbox"/>	4 Daily (> 5) <input type="checkbox"/>	
15 Have you ever consumed alcohol?		1 Never <input type="checkbox"/>	2 Former <input type="checkbox"/>	3 Current <input type="checkbox"/>
16 If you consume alcohol currently, how frequent?				
1 Occasionally <input type="checkbox"/>	2 Frequently <input type="checkbox"/>	3 Daily <input type="checkbox"/>		
17 Have you ever consumed illicit liquor?		1 Never <input type="checkbox"/>	2 Occasionally <input type="checkbox"/>	3 Frequently <input type="checkbox"/>
18 Have you ever chewed tobacco/ lime?		1 Never <input type="checkbox"/>	2 Former <input type="checkbox"/>	3 Current <input type="checkbox"/>

Janakan / Epidemiology Unit / 1 Sept 2008

ENVIRONMENTAL FACTORS

19 Your main source of drinking water for the last 5 years?		1 Well <input type="checkbox"/>	2 Tube well <input type="checkbox"/>
3 Pipe borne <input type="checkbox"/>	4 Tank <input type="checkbox"/>	5 Others	<input type="checkbox"/>
20 Have you used water from any other sources (other than above) for more than 5 years? (more than one option is possible)			
1 Well <input type="checkbox"/>	2 Tube well <input type="checkbox"/>	3 Pipe borne <input type="checkbox"/>	
4 Tank <input type="checkbox"/>	5 Others	<input type="checkbox"/>	
21 During your lifetime, to your knowledge have you had any exposure to agro-chemicals (fertilizers, pesticides etc)			
1 No exposure <input type="checkbox"/>	2 Occasional exposure <input type="checkbox"/>	3 Frequent exposure <input type="checkbox"/>	4 Very frequent exposure <input type="checkbox"/>

HEALTH STATUS

(Please cross check patient's response with the medical records)

22 Have you had any of the following symptoms in the past, especially during your childhood? (Swelling of face/ legs, passing blood stained urine, reduced urine output)				1 Yes <input type="checkbox"/>	2 No <input type="checkbox"/>
23 Have you had any of the following diseases/ conditions in the past? (more than one option is possible)					
1 Snakebite <input type="checkbox"/>	2 Leptospirosis <input type="checkbox"/>	3 Stones in the urinary tract <input type="checkbox"/>			
4 Glomerular nephritis (AGN) <input type="checkbox"/>	5 Prostate problems <input type="checkbox"/>	6 Any significant illnesses	<input type="checkbox"/>		
24 Have you been getting treatment for any chronic / severe illnesses?				1 Yes <input type="checkbox"/>	2 No <input type="checkbox"/>
25 If yes, what are those illnesses? (more than one option is possible)				1 Diabetes mellitus <input type="checkbox"/>	
2 Hypertension <input type="checkbox"/>	3 Polycystic kidney disease <input type="checkbox"/>	4 Others	<input type="checkbox"/>		
26 Does any one from your family suffer from following diseases/ conditions?				1 Polycystic kidney disease <input type="checkbox"/>	
2 Systemic lupus erythematosus (SLE) <input type="checkbox"/>	3 Deafness <input type="checkbox"/>	4 Others	<input type="checkbox"/>		

ANTHROPOMETRIC MEASURES

27 Height: (in cm)	<input type="text"/> <input type="text"/> <input type="text"/>			
	1 st available reading	2 nd available reading	3 rd available reading	4 th available reading
28 Weight: (in kg)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
29 Body Mass Index: (BMI)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
30 Blood Pressure:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

LABORATORY INVESTIGATIONS

	1 st available reading	2 nd available reading	3 rd available reading	4 th available reading
31 Urine Albumin	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
32 Urine Microalbumin	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
33 S Creatinine	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
34 GFR	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
35 FB Sugar	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
36 PPB Sugar	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
37 Hb A1c	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
38	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Year of diagnosis	Chronic Kidney Disease	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	End Stage Renal Disease	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Treatment	Medication <input type="checkbox"/>	Peritoneal Dialysis <input type="checkbox"/>	Haemodialysis <input type="checkbox"/>	Transplantation <input type="checkbox"/>
Interviewer's code:	<input type="text"/> <input type="text"/>	Date of interview:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
OFFICIAL USE:				



Introduction and background

As the prevalence of CKDu is not known, a population prevalence study was conducted during 2010-2012. In addition the role of known nephrotoxins arsenic (As), cadmium (Cd) and lead (Pb) pesticides (14-16) and other metals and pesticides that could influence the natural history of kidney disease (aluminium, copper, chromium, sodium, potassium, calcium, magnesium, copper, zinc, selenium, titanium and strontium) (17), in the pathogenesis of CKDu have not been hitherto investigated comprehensively. The population prevalence study as well as the analytical and environmental study was conducted and for both these studies geographical mapping was done.

Scientific scope and objectives

This study was therefore undertaken to map the following:

- All sampling populations (Household level) in population prevalence study To confirm or refute previously reported wide ranges in the prevalence of CKDu.
- Collection sites of environmental samples including water, soil, weedicides and fertilizers obtained from endemic and non-endemic areas

Materials and Methods

Selected households for the population prevalence study were mapped by the use of GPS receivers and were linked to the database containing attributes of the survey data collected. Furthermore, they were also linked to data tables of the results of the various analyses performed. Locations of the matched controls for different case control studies were also mapped. Similarly, locations of all environmental samples were mapped.

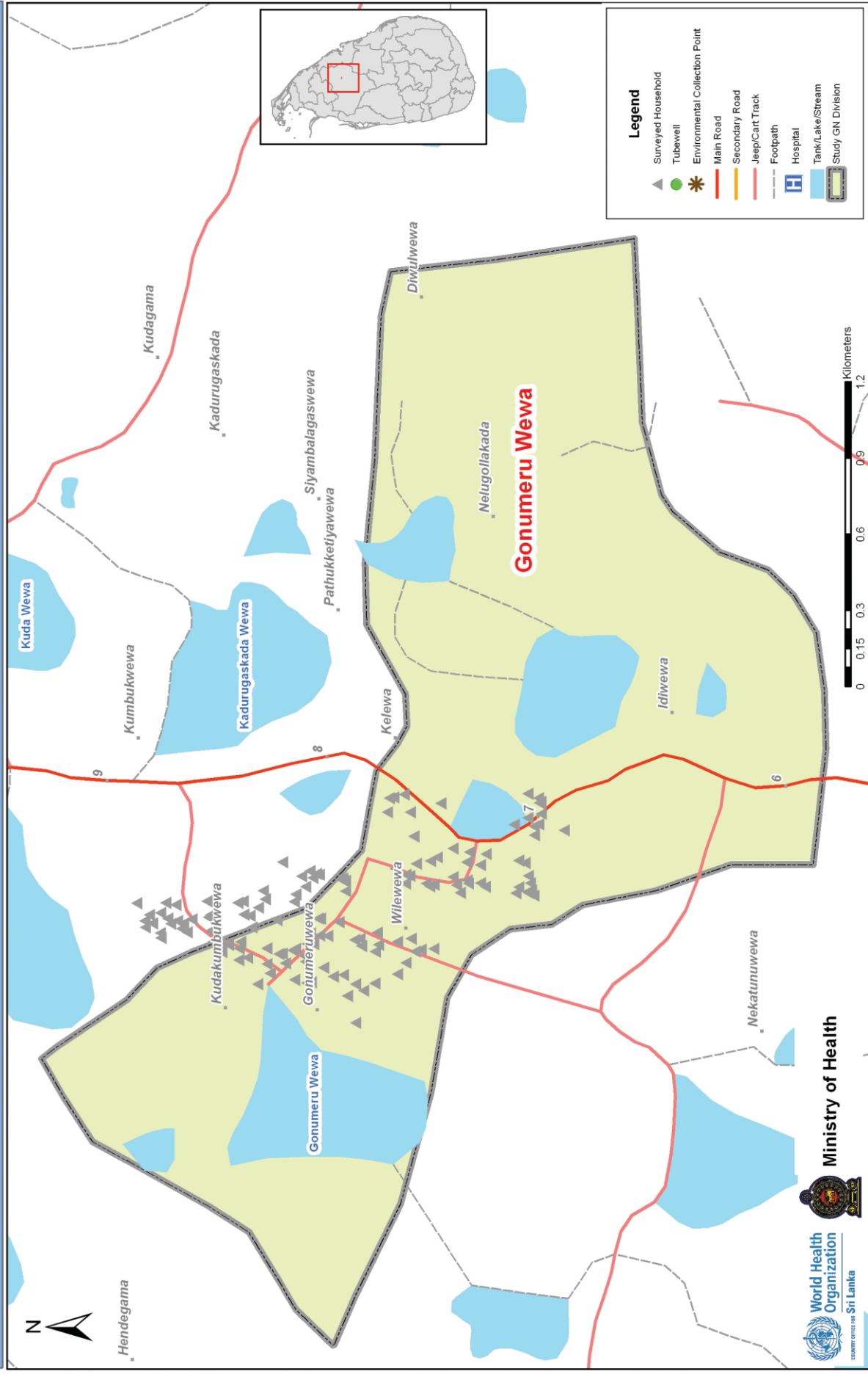
The List of maps prepared for the research project

- a) Summary of CKD prevalence Study (x2 maps)
- b) Household Maps – All households surveyed in the 22 GN divisions (22 Maps) and 2 GN divisions in the control area of Hambantota
- c) Cross sectional comparison of potential environmental toxins in high and low prevalent areas for CKDu - Environmental Sample Collection sites – Anuradhapura, Badulla, Polonnaruwa & Hambantota Districts
- d) Drinking Water collection sites - Anuradhapura, Badulla, Polonnaruwa & Hambantota Districts

MAPS OF HOUSEHOLDS SURVEYED

District	D.S. Division	G.N. Division
Anuradhapura	Kahatagasdigiliya	Gonumeru Wewa
		Mee-Kumbukwewa
		Kokmaduwa
	Galenbindunuwewa	Ellawewa
		Getalawa
		Hurulunikawewa
		Hurulumeegahapattiya
	Padaviya	Padaviya
		Parakramapura
		Elikimbulagala
		Kumbukwewa
		Bogahawewa
	Medawachchiya	Katuwela
		Kanadara Divulwewa
		Kirigalwewa
		Madawachchiya East
		Poonewa
Polonnaruwa	Medirigiriya	Thissapura
		Ambagaswewa
		Thalakolawewa
Badulla	Mahiyangana	Belaganwewa
		Girandurukotte
Hambantotata	T	Aluth
	Thissamaharama	Rohanapura

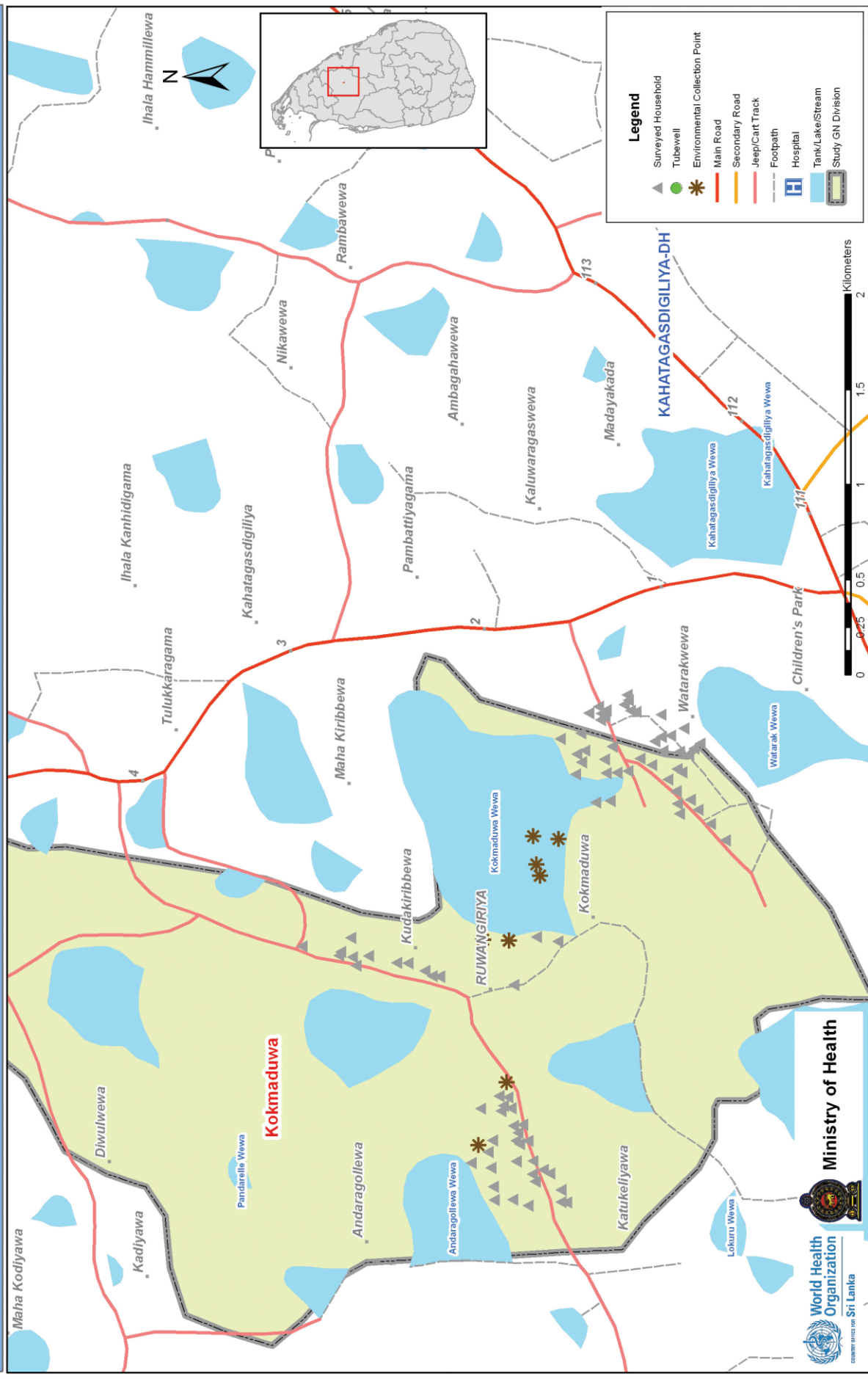
Households surveyed in Gonumerwewa Grama Niladhari Division



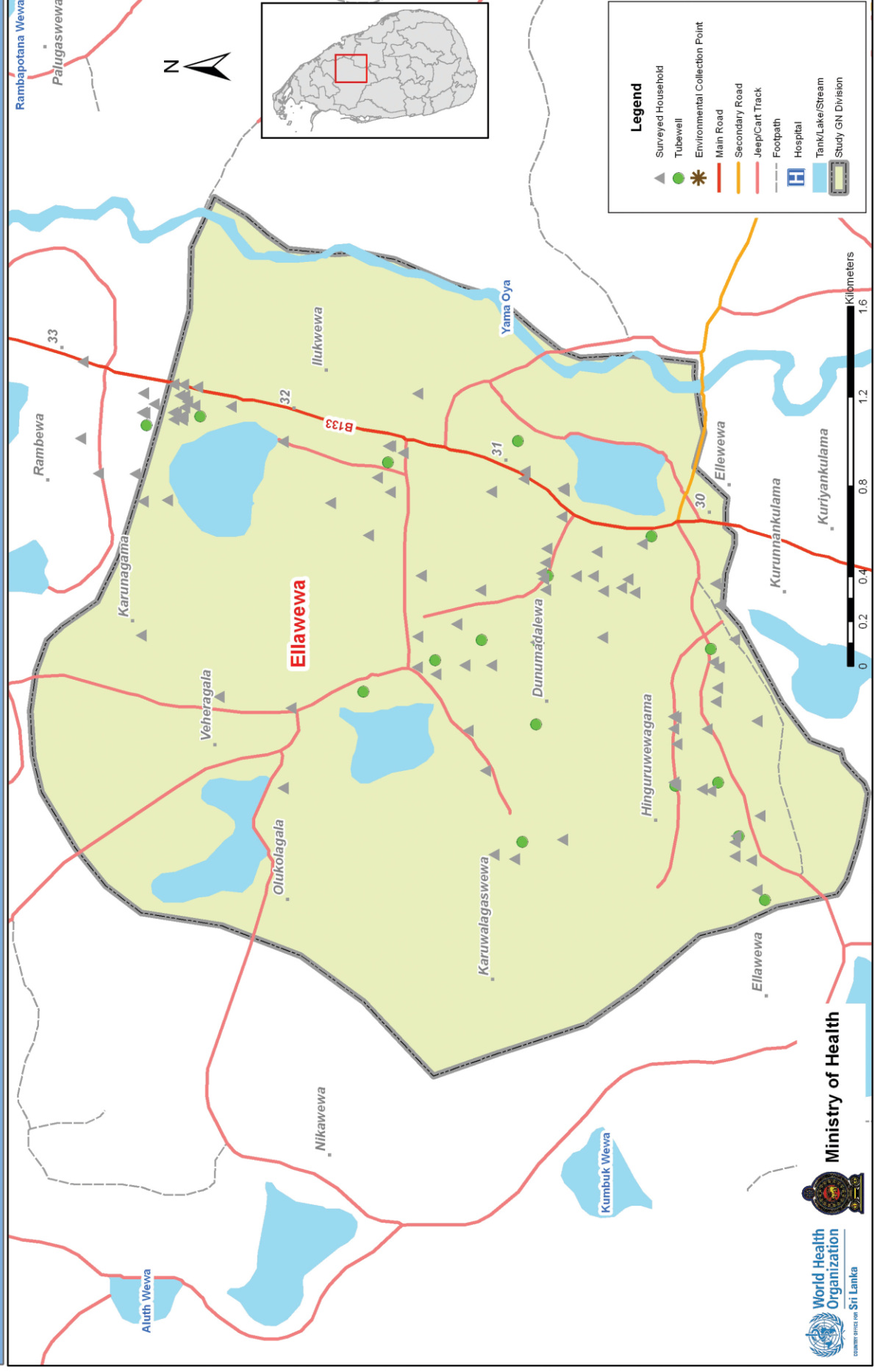
Households surveyed in Mee – Kubukwewa Grama Niladhari Division



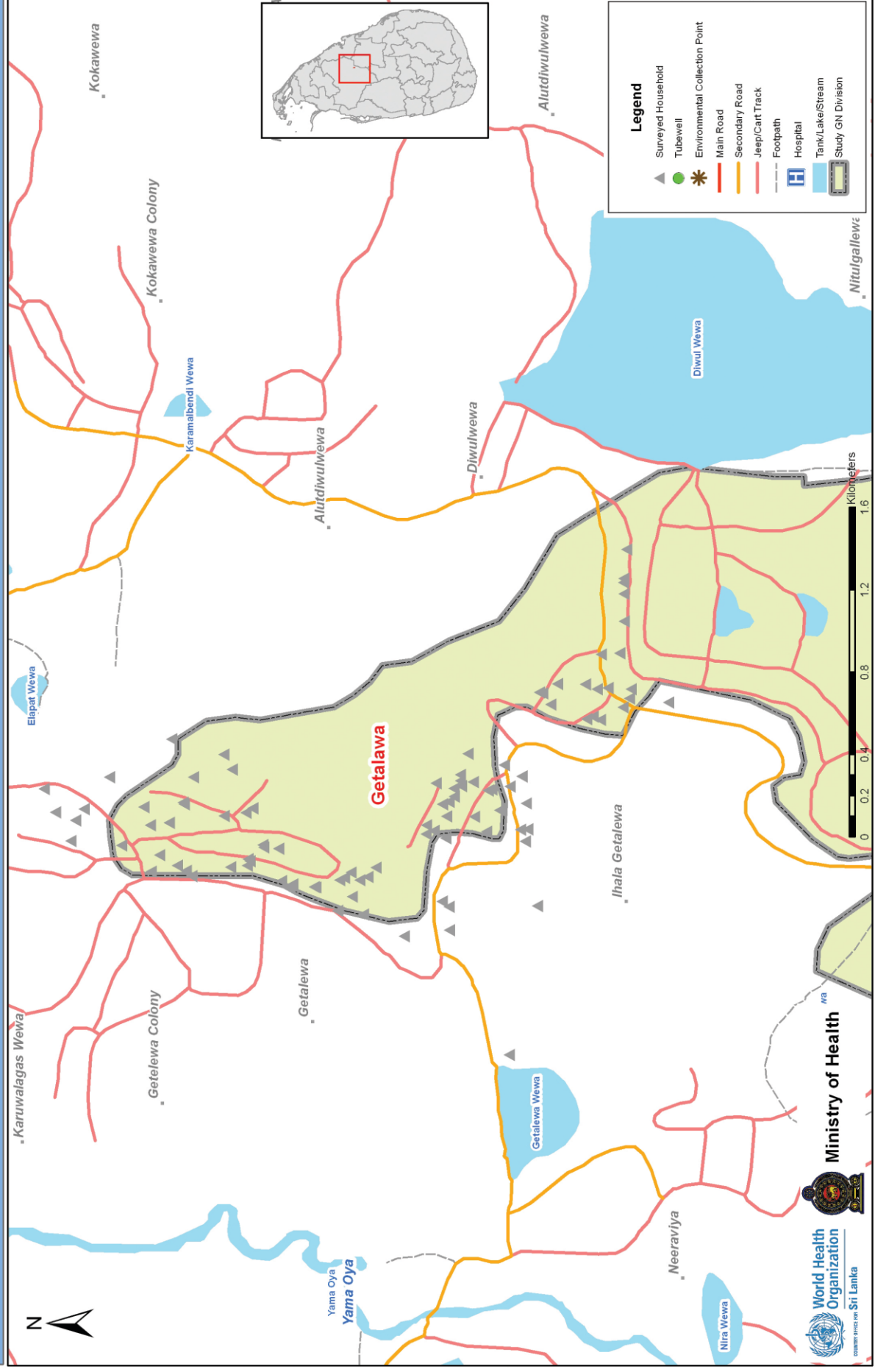
Households surveyed in Kokmaduwa Grama Niladhari Division



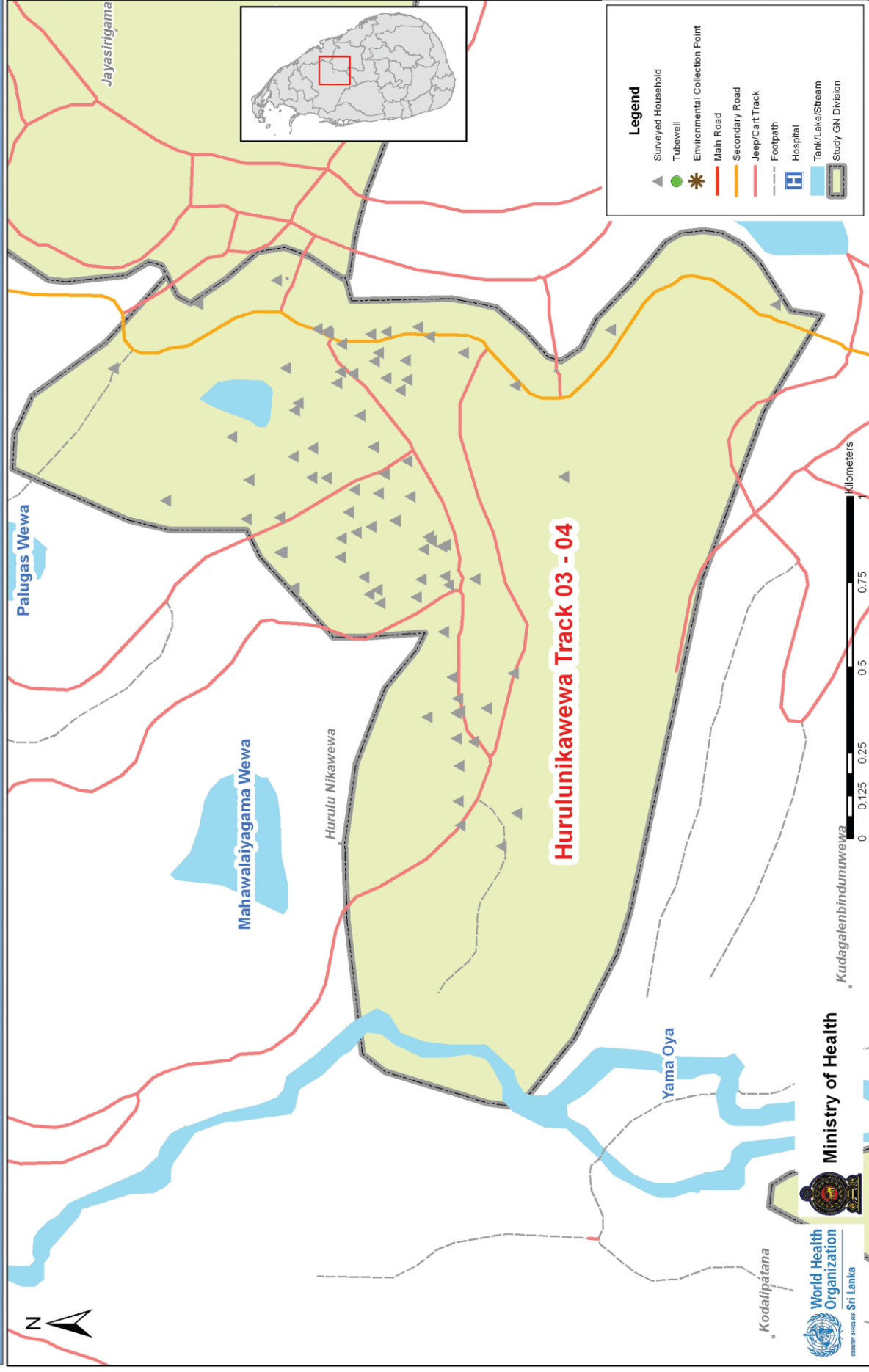
Households surveyed in Ellewewa Grama Niladhari Division



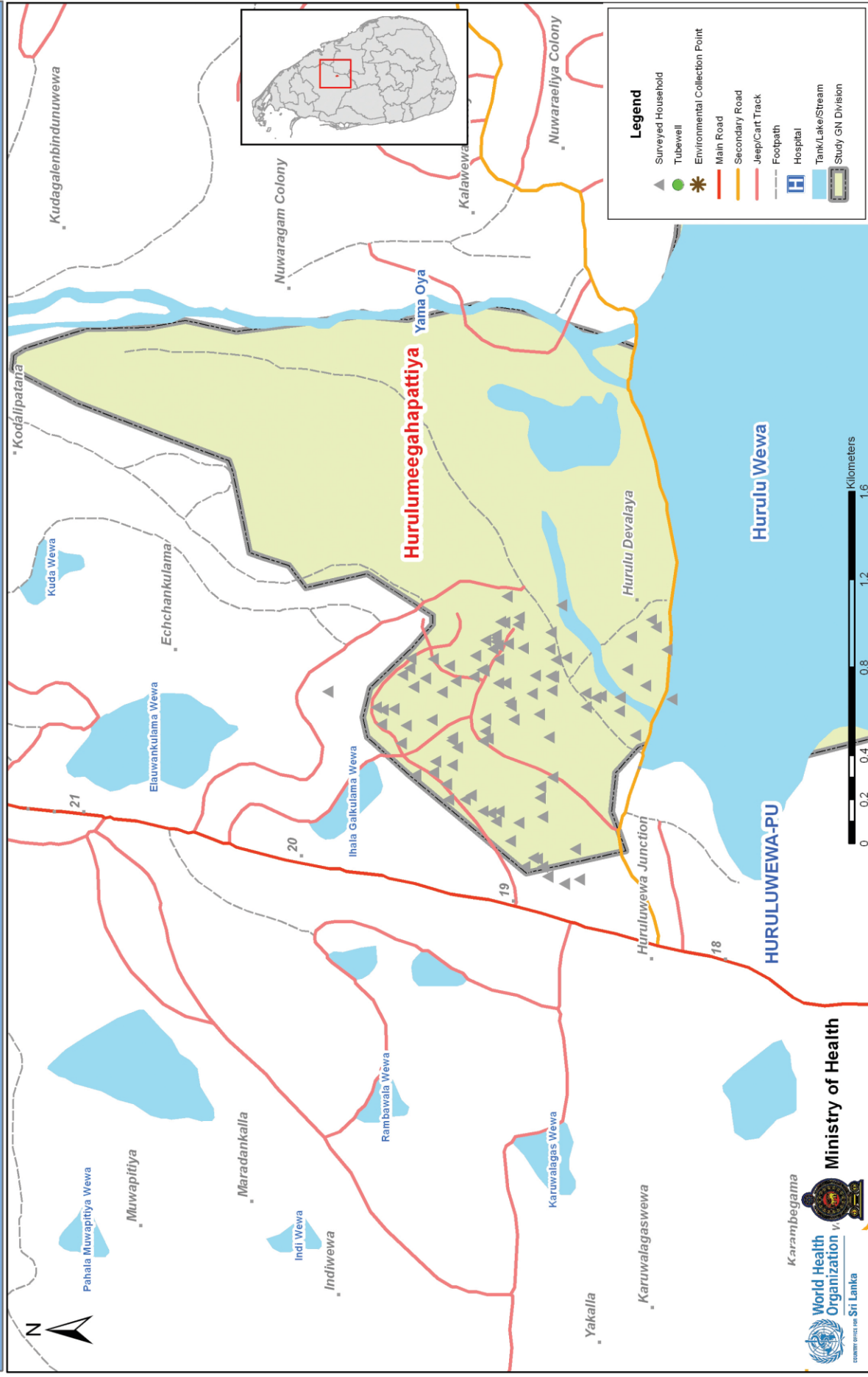
Households surveyed in Getalawa Grama Niladhari Division



Households surveyed in Hurulunikawewa Grama Niladhari Division



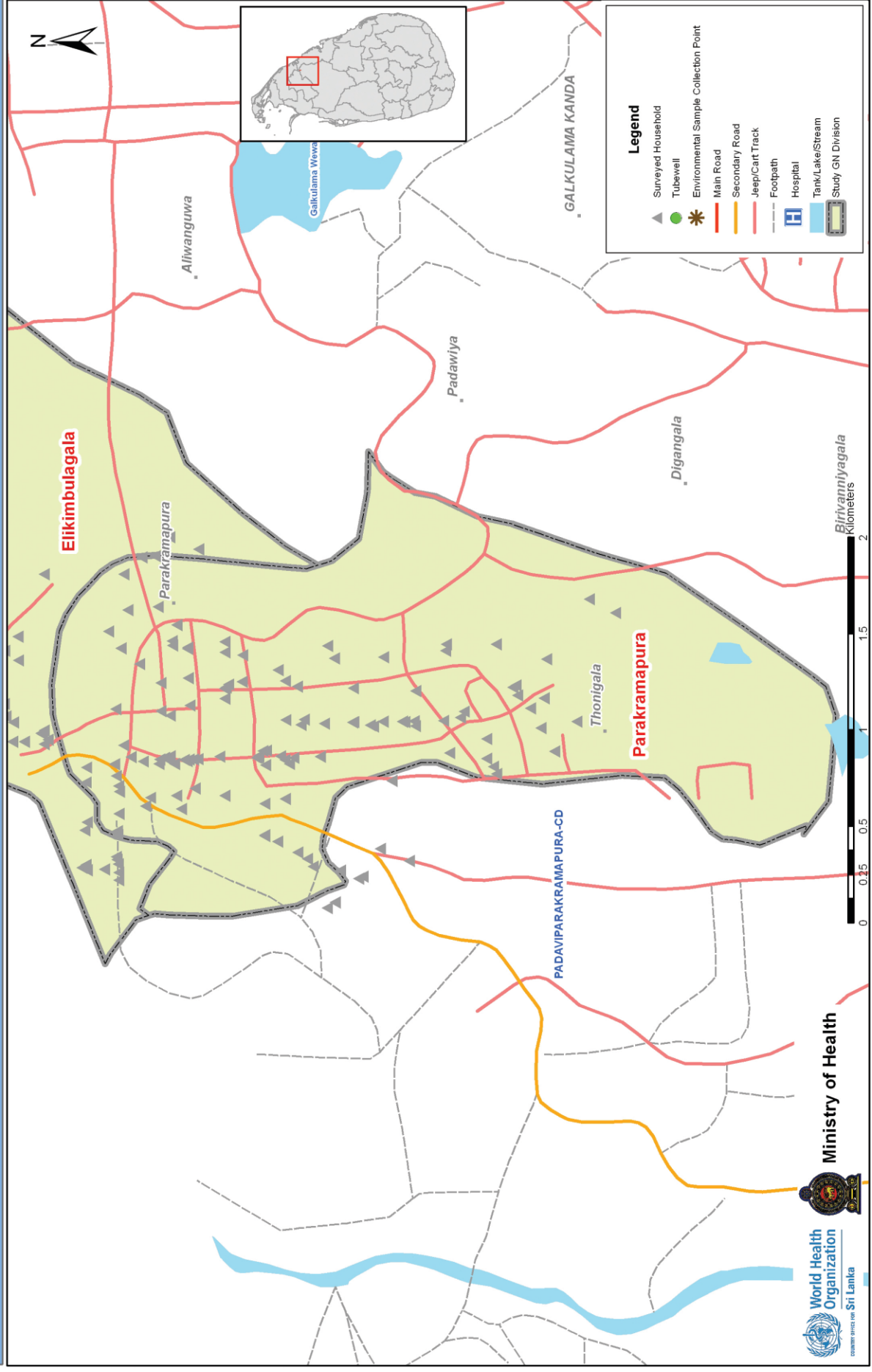
Households surveyed in Hurulumeegahapattiya Grama Niladhari Division



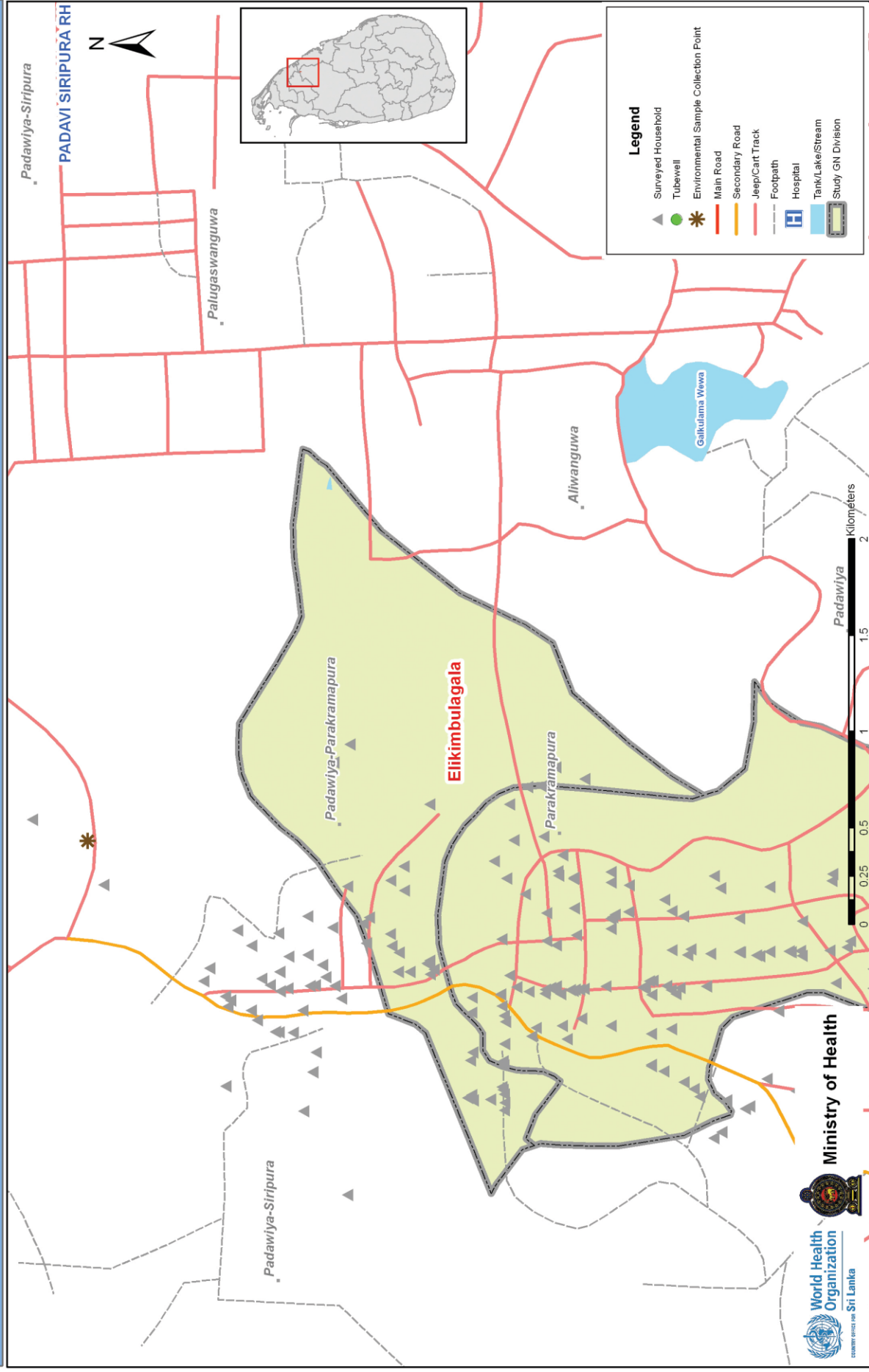
Households surveyed in Padaviya Grama Niladhari Division



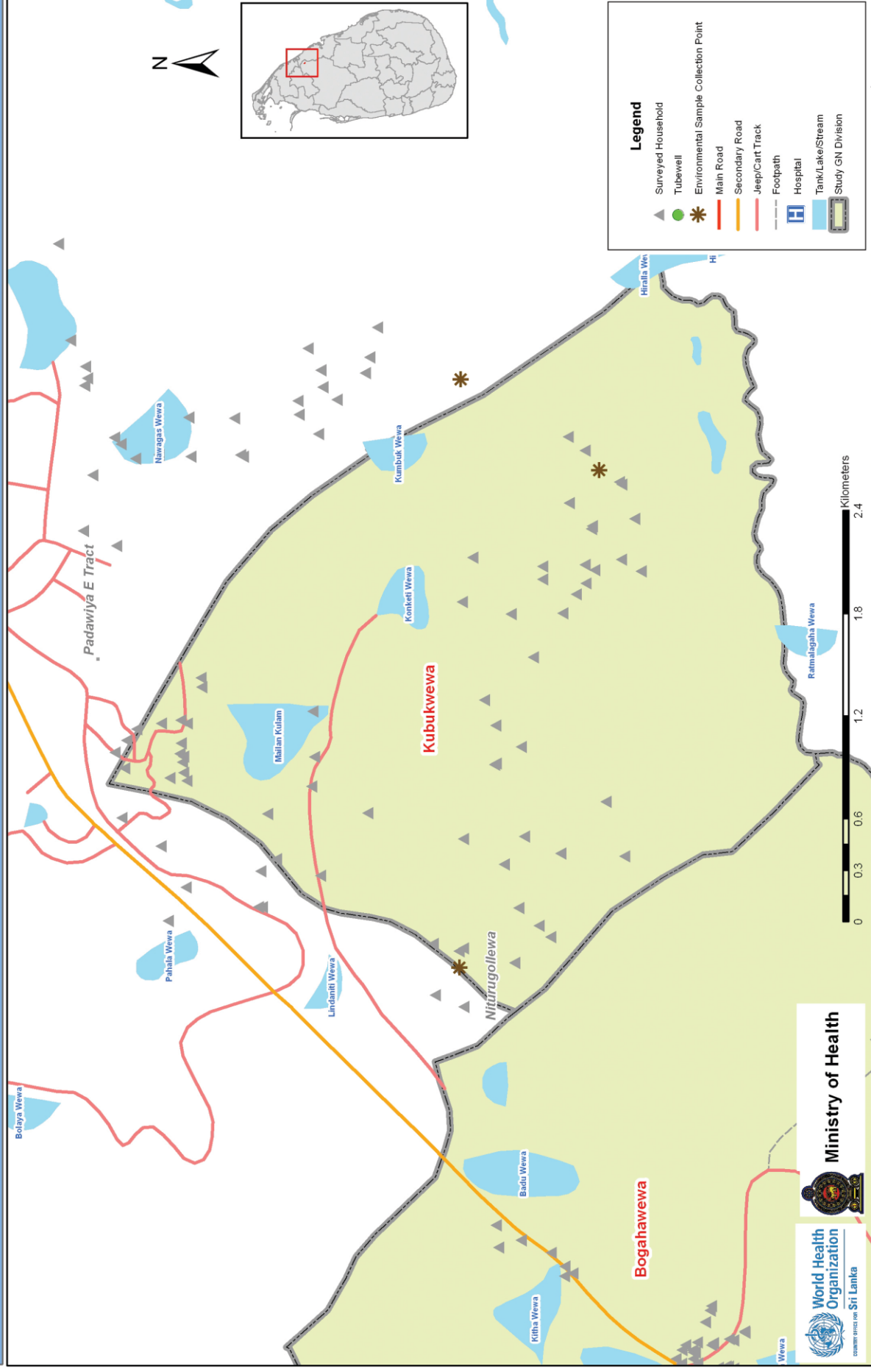
Households surveyed in Parakramapura Grama Niladhari Division



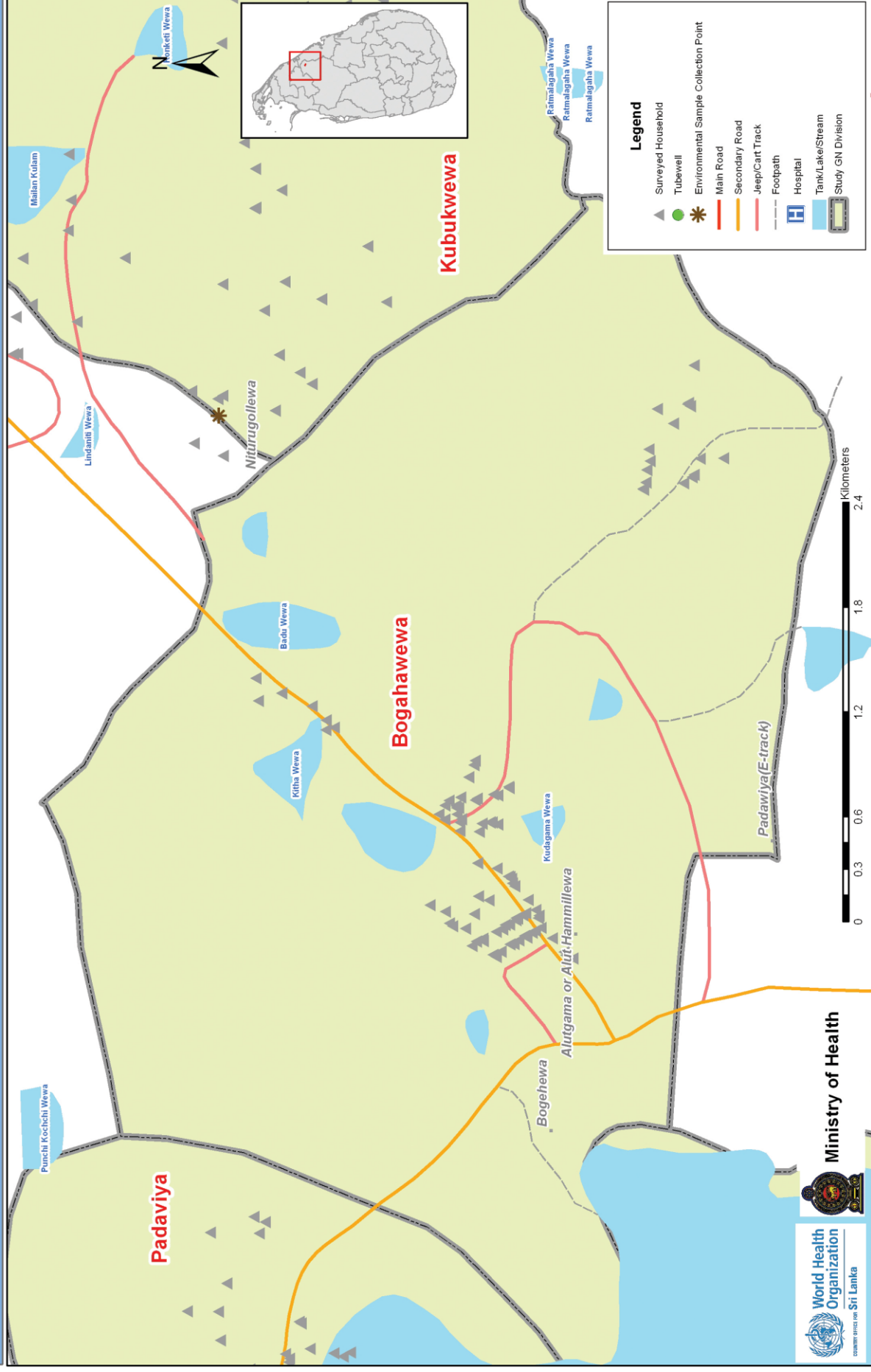
Households surveyed in Elikimbulagala Grama Niladhari Division



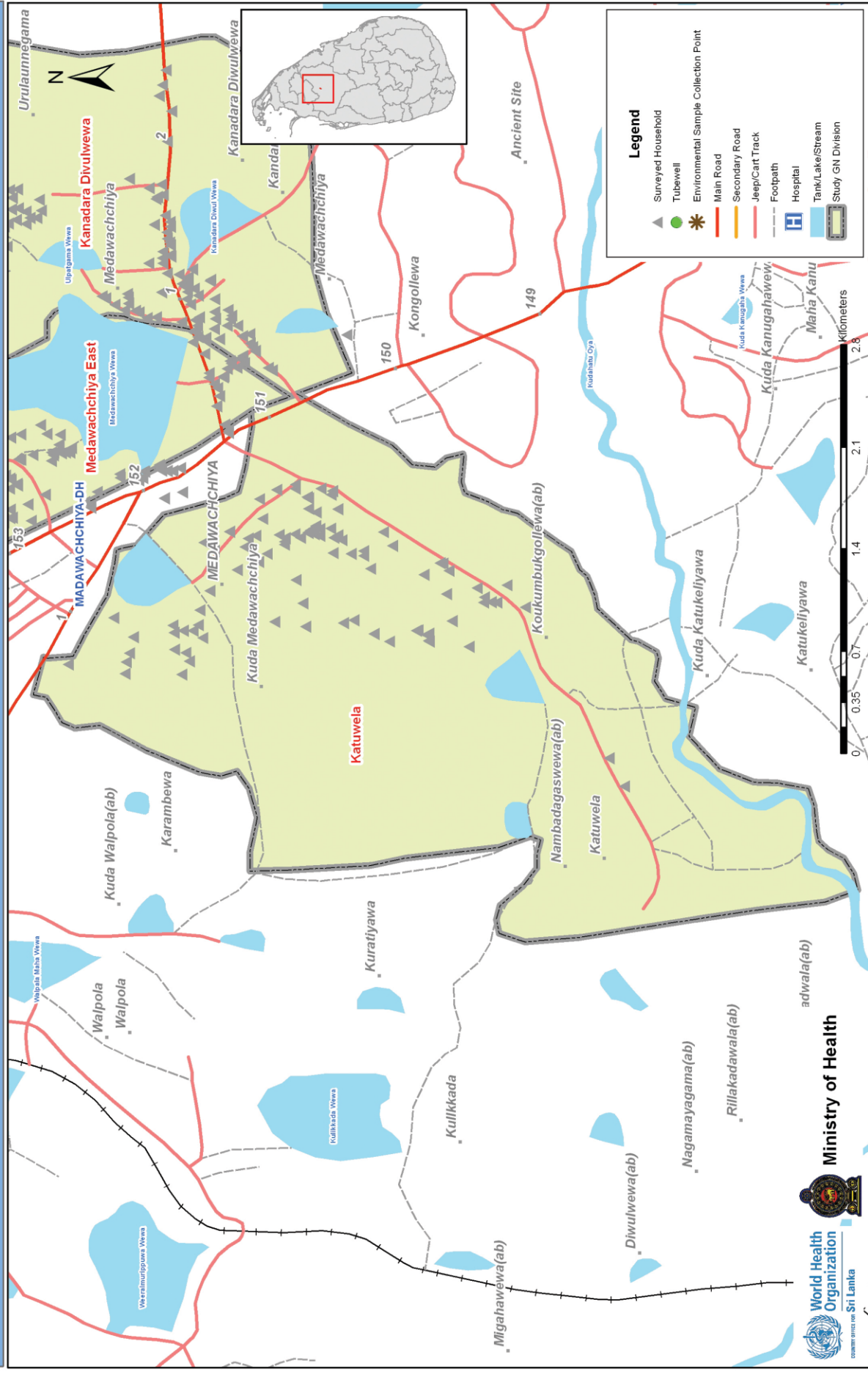
Households surveyed in Kubukwewa Grama Niladhari Division



Households surveyed in Bogahawewa Grama Niladhari Division



Households surveyed in Katuwela Grama Niladhari Division



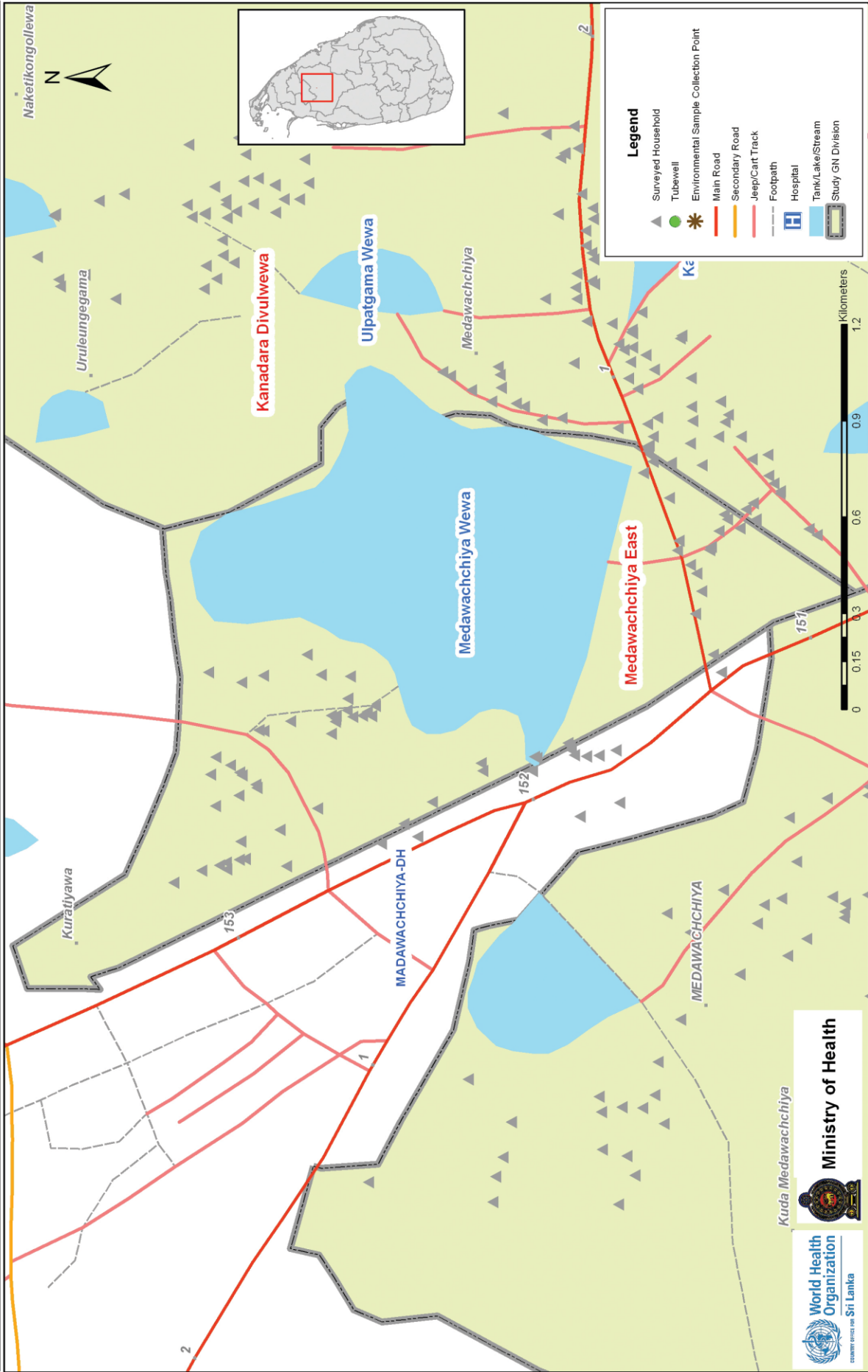
Households surveyed in Kanadaradivulwewa Grama Niladhari Division



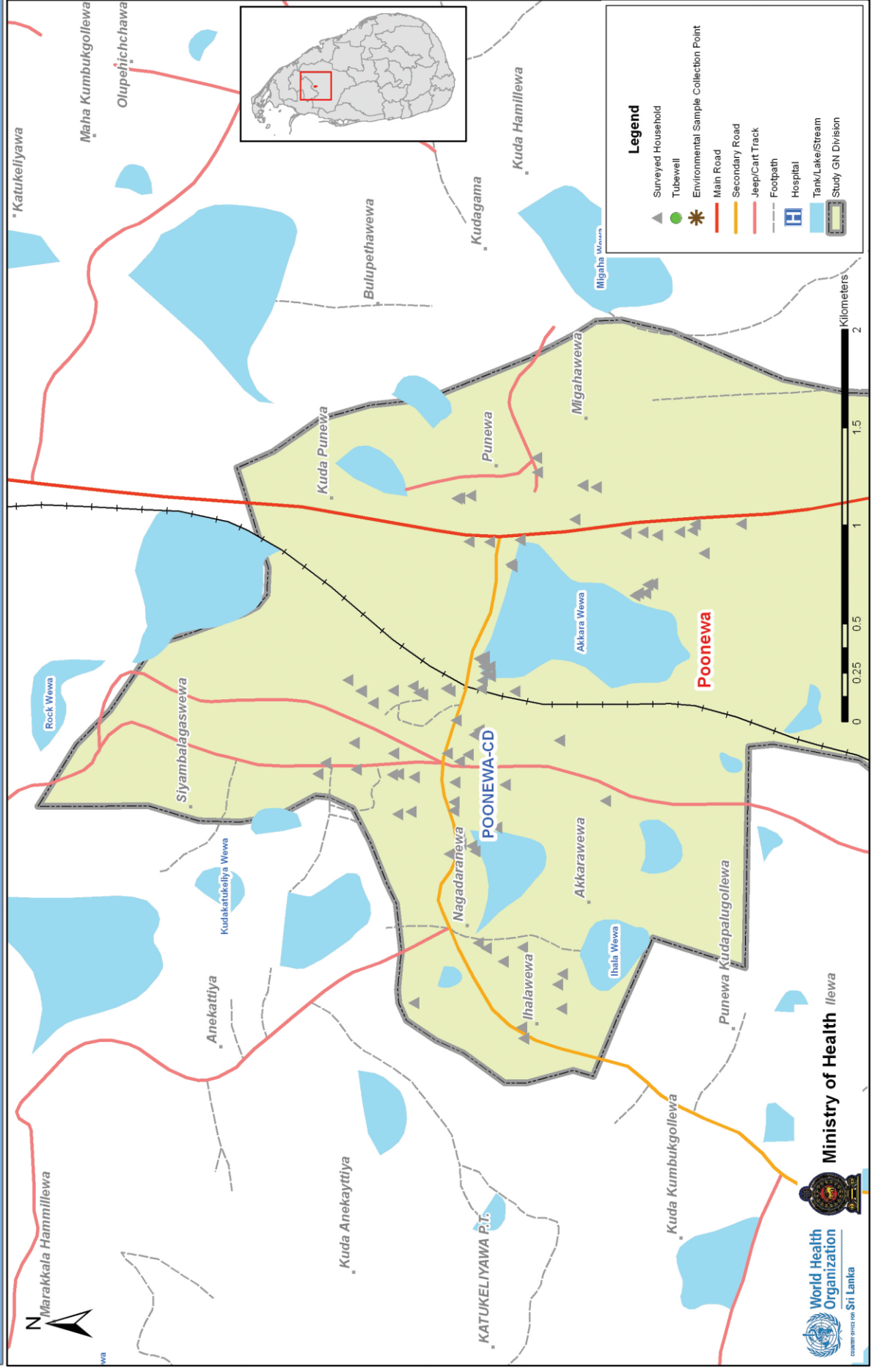
Households surveyed in Kirigalwewa Grama Niladhari Division



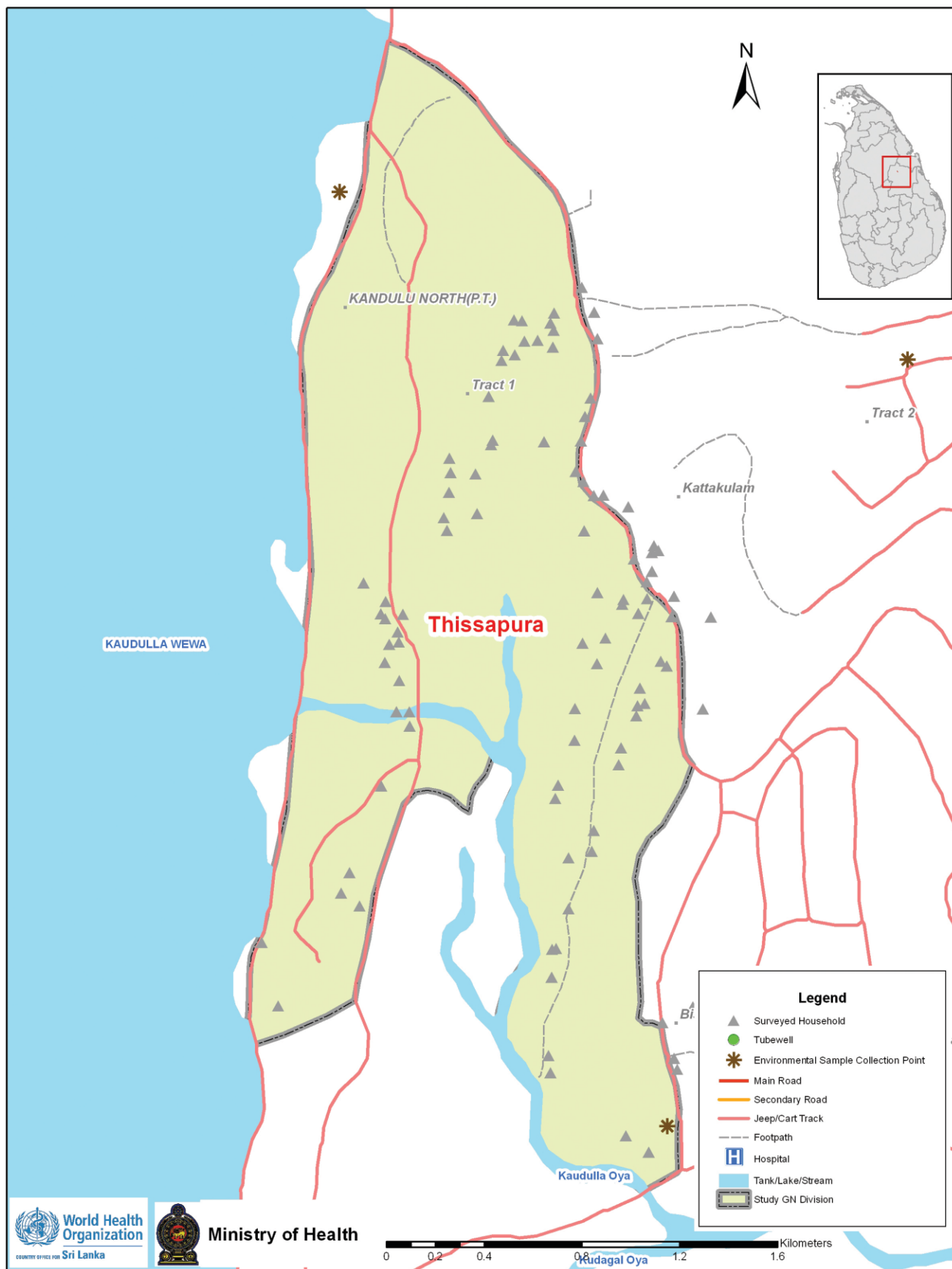
Households surveyed in Medawachchiya East Grama Niladhari Division



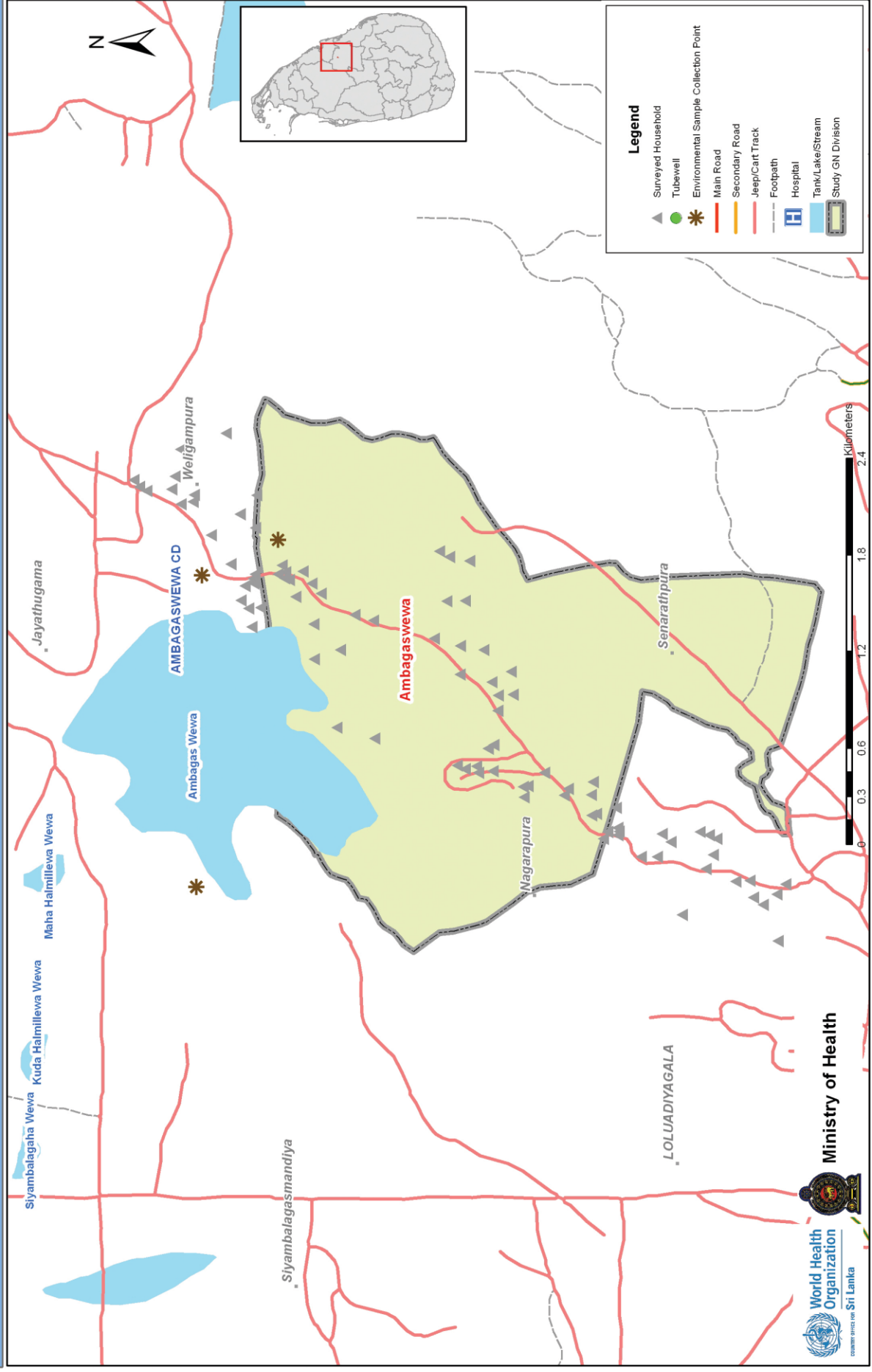
Cases of CKDu Identified in Poonewa Grama Niladhari Division



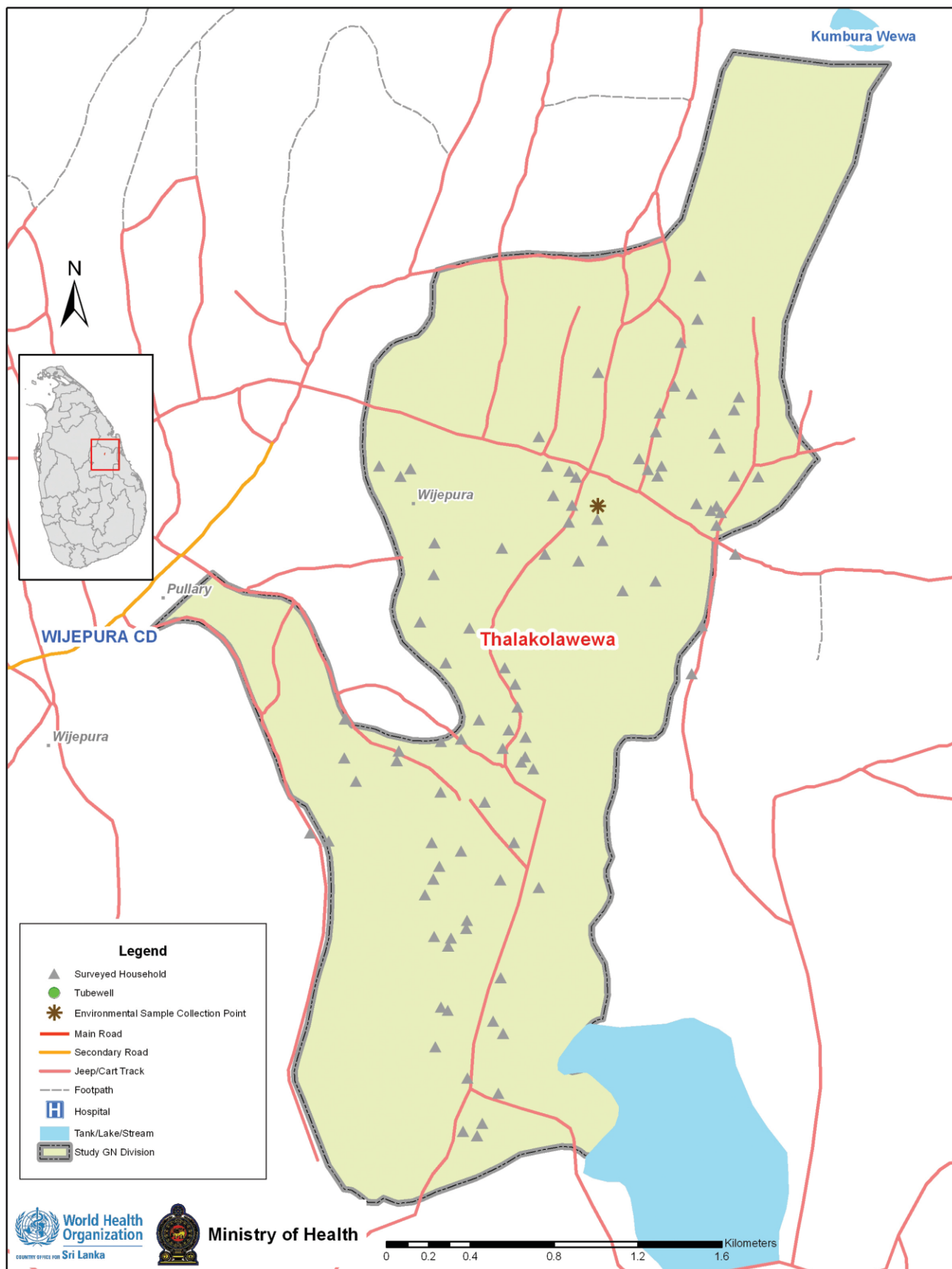
Households surveyed in Thissapura Grama Niladhari Division



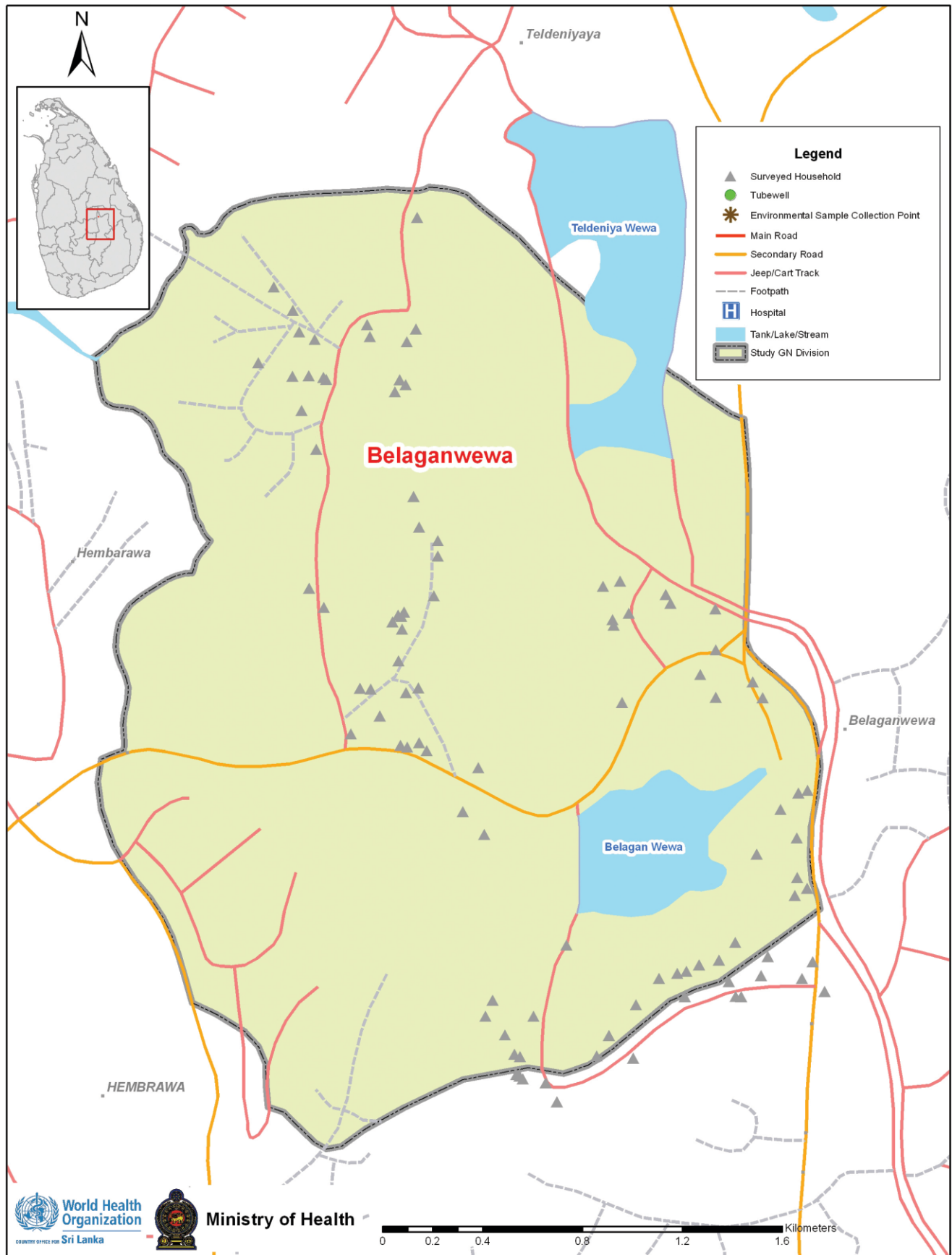
Households surveyed in Ambagaswewa Grama Niladhari Division



Households surveyed in Thalakolawewa Grama Niladhari Division

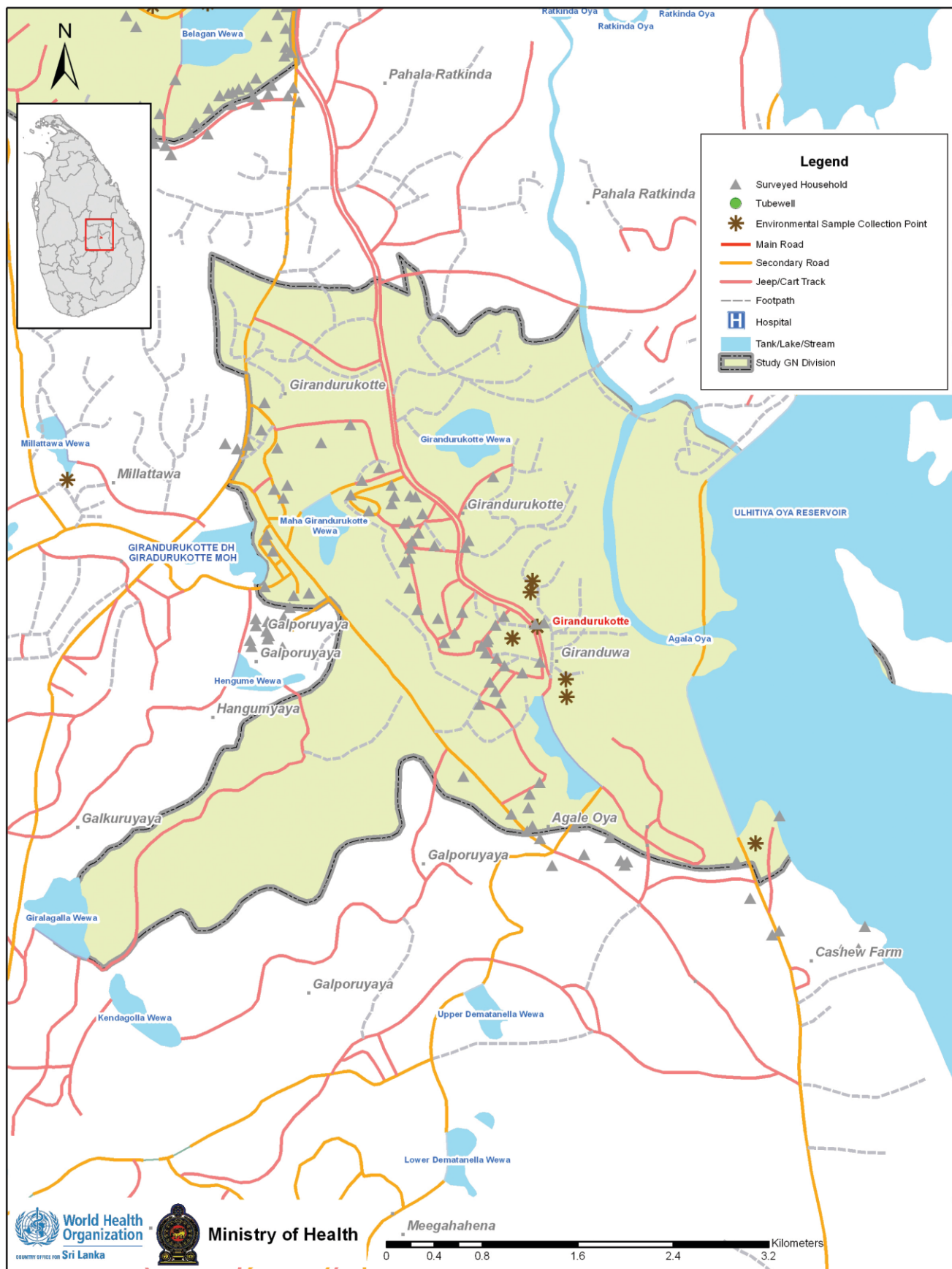


Households surveyed in Belaganwewa Grama Niladhari Division

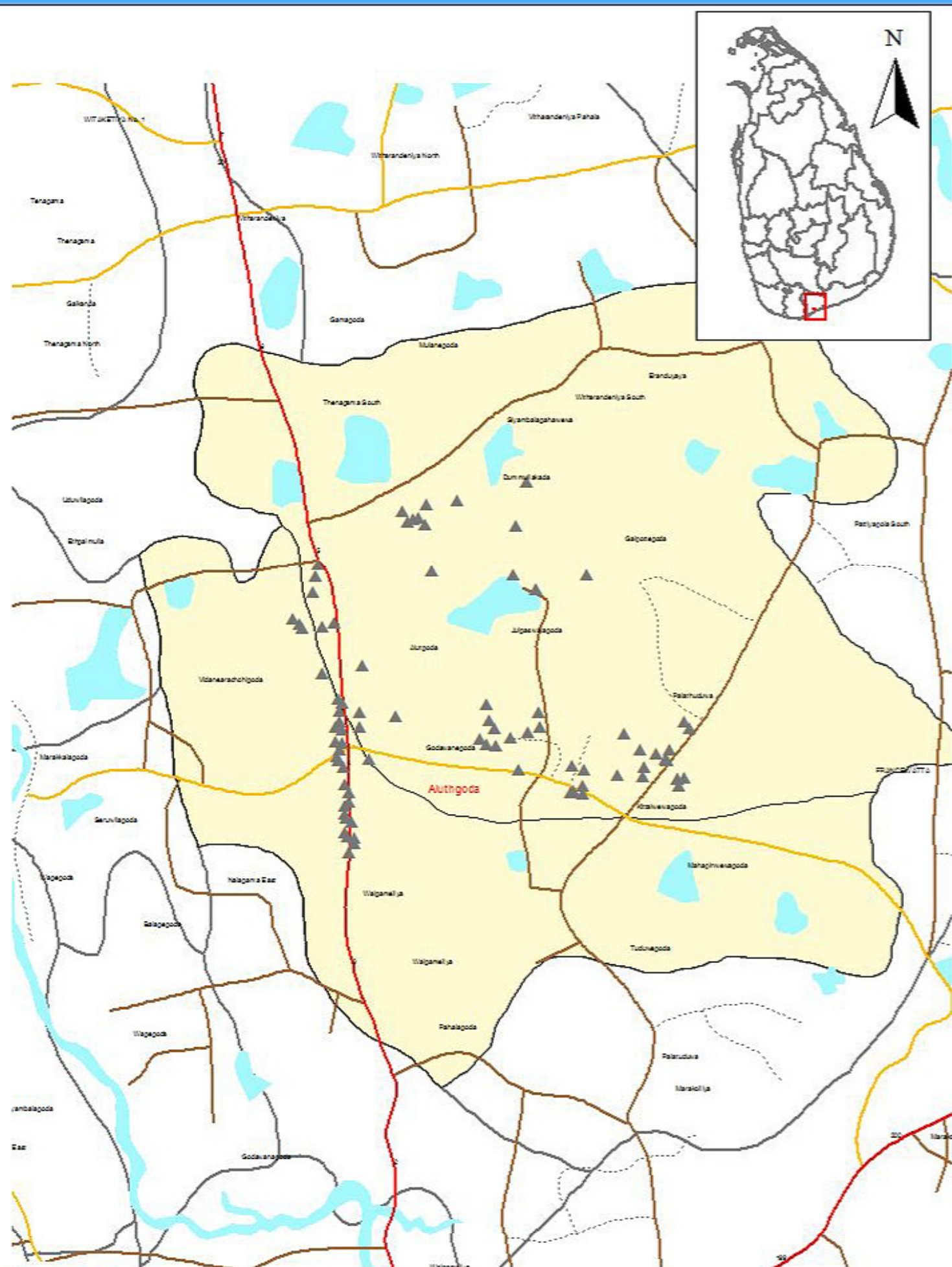


Note: The boundaries and names shown and the designations used in this map do not imply official endorsement by the United Nations.

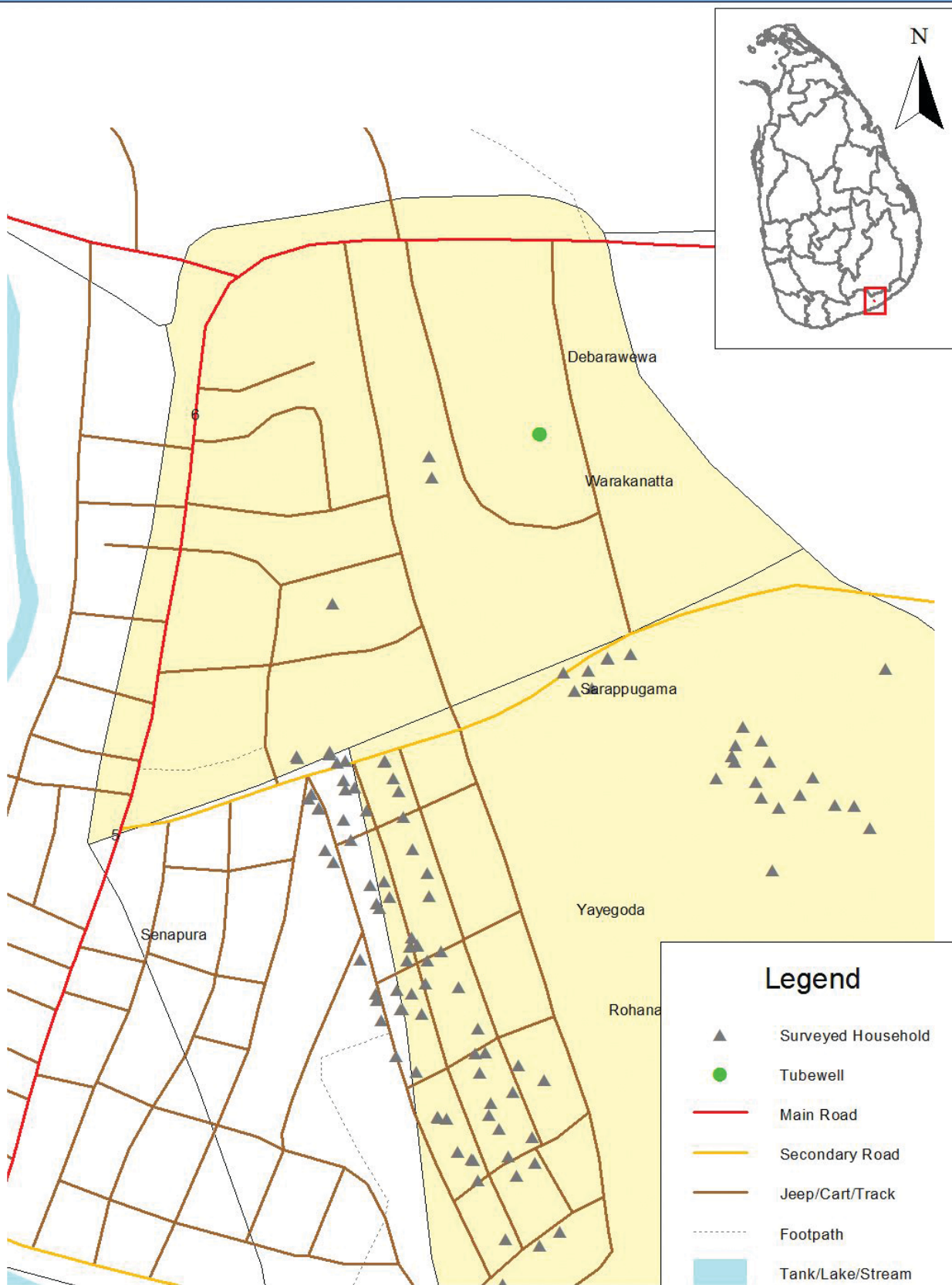
Households surveyed in Girandurukotte Grama Niladhari Division



Households surveyed in Aluthgoda Grama Niladhari Division



Households surveyed in Rohanapura Grama Niladhari Division



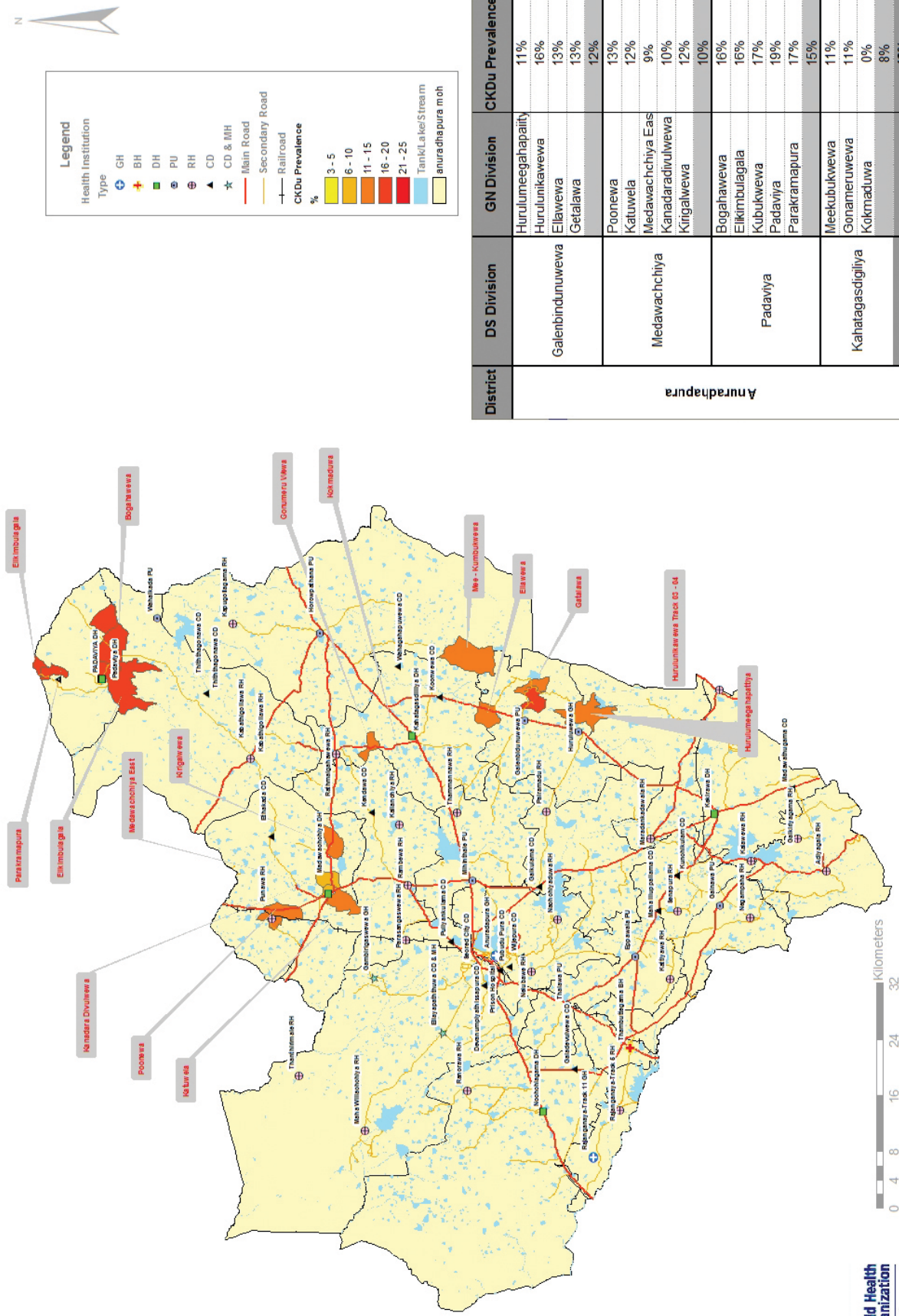
Legend

- ▲ Surveyed Household
- Tubewell
- Main Road
- Secondary Road
- Jeep/Cart/Track
- Footpath
- Tank/Lake/Stream
- Study GN Division

MAPS OF PREVALENCE OF CKDu

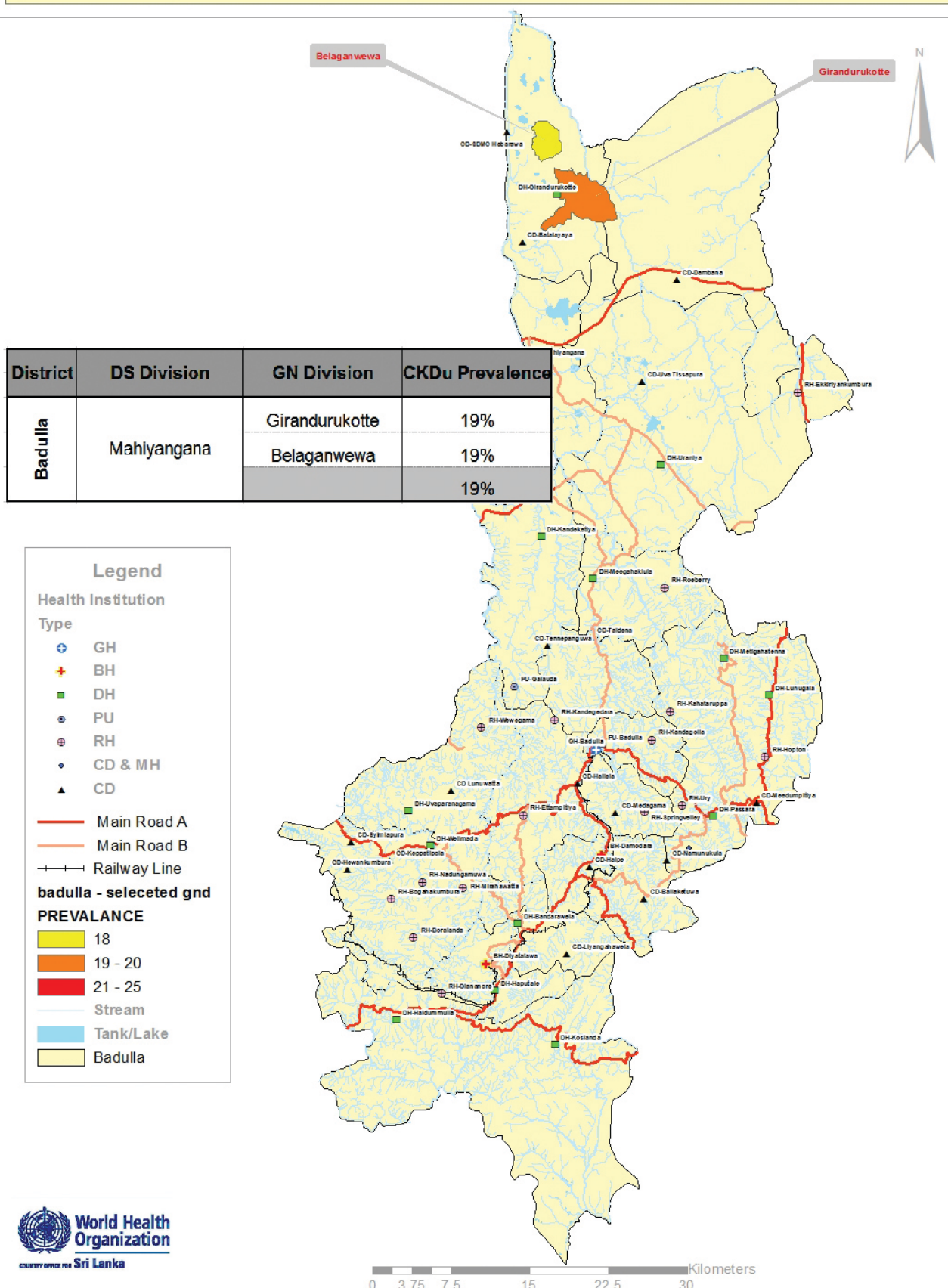
District	D.S. Division
Anuradhapura	Kahatagasdigiliya
	Galenbindunuwewa
	Padaviya
	Medawachchiya
Polonnaruwa	Medirigiriya
Badulla	Mahiyangana

CKDu Prevalence - Anuradhapura

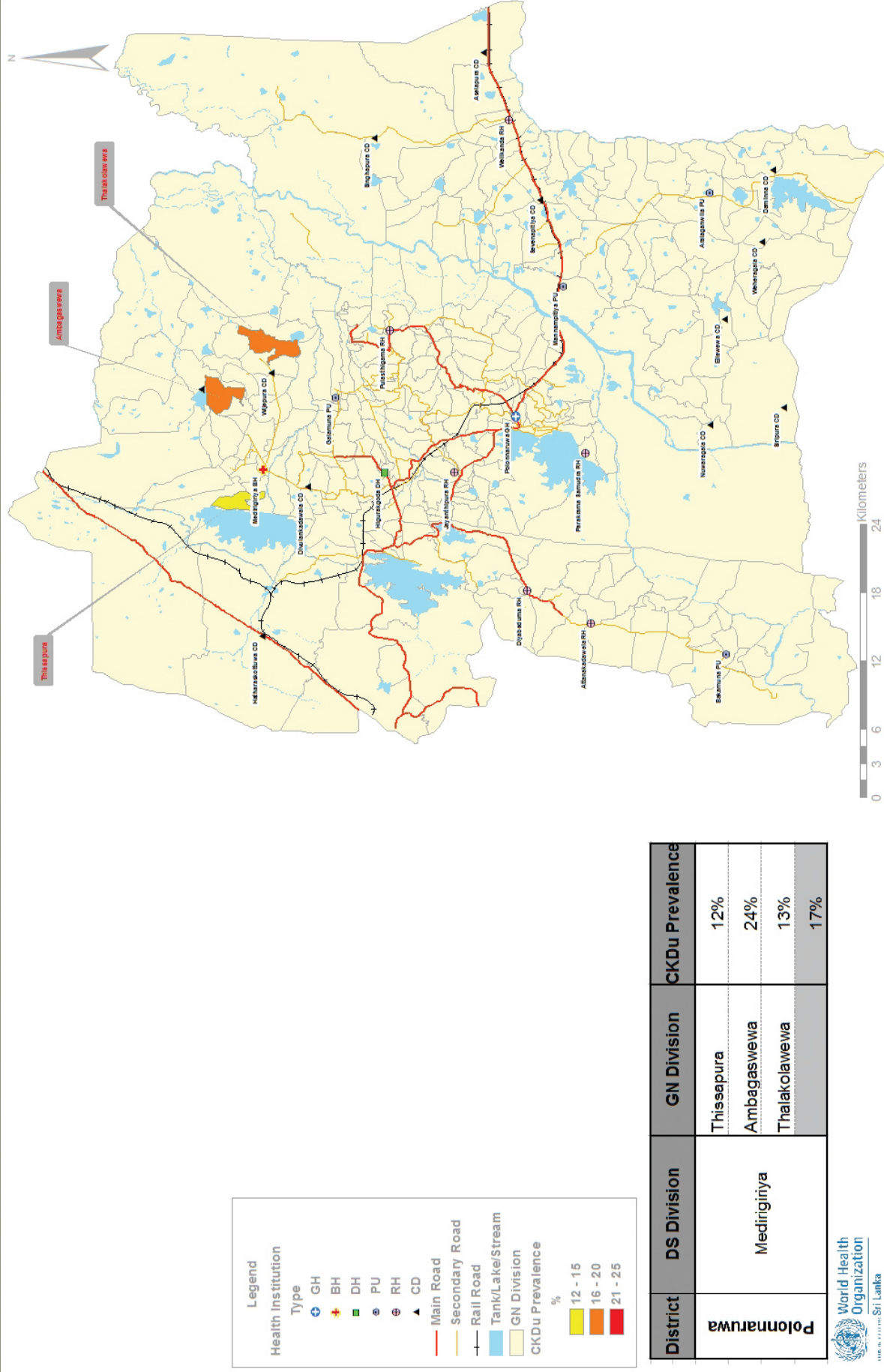


Note: The boundaries and names shown and the designations used in this map do not imply official endorsement by the United Nations.

CKDu Prevalence - Badulla



CKDu Prevalence - Polonnaruwa



**Cross sectional comparison of potential environmental
toxins in endemic & non endemic areas for CKDu**

Drinking Water Sample Collection sites

District	D.S. Division
Anuradhapura	Kahatagasdigiliya
	Galenbindunuwewa
	Padaviya
	Medawachchiya
Polonnaruwa	Medirigiriya
Badulla	Mahiyangana

Legend

- Ckdu water analysis
- CKDu Cases
- Main Road
- Minor Road
- Jeep or Cart Track
- +—+—+ Railway Line
- Tanks
- GN Division

Map Labels:

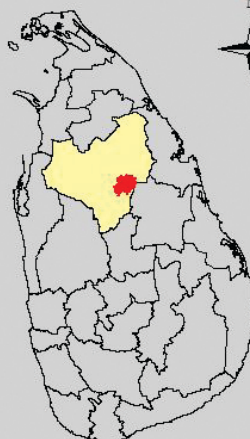
Water Analysis Points (Red Dots):

- 7127010020
- 7127010016
- 7127010047
- 7127010081
- 7127095020
- 7127095005
- 7127130046
- 7127130049
- 7127130020
- 7127180012

GN Divisions: Keleniwewa, Konwewa, Elluwewa, Kataranpura, Perettupala Gama, Dutuwewa Paranagama, Kokawewa, Palugollagama, Karuwalagaswewa, Aluth Divulwewa, Hurulu Nikawewa, Gatalaw, Hurulunkawewa Tract 03 - 04, Janasirigama, Kurunegala Colony, Nuwarseli Colony, Padikaramaduwa, Hurulu Wewa, Ihala Galkulama, Sunanda Mawatha, Gonarankella, Kuda Galenbindunuwewa, Ilukbadayagama, Ihalagama, Mailagaswewa, Himbutugollewa, Upuldeniya, Upathgama, 21 Colony West, 21 Colony East, Thammennagama, Sivalakulama, Galwaduwagama, Muriyakadawala, Yakalla, Hurulu Jayapura, Ihala Galkulama, Hurulu Wewa, Hurulu Wewa, Hurulu Wewa.

Inset Map: Shows the location of the Nuwara-Eliya Division within Sri Lanka.

Logos: Ministry of Health, World Health Organization.



7127010020

7127010016

7127010047

7127010081

7127095020

7127095005

7127130046

7127130049

7127130020

7127180012

- Ckdu water analysis

- CKDu Cases

— Main Road

— Minor Road

—— Jeep or Cart Track

+++++ Railway Line

 Tanks

GN Division

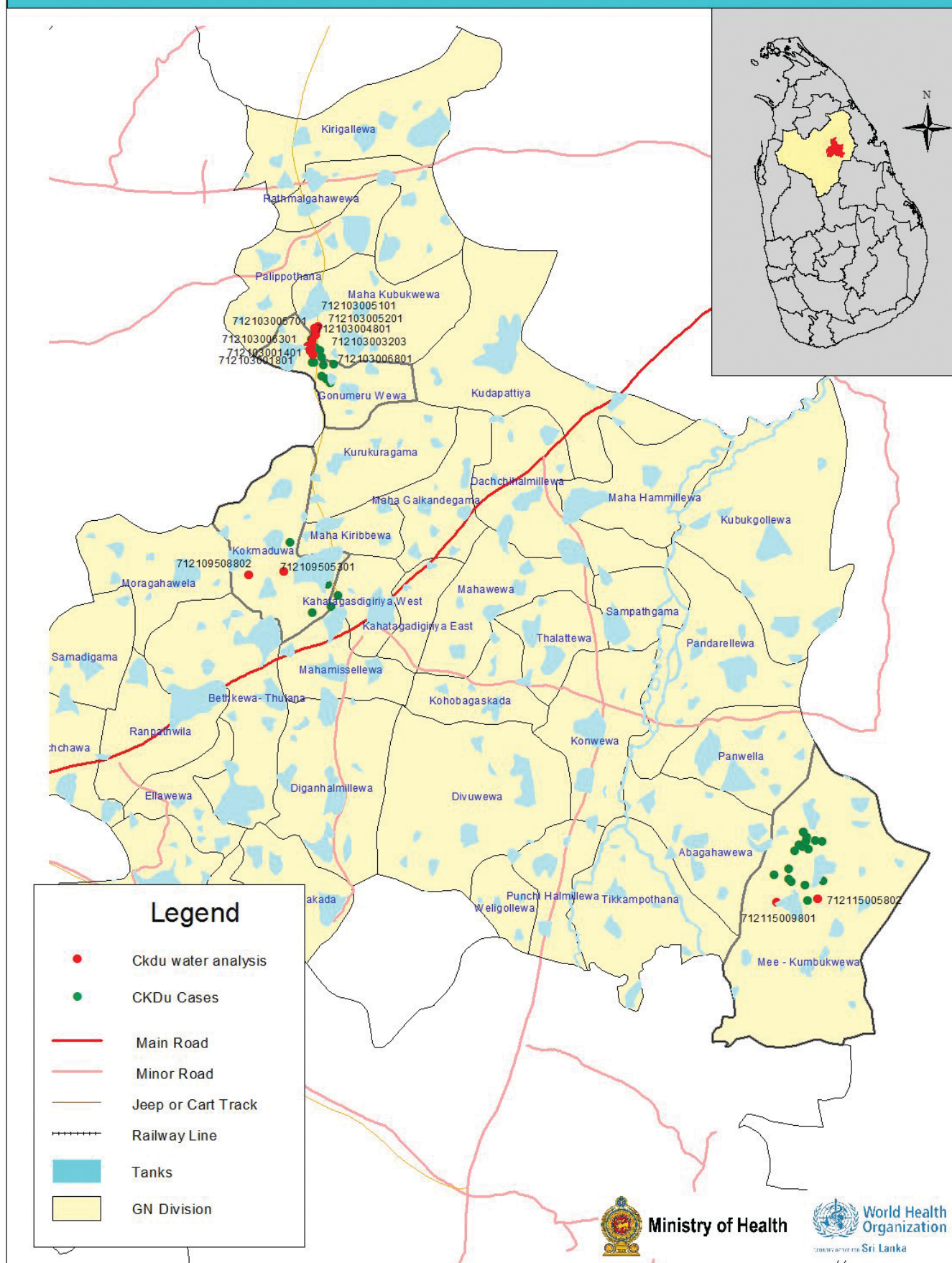


Ministry of Health

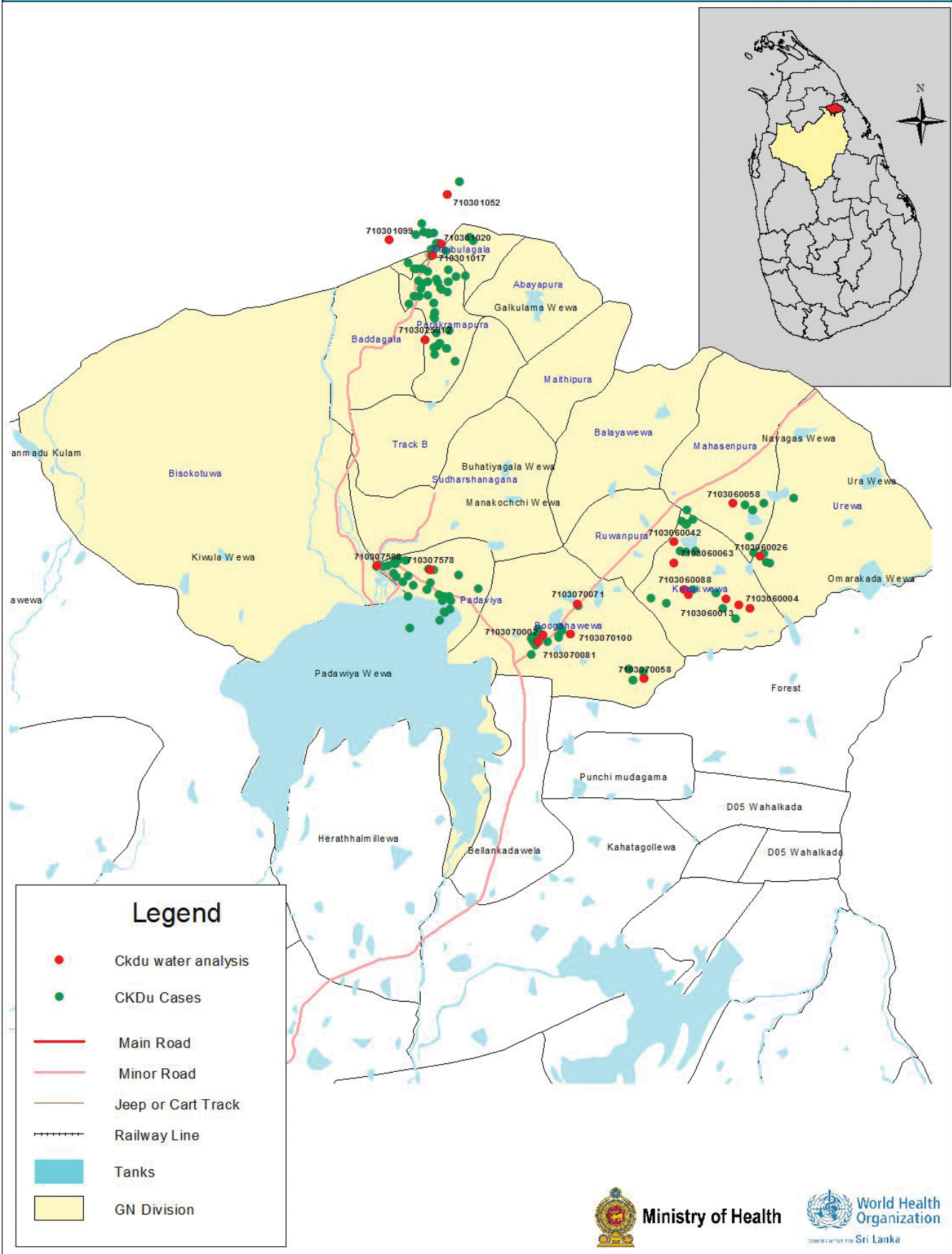


World Health
Organization
Sri Lanka

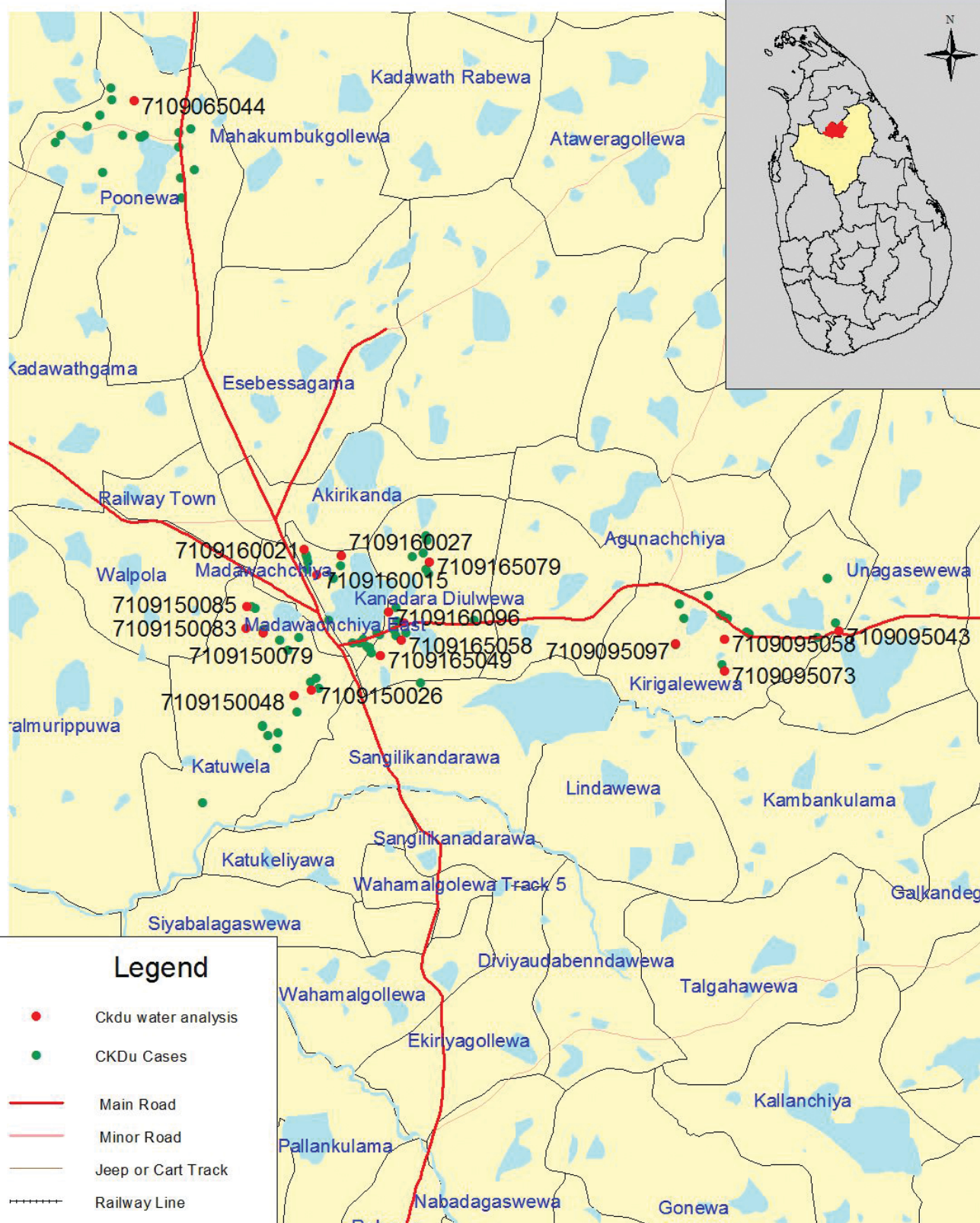
Collection of Drinking Water Samples from CKDu Patients for Metal Analysis Kahatagasdigiliya Divisional Secretariat Division



Collection of Drinking Water Samples from CKDu Patients for Metal Analysis
Padaviya Divisional Secretariat Division



Collection of Drinking Water Samples from CKDu Patients for Metal Analysis Medawachchiya Divisional Secretariat Division

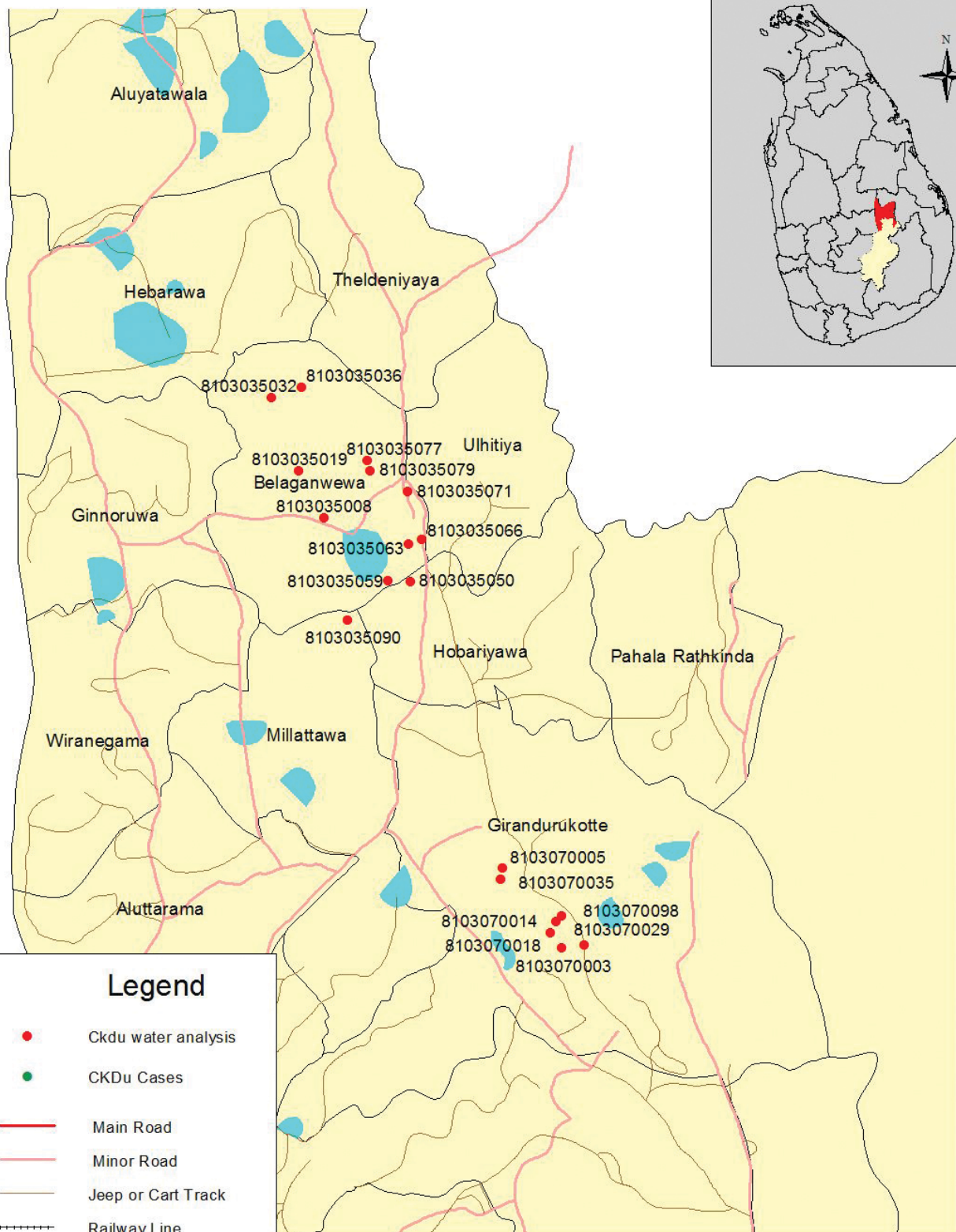


Ministry of Health



World Health Organization
Sri Lanka

Collection of Drinking Water Samples from CKDu Patients for Metal Analysis Mahiyanganaya Divisional Secretariat Division

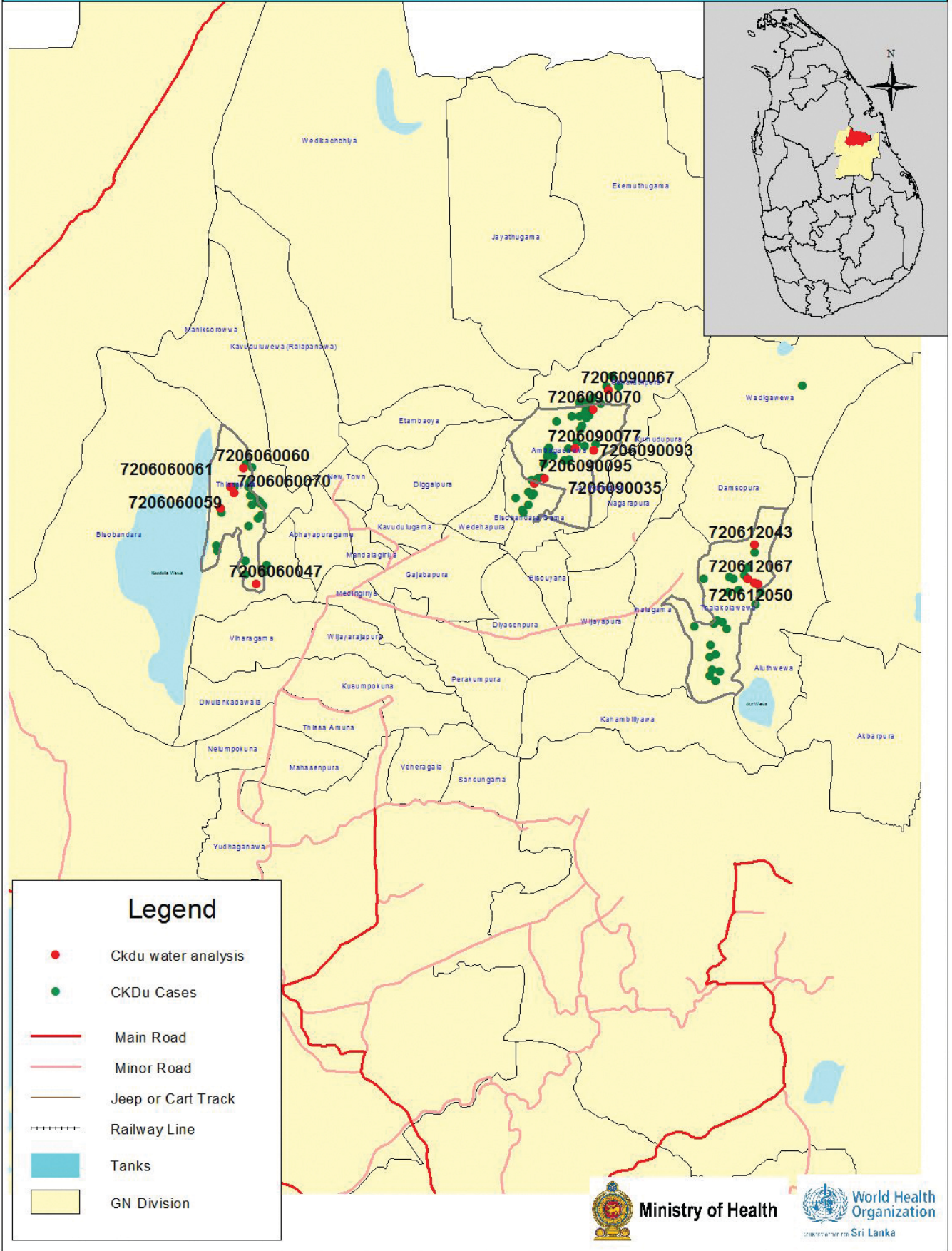


Ministry of Health



World Health Organization
Sri Lanka

Collection of Drinking Water Samples from CKDu Patients for Metal Analysis
Medirigiriya Divisional Secretariat Division



**Cross sectional comparison of potential environmental
toxins in endemic & non endemic areas for CKDu**

Environmental Sample Collection sites

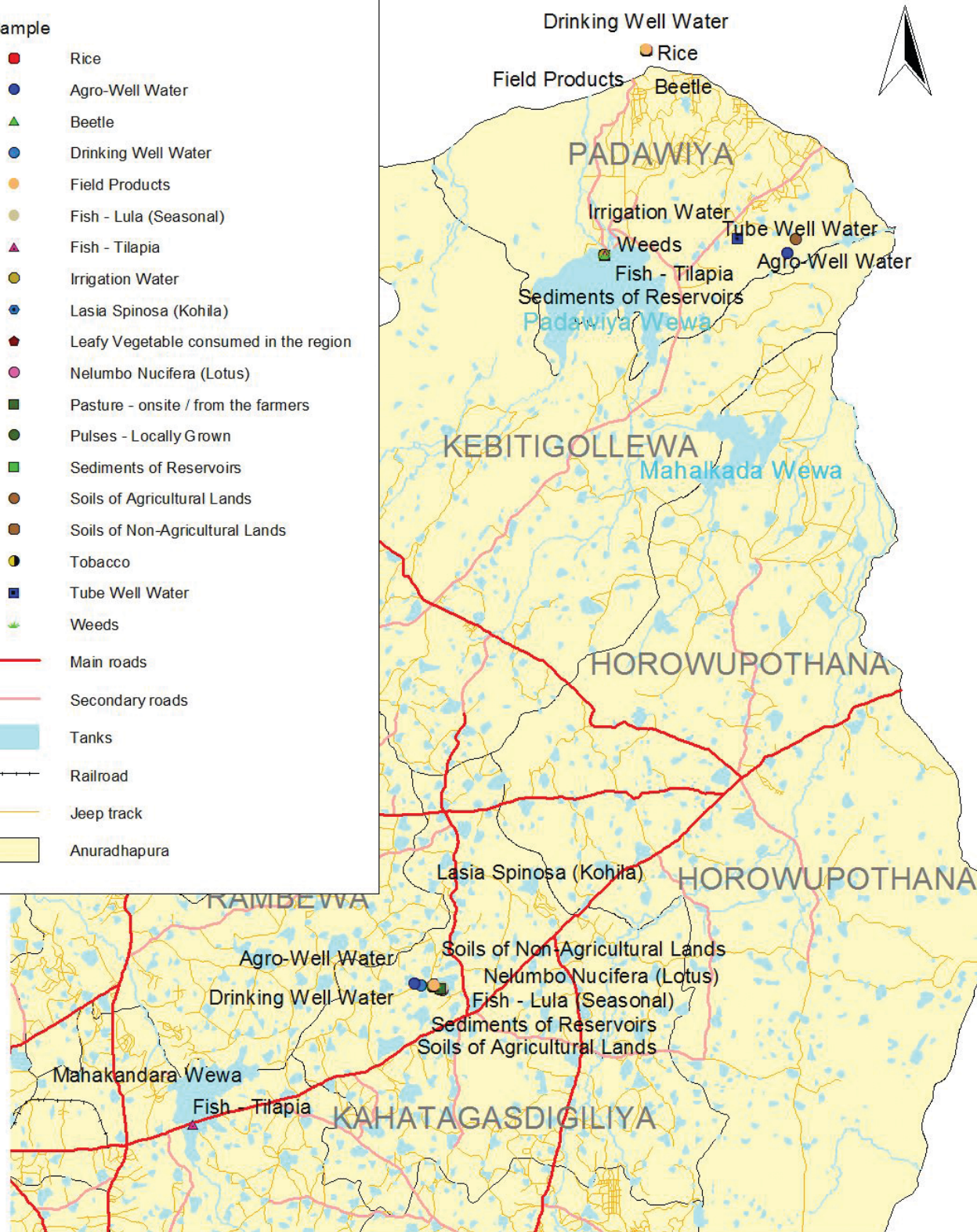
District	D.S. Division
Anuradhapura	Kahatagasdigiliya
	Galenbindunuwewa
	Padaviya
	Medawachchiya
Polonnaruwa	Medirigiriya
Badulla	Mahiyangana
Hambantota	Tangalle
	Tissamaharama

Environment samples collected from study area - Anuradhpura

Legend

Sample

- Rice
- Agro-Well Water
- ▲ Beetle
- Drinking Well Water
- Field Products
- Fish - Lula (Seasonal)
- ▲ Fish - Tilapia
- Irrigation Water
- Lasia Spinosa (Kohila)
- Leafy Vegetable consumed in the region
- Nelumbo Nucifera (Lotus)
- Pasture - onsite / from the farmers
- Pulses - Locally Grown
- Sediments of Reservoirs
- Soils of Agricultural Lands
- Soils of Non-Agricultural Lands
- Tobacco
- Tube Well Water
- Weeds
- Main roads
- Secondary roads
- Tanks
- Railroad
- Jeep track
- Anuradhapura

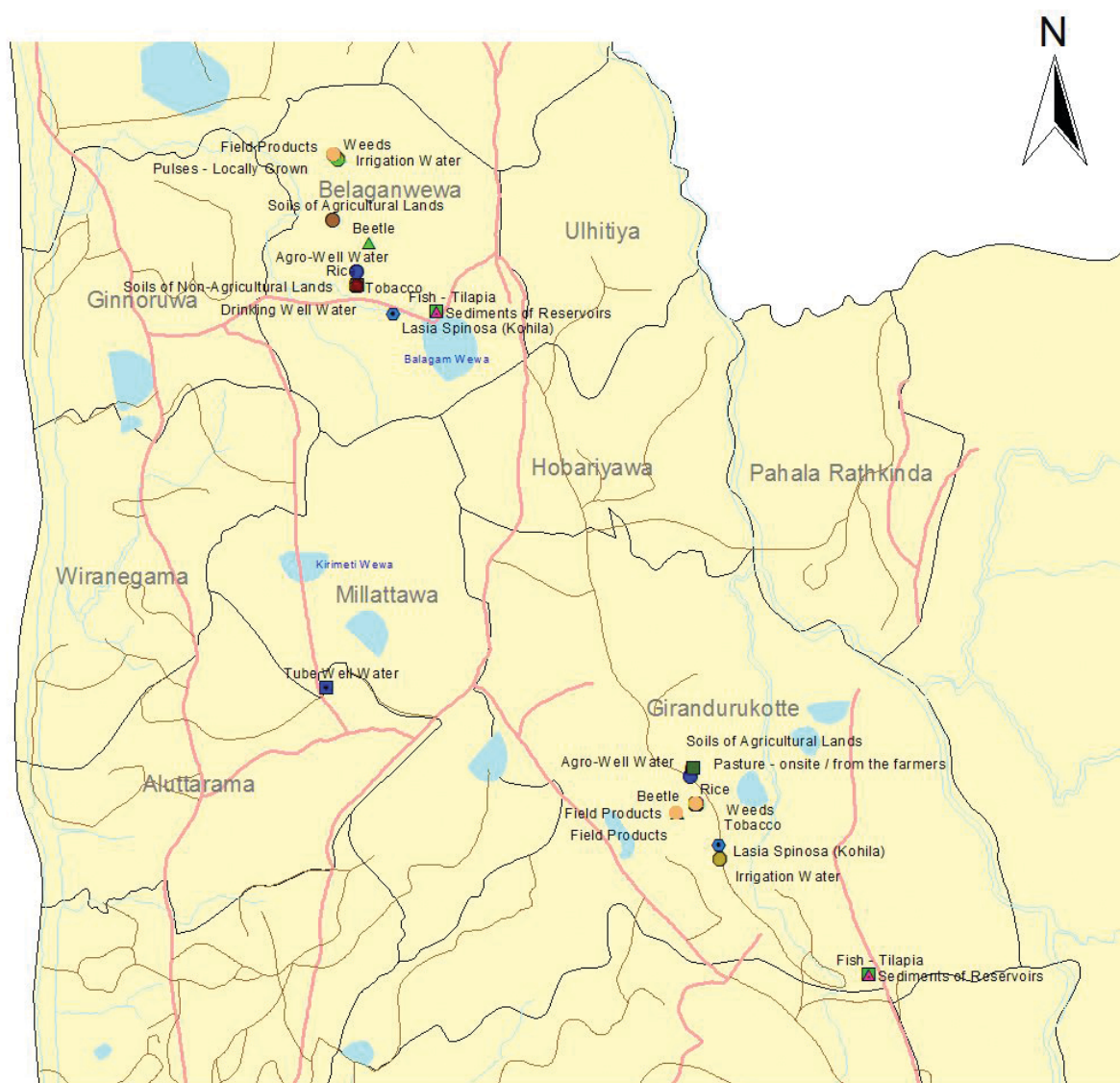


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World Health Organization
Sri Lanka

Environment samples collected from study area - Badulla



Legend

Sample

● Rice	● Nelumbo Nucifera (Lotus)	— Main roads
● Agro-Well Water	■ Pasture - onsite / from the farmers	— Secondary roads
▲ Beetle	● Pulses - Locally Grown	■ Tanks
● Drinking Well Water	■ Sediments of Reservoirs	— Railroad
● Field Products	● Soils of Agricultural Lands	— Jeep track
● Fish - Lula (Seasonal)	● Soils of Non-Agricultural Lands	■ Anuradhapura
▲ Fish - Tilapia	● Tobacco	
● Irrigation Water	■ Tube Well Water	
● Lasia Spinosa (Kohila)	● Weeds	
● Leafy Vegetable consumed in the region		

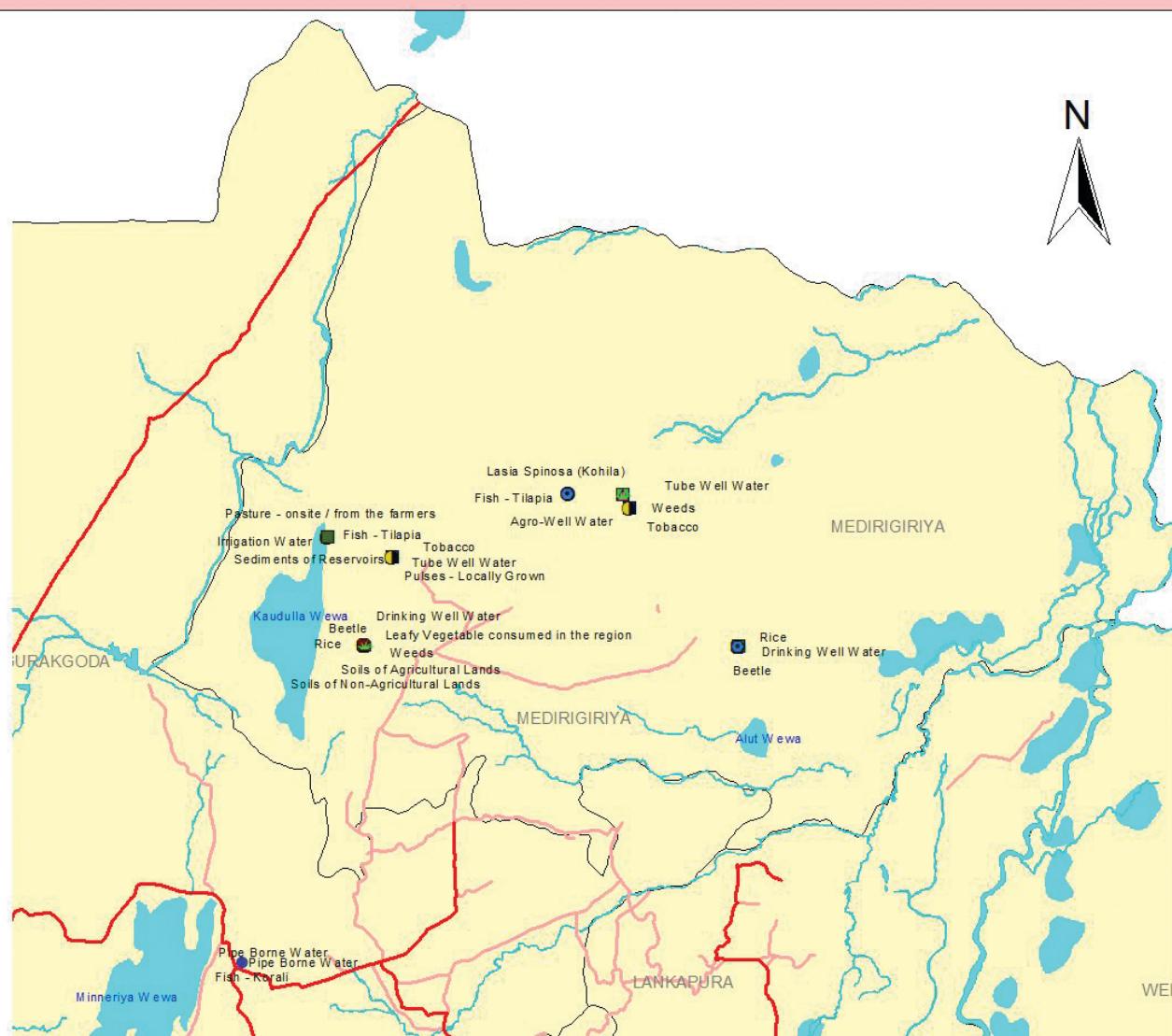


Ministry of Health



World Health Organization
Sri Lanka

Environment samples collected from study area - Polonnaruwa



Legend

Sample

- Rice
- Agro-Well Water
- ▲ Beetle
- Drinking Well Water
- Field Products
- Fish - Lula (Seasonal)
- ▲ Fish - Tilapia
- Irrigation Water
- Lasia Spinosa (Kohila)
- Leafy Vegetable consumed in the region

- Nelumbo Nucifera (Lotus)
- Pasture - onsite / from the farmers
- Pulses - Locally Grown
- Sediments of Reservoirs
- Soils of Agricultural Lands
- Soils of Non-Agricultural Lands
- Tobacco
- Tube Well Water
- Weeds

- Main roads
- Secondary roads
- Tanks
- Railroad
- Jeep track
- Anuradhapura

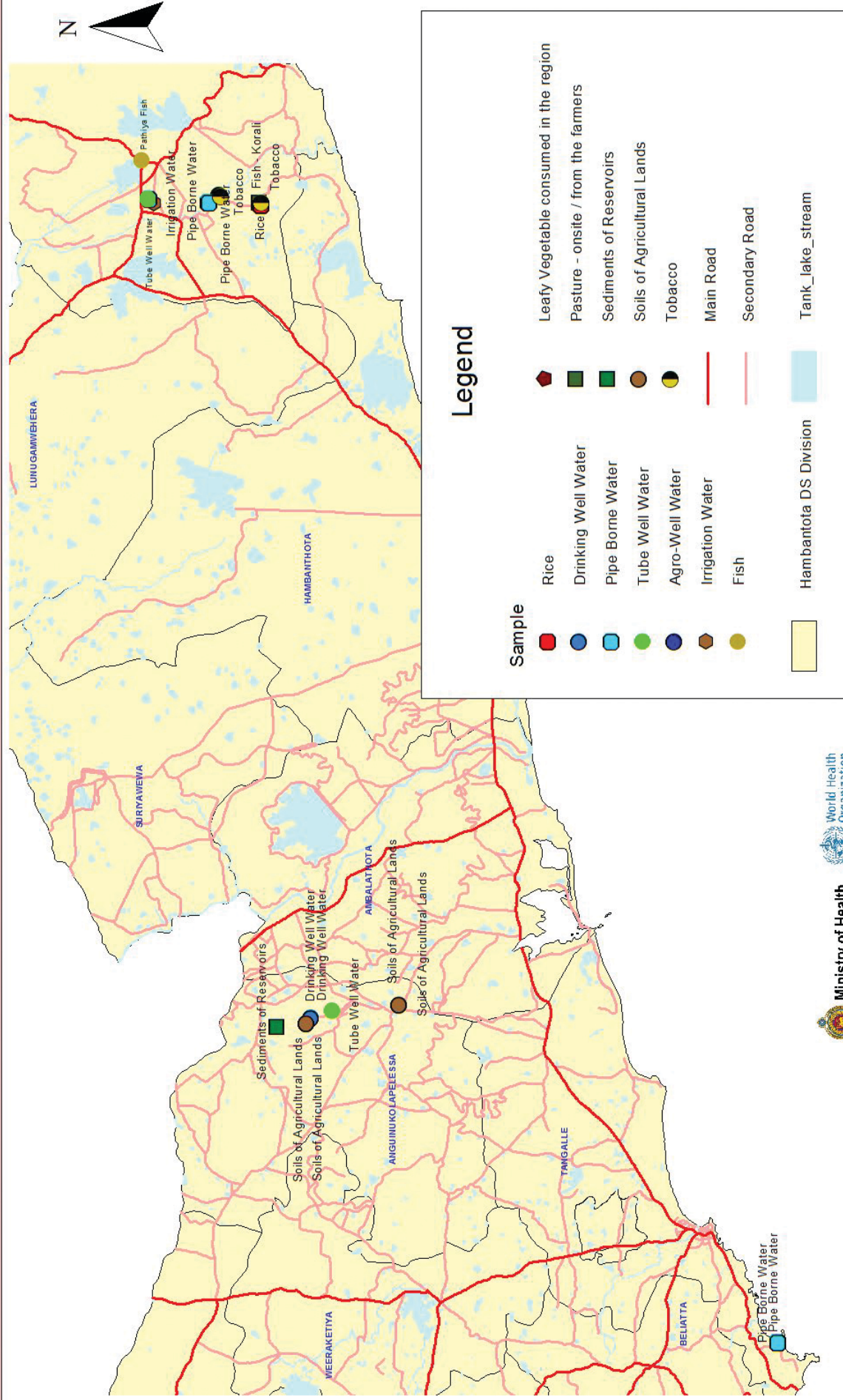


Ministry of Health



World Health Organization
Sri Lanka

Environment samples collected from study area - Hambantota



A GIS assistant based at the WHO country office was supported this exercise and the ToR of the GIS assistant is as follows:

Terms of reference – GIS Assistant

Contract Pried 01 December 2010 to 31 May 2011

- Collection of environmental samples for CKD project and ensure standards are met during collection and transportation of samples to reference laboratories
- Follows up with documentation relating to S & E, DFC, IPO and APW of CKD related activities
- Assisting in conducting of consultative meetings on CKDu research work, liaising with stakeholders and coordinating
- Maintain office records, related to the CKD subjects.
- Maintain databases on CKD related work
- Production of reports, maps and statistical information sheets on findings etc.
- Provision of IT support for workshops
- GIS mapping of environmental sample locations, pilot study sites and maintain comprehensive and up-to date databases on them
- Ability to work with GSM



Establishment of a literature repository for CKD

Introduction & Background

There are several studies that have investigated the prevalence, aetiology, clinical and histopathological features of CKD and CKDu. Collating these data (published/ unpublished/ grey literature related to CKD/ CKDu) into a repository can contribute to the national research effort by facilitating knowledge sharing between researchers and dissemination of results of studies to other stakeholders and policy makers. A request was made to researchers, academics and all other stakeholders to share copies of relevant research work especially papers published in peer-reviewed journals during the period 2000 - 2012. The literature/ data collected were compiled under different topics.

This was not an identified activity under the original proposal. However, considering the need for scholarly communication and a literature base for future research on the subject, the Scientific Committee had made a decision to establish a literature repository for CKD. Both hard and soft copies of compilation that includes scientific papers published in peer reviewed journals, presentations made at various forums, newspaper articles and grey literature are now available for reference.

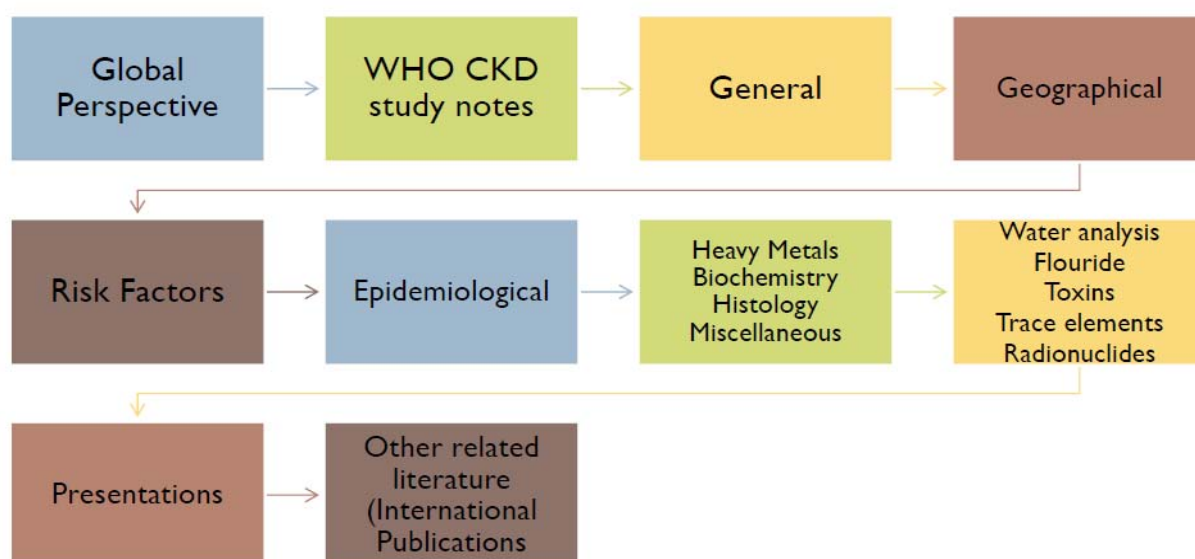
Scientific Scope of the Project

Establishing a literature repository on CKD especially CKDu was a long felt need. Since early 2000, CKDu has caught the attention of many clinicians, epidemiologists, policy makers and researchers. Many of them have conducted studies ranging from case studies to population based studies. In addition, Ministry of health, regional health authorities, universities, NGOs and international organizations have conducted several meetings and seminars and produced discussion papers and reports. Unfortunately, many of these documents remain as 'grey literature' and not accessible to those who are interested in this subject.

It is known that repositories facilitate a scholarly communication process. The dissemination and the wide use of the repository would facilitate, engender and encourage the ongoing collaborative and interdisciplinary research on CKDu.

Materials and Methods

Two editorial assistants were recruited to collect and collate information to produce the literature repository. In addition to the publication a CD was also produced which includes international publications, slide presentations and newspaper articles. Literature was collected under the following sub headings.



Results/Outputs

The publication and the CD produced is annexed together with the main report

Discussion & Conclusions

This publication will be a useful resource

II. Randomized Clinical trial to examine the renal effects of an Angiotensin Converting enzyme Inhibitor (Enalapril) in adults with CKDu

Introduction & Background

Chronic Kidney Disease of uncertain (CKDu) aetiology, which cannot be attributed to diabetes mellitus, hypertension, glomerular nephritis, chronic pyelonephritis or other known aetiologies has emerged particularly in the North Central province of Sri Lanka. Exposure to cadmium, nephrotoxic pesticides, together with deficiency of selenium and genetic susceptibility have been shown to play a role in the pathogenesis of the condition (1). CKDu is slowly progressive, probably starting in the second decade of life, and asymptomatic until very advanced. It has become a major public health problem causing serious economic and health impacts particularly in the lower socioeconomic communities in this region. The health care costs for the management of these patients are considerable as those in end stage kidney disease require haemodialysis or transplantation. Further, these high technology interventions are not readily accessible to the majority with CKDu due to economic constraints. This highlights the need to find strategies for prevention and slowing the progression of CKDu.

Main treatment modalities to slow down the progression to chronic renal disease are likely to be through control of blood pressure and proteinuria. The importance of proteinuria as a significant risk factor for end stage kidney disease is well recognized (2). Treatment that is targeted at reducing proteinuria has been shown to reduce progression of renal disease (3–6). In most forms of proteinuric chronic renal disease, glomerular filtration rate continues to decline even when the initial insult has been removed. Angiotensin converting enzyme inhibitors (ACEI) have been shown to be effective in retarding the progress of some forms of proteinuric kidney disease. The effect of ACEI on CKDu is not known. If ACEI are found to be effective in retarding the progress of CKDu it will be a cost effective secondary prevention intervention for this major public health problem in Sri Lanka.

Scientific Scope of the project

The objective of this double blind controlled study was to investigate the effect of enalapril on the progression of CKDu by comparing and evaluating the effect of enalapril to a placebo on estimated GFR and albuminuria.

Materials and methods

Subjects living in two districts (Anuradhapura and Polonnaruwa) in the North Central province of Sri Lanka, diagnosed as having CKDu in a population prevalence study, who satisfied inclusion criteria of the trial were invited to participate. Ethical clearance for the

study was obtained from the Ethical Review Committee, Medical Research Institute, Ministry of Health, Sri Lanka. All participants gave written informed consent. Patients were potentially eligible if they were between 30 and 70 years and had albumin to creatinine ratio $>30\text{mg/g}$ and estimated glomerular filtration rate $>15\text{ ml/min}$. The response rate was 70.87% ($n=427$). Patients who were already on treatment with either an ACEI or an angiotensin receptor blocker were excluded ($n=41$). Another 54 patients were excluded based on other exclusion criteria (pregnancy-4, breast feeding - 16, renal calculus with urinary tract dilatation - 4, diabetes mellitus - 7, malignancy - 2, $\text{eGFR} < 15\text{ml/min}$ - 8, recent history of acute kidney injury following snake bite - 2, rheumatoid arthritis - 2, glomerulonephritis-2, not willing to take western medicine-7). At the baseline visit, laboratory tests were done for urine sediment analysis, urine albumin creatinine ratio, hemoglobin, white cell count and differential count, glucose, urea, HbA1C, uric acid, cholesterol, triglycerides, liver enzymes, bilirubin and 24 hour urine analysis. Repeat urine albumin creatinine ratio was $<30\text{ mg/g}$ in 69 patients. They were excluded from the study. Patients who had no exclusion criteria ($n=263$) were randomized to treatment and placebo groups (Figure 1), and followed up at the Teaching Hospital Anuradhapura and Base Hospitals Padaviya and Medirigriya.

Participants were seen at two pre-randomization visits, and every month after randomization for 12 months. Those who were randomized were commenced on enalapril or placebo. Enalapril or placebo were started at low dose and titrated up based on blood pressure, proteinuria and serum potassium level. During each visit compliance, symptoms, blood pressure, serum creatinine, serum potassium and urine albumin to creatinine levels were assessed. All treatments other than enalapril were continued at the discretion of the responsible physician. Blood pressure was measured as the mean of two measurements made in the seated position using an xx sphygmomanometer at each study visit. Serum creatinine and electrolyte levels were measured at registration and randomization and at x and x-month visits. Measurement of urinary albumin creatinine ratio was performed on spot urine samples at the registration visit, every month after randomization and at the end of follow-up. The abbreviated Modification of Diet in Renal Disease (MDRD) equation was used to estimate eGFR.

Confidentiality of participants' data was protected by identifying patients on all study forms by a unique patient identification number. No study forms or other documents collected for the purpose of this study revealed the participant's name. No subject identifiers were presented on any files transmitted to any committee or any institution.

Statistical Analysis:

In order to calculate the sample size and the power estimates two indices of improvement were selected; Estimated Glomerular Filtration rate (eGFR) and urine Albumin Creatinine Ratio (ACR). To ensure a power of at least 80%, at $\alpha=5\%$ and to detect up to 14.04 ml/min discrepancies in eGFR rate and up to 20.77 mg/gr discrepancies in ACR rate, 51 cases and 51 controls were required. Assuming that eGFR rate and ACR rate follow a normal distribution with standard deviations of $\sigma =30.84\text{ ml/min}$ and $\sigma =50.52\text{ mg/gr}$ respectively, a sample size of 100 in each arm was required to ensure a statistical power of the test at least 80% at $\alpha=5\%$ and account for 25% loss of cases and controls during follow up.

Data collected during the baseline visit and the 12 follow up visits were analyzed to test the change in albuminuria and estimated glomerular filtration rate in participants receiving enalapril and compared to participants receiving the placebo. Intention to treat analysis was used where the baseline allocation to active treatment or control treatment was used over all of the study period. Due to non-symmetric distributions the Wilcoxon rank-sum (Mann-Whitney) test was used for continuous data. Proportions were tested using Fischer's exact test.

Results / Outputs

As shown in table below, there was no significant difference in the baseline characteristics (age, sex distribution, albumin to creatinine ratio and eGFR) in the enalapril and placebo groups.

Baseline Characteristics of the patients

Characteristic	Enalapril group	Placebo group	P value
Age (years)			
(mean, SD)	47.7 (13.3)	48.3 (13.6)	0.18
Male sex (number, %)	61 (46.92)	51 (38.35)	0.17
Blood pressure (mmHg)			
Systolic (mean, SD)	124.5 (17.9)	125.2 (18.9)	0.76
Diastolic (mean, SD)	78.3 (10.6)	80.4 (11.6)	0.14
Albumin creatinine ratio			
(mean, SD)	162.0 (321.7)	197.9 (461.6)	0.47
Estimated glomerular filtration rate			
(mean, SD)	71.7 (22.2)	73.8 (24.2)	0.46

The mean systolic and diastolic blood pressure levels declined significantly in both enalapril and placebo groups. The mean reduction in systolic blood pressure was 11.6 and 9.9 mmHg ($p=0.005$, 0.031), respectively. The mean reduction in diastolic blood pressure was 9.7 and 8.3 mmHg ($p<0.001$), respectively. There was no significant difference between the treatment and placebo groups in the reduction in systolic blood pressure and diastolic blood pressure.

There was a significant improvement in the albumin to creatinine ratio in the enalapril group compared to the placebo group ($p=0.005$). In the enalapril group, the mean albumin to creatinine ratio declined from 162.0 mg/g (SD 321.7) at baseline, to 55.4 mg/g (SD 122.4) at one year follow up. In the placebo group, the mean albumin to creatinine ratio

increased from 197.9 mg/g (SD 461.6) at baseline to 253.2 mg/g (SD 558.7), at one year follow up.

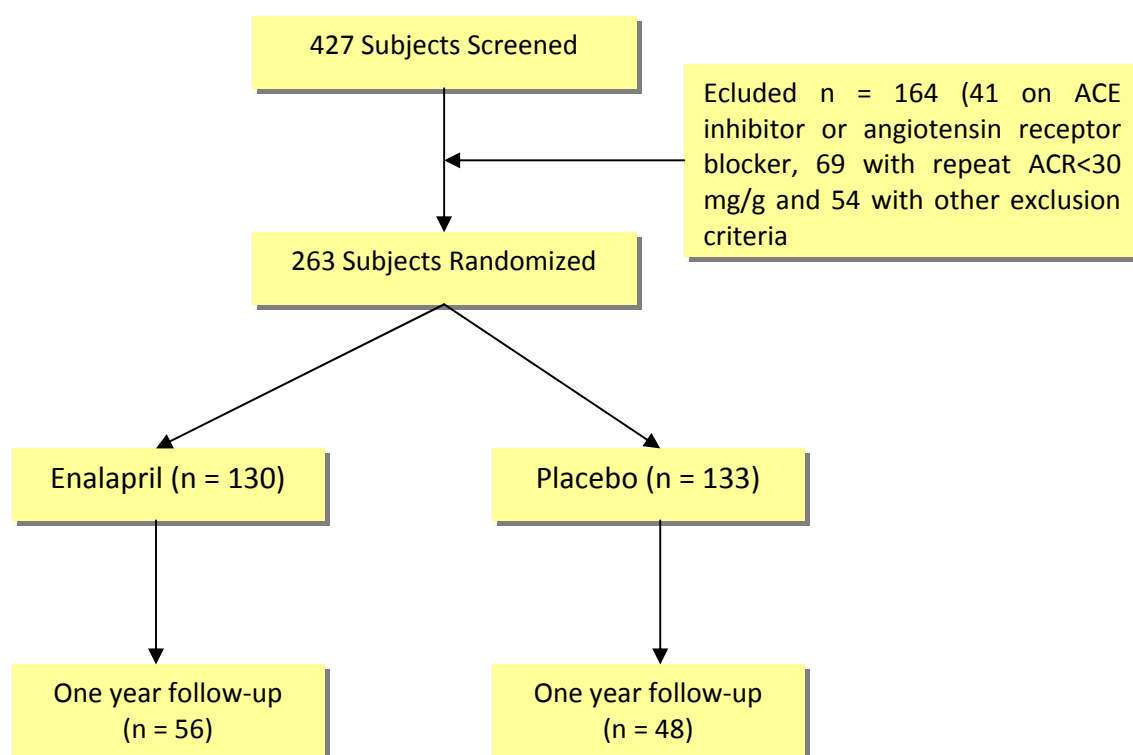
In both groups, the eGFR declined significantly ($p < 0.001$), during the 12 month followup. In the enalapril group the mean eGFR declined from 71.7 ml/min (SD 22.2) to 57.1 ml/min (SD 16.1). In the placebo group the mean eGFR declined from 73.8 ml/min (SD 24.2) to 54.7 ml/min (SD 20.3). There was no significant difference in the rate of decline between the two groups.

During the course of the study, 5 cases in the enalapril group and one case in the placebo group were switched over to losartan due to persistent dry cough. Five cases were withdrawn due to other reasons (Figure below). Loss of appetite and hyperkalaemia necessitated the discontinuation of treatment in 2 patients in the enalapril. One patient in the placebo group was withdrawn from the study due to pregnancy. In the enalapril group, one patient suffered a myocardial infarction and one patient suffered a stroke.

Outcomes according to study group at the end of the study

Variable	Enalapril group	Placebo group	P
Systolic blood pressure (mmHg) mean, (standard deviation)	112.9 (15.5)	115.3 (12.2)	0.58
Diastolic blood pressure (mmHg) mean, (standard deviation)	68.6 (12.4)	72.1 (7.1)	0.14
Albumin creatinine ratio (mg/g) mean, (standard deviation)	55.4 (122.4)	253.2 (558.7)	0.005
e GFR (ml/min) mean, (standard deviation)	57.1 (16.1)	54.7 (20.3)	0.63

Recruitment , randomization and follow-up of study subjects



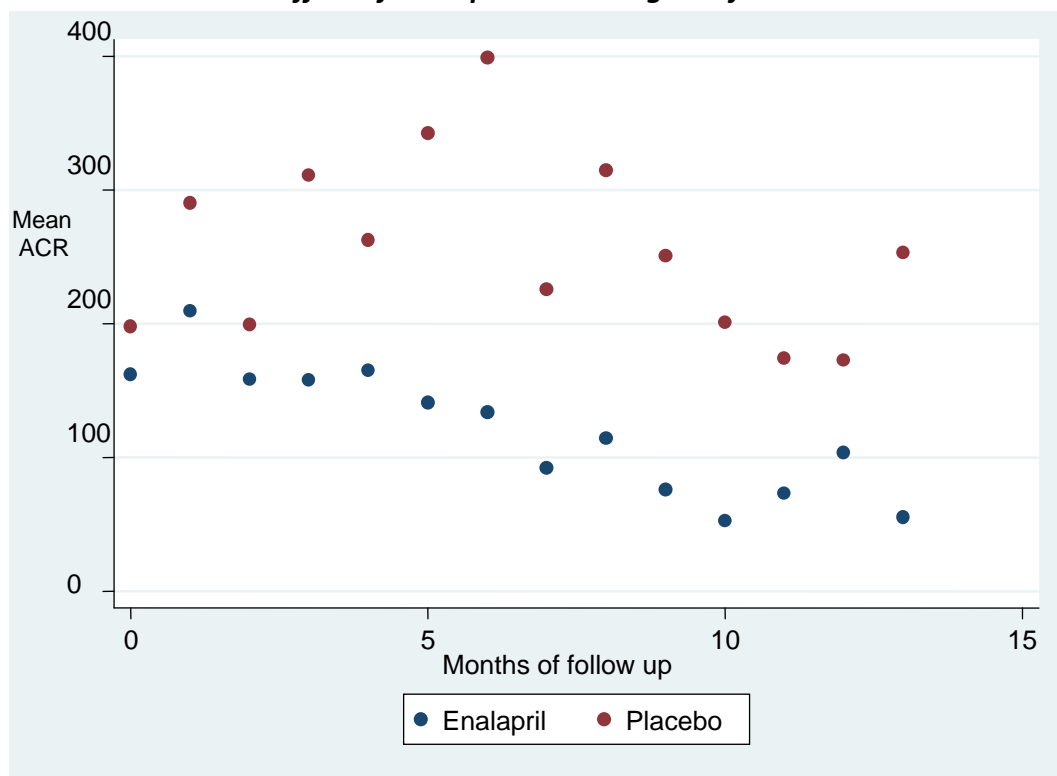
Discussion and conclusions

There was equal control of blood pressure in the enalapril and placebo groups. Treatment with enalapril was associated with a reduction in albuminuria. However there was no slowing of the rate of progression of nephropathy in the enalapril group or the placebo group, as reflected in the eGFR. We interpret these results as demonstrating that enalapril was effective in reducing albuminuria in these patients with nephropathy due to exposure to environmental toxins.

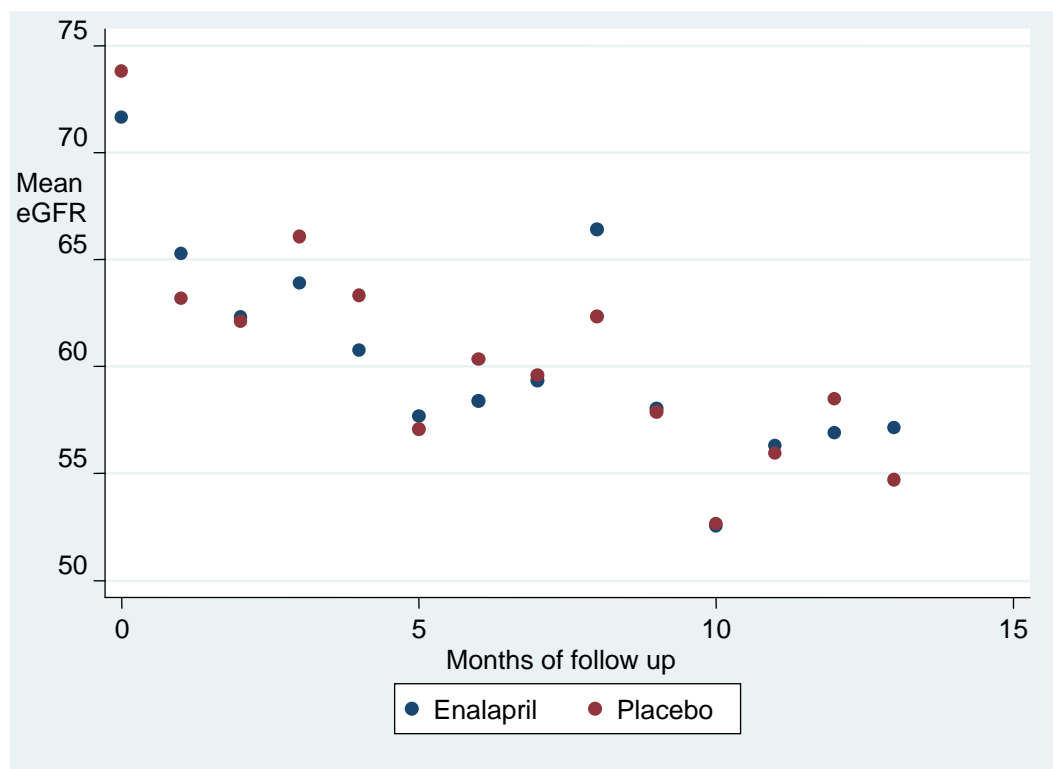
Data from observational studies suggest that proteinuria contributes to progressive renal damage, ultimately leading to end stage renal disease (7). In diabetic nephropathy, a 50% reduction in albuminuria was associated with a relative risk reduction for end stage renal disease of approximately 50% (8). However, despite current available treatments, most patients still continue to have residual proteinuria and progression of disease (4, 6, 7, 9). For example, in controlled trials, about one fifth of patients with severe diabetic nephropathy who have been intensively treated still progress to end stage renal disease in about 3 years (4, 6). There is a need for the development of new strategies to reduce exposure to nephrotoxins and arrest the rate of loss of renal function.

Limitations: Attrition of subjects at different stages was the main limitation of the study.

Effect of Enalapril on the degree of Albuminuria



Effect of enalapril on the estimated glomerular filtration rate



References

1. Jayatilake N, Mendis S, Maheepala P, Mehta F.R. Chronic kidney disease of uncertain aetiology; prevalence and causative factors in a developing country. *BMC Nephrol* 2013, Aug 27;14(1):180
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Formats Used

Study on Renal Effects of ACEI in CKDu Patients

Baseline Assessment

1. Name		2. Address	
3. GN Division:		4. Closest Hospital:	
5. Identification No:	□□□□□□□ □□□□	6. Date of Visit (d/m/y):	□□ □□ □□□□
7. Gender:	Male <input type="checkbox"/> Female <input type="checkbox"/>	8. Date of Birth (d/m/y):	□□ □□ □□□□
9. Weight (kg):	□□ . □	10. Height (m):	□ . □□

11. Blood Pressure reading (mm Hg)	1 st : Systolic <input type="text"/> <input type="text"/> <input type="text"/> Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	2 nd : Systolic <input type="text"/> <input type="text"/> <input type="text"/> Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	3 rd : Systolic <input type="text"/> <input type="text"/> <input type="text"/> Diastolic <input type="text"/> <input type="text"/> <input type="text"/>
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12. Concomitant diseases:	
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Past Medical History:	If necessary, provide details
13. Evidence or suspicion of renovascular disease, obstructive uropathy or other renal disease	Yes <input type="checkbox"/> No <input type="checkbox"/>
14. Treatment with corticosteroids, non-steroidal anti-inflammatory drugs, or immunosuppressive drugs	Yes <input type="checkbox"/> No <input type="checkbox"/>
15. Acute myocardial infarction or cerebrovascular accident in the previous 6 months	Yes <input type="checkbox"/> No <input type="checkbox"/>
16. Suspicion or evidence of connective tissue disease e.g. arthropathy, skin lesions, Reynaud's phenomenon etc.	Yes <input type="checkbox"/> No <input type="checkbox"/>
17. Suspicion or evidence of cancer	Yes <input type="checkbox"/> No <input type="checkbox"/>
18. Suspicion or evidence of non renal secondary hypertension: episodic sweating, palpitation etc.	Yes <input type="checkbox"/> No <input type="checkbox"/>
19. Presence of chronic cough	Yes <input type="checkbox"/> No <input type="checkbox"/>
20. Suspicion or evidence of drug abuse	Yes <input type="checkbox"/> No <input type="checkbox"/>
21. Pregnancy and breast feeding	Yes <input type="checkbox"/> No <input type="checkbox"/>

General examination:				
Hyper pigmentation:	22. General:	Yes <input type="checkbox"/> No <input type="checkbox"/>	23. Palm & sole:	Yes <input type="checkbox"/> No <input type="checkbox"/>
24. Arsenic keratosis:	Yes <input type="checkbox"/> No <input type="checkbox"/>	25. Gout:	Yes <input type="checkbox"/> No <input type="checkbox"/>	

26. Gingival lead line:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	27. Wrist/ foot drop:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
28. Tremors:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	29. Pitting ankle oedema:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
30. Pallor:	Yes <input type="checkbox"/>	No <input type="checkbox"/>			

Cardiovascular examination:

31. Heart rate (per minute):		<input type="text"/> <input type="text"/> <input type="text"/>		32. Shifted cardiac apex:		Yes	<input type="checkbox"/>	No	<input type="checkbox"/>		
33. Heart sounds:		34. Diastolic murmurs:	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>	35. Systolic murmurs:	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
36. Findings of 2D Echocardiography: (Indication: shifting of cardiac apex/ murmurs)											

Respiratory system examination:

37. Crackles:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	38. Wheeze:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
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Abdominal examination:

39. Palpable left kidney:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	40. Palpable right kidney:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
41. Distended bladder:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	42. Renal bruit:	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Fundus examination:

43. Haemorrhages:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	44. Hard exudates:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
45. Soft exudates:	Yes <input type="checkbox"/>	No <input type="checkbox"/>	46. Papilloedema:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
47. Optic atrophy:	Yes <input type="checkbox"/>	No <input type="checkbox"/>			

Treatment protocol:

48. Already on prescribed treatment:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
49. If yes, name of the hospital/ clinic where treatment obtained:		
50. List the drugs, dosages & duration of use (in months):		

Notes:

Study on Renal Effects of ACEI in CKDu Patients
Baseline Investigations

Identification Data:				
Name		Address		
Gender:	Male <input type="checkbox"/>	Female <input type="checkbox"/>	Date of Birth (d/m/y):	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Identification No:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Date of Visit (d/m/y):	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	

Results of Investigations

Investigations - Urine				
Urine Full Report	Protein:		Sugar:	
	Deposits:			
Urine Albumin Creatinine Ratio (ACR):				
24 Hours Urine Analysis	Na:	K:	Protein:	
	Urea:		Creatinine:	
Urine protein electrophoresis: (For a sub-sample)				

Investigations - Blood					
WBC (total count)		N (absolute):		L (absolute):	
		M (absolute):		E (absolute):	
Haemoglobin:		Platelets:		HbA ₁ C:	
ALT:		AST:		Alk. phosphatase:	
Serum Bilirubin:		Serum K:		Serum Na:	
Serum Creatinine:		Urea:		Uric acid:	
Serum Albumin		Serum Globulin:		Total Cholesterol:	
Estimated glomerular filtration rate (eGFR):					
USS KUB findings:					

Notes:

1st Follow up Visit Assessment (Randomisation) - Format

Study on Renal Effects of ACEI in CKDu Patients

1st Follow-up Visit Assessment (Randomization)

1. Patient Initials:		2. Unique Patient ID:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
3. Gender:	Male <input type="checkbox"/> Female <input type="checkbox"/>	4. GN No. & Name:	
5. Weight (kg):	<input type="text"/> <input type="text"/> . <input type="text"/>	6. Date of Visit (d/m/y):	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

History & Examination:

7. Symptoms reported:

8. Blood Pressure reading (mm Hg)	1 st : Systolic <input type="text"/> <input type="text"/> <input type="text"/>	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	2 nd : Systolic <input type="text"/> <input type="text"/> <input type="text"/>	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	3 rd : Systolic <input type="text"/> <input type="text"/> <input type="text"/>	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>
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9. Examination:

Treatment protocol:

10. Medicines currently used by the patient (list the drugs, dosages & duration):

11. Study drug:

12. Dosage:

13. Other medications prescribed (list the drugs, dosages & duration):

14. Drug monitoring chart issued:

Yes ☐ No ☐

15. Advice on medication given:

Yes ☐ No ☐

16. Any previously recognized issues & action taken:

17. Whom to contact in case of concern:

Annexure VIId – 2nd Follow up Visit Assessment (One Month After Intervention) - Format

Study on Renal Effects of ACEI in CKDu Patients
2nd Follow-up Visit Assessment (One month after intervention)

1. Patient Initials:		2. Unique Patient ID:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
3. Gender:	Male <input type="checkbox"/> Female <input type="checkbox"/>	4. GN No. & Name:	
5. Weight (kg):	<input type="text"/> <input type="text"/> . <input type="text"/>	6. Date of Visit (d/m/y):	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

History & Examination:

7. Symptoms reported:

8. Blood Pressure reading (mm Hg)	1 st : Systolic <input type="text"/> <input type="text"/> <input type="text"/>	2 nd : Systolic <input type="text"/> <input type="text"/> <input type="text"/>	3 rd : Systolic <input type="text"/> <input type="text"/> <input type="text"/>
	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>	Diastolic <input type="text"/> <input type="text"/> <input type="text"/>

9. Examination:

Details of study drug:

10. Study drug:		11. Dosage:	
12. Did the patient fail to take study drug during the last month?		Yes <input type="checkbox"/> No <input type="checkbox"/>	
13. If yes, for how many days?		<input type="text"/> <input type="text"/> days	
14. How many tablets of study drug remaining with the subject?		<input type="text"/> <input type="text"/> tablets	
15. Reasons given by the subject for not taking the study drug regularly:			
16. Any adverse effects due to study drug/ subject believes due to study drug:			
17. If adverse effects reported, details of action taken?			

Details of other medications:

18. Medicines currently used by the patient (other than study drug) & dosages:

19. Details of new medications prescribed at this visit (If any, dosages & duration):

Investigations:

20. Serum Creatinine		21. Estimated GFR (eGFR)	
22. Urine albumin creatinine ratio (ACR)		23. Serum Potassium (K)	

Study on Renal Effects of ACEI in CKDu PatientsC

Consent Form (Sinhala)

තැමැත්ත ප්‍රකාශ කිරීමේ සහතිකය

මෙම පර්යේෂණයේ අරමුණ නිශ්චිත වකුගඩු රෝගීන්ගේ වකුගඩු වල ක්‍රියාකාරීත්වය තවදුරටත් දුර්වල වීම වලක්වා ගැනීමට එනලප්‍රිල් (Enalapiril) ඖෂධය සතු හැකියාව සොයා බැලීමත්, එම ඖෂධය දැනට භාවිතා වන ප්‍රතිකාර සමග විද්‍යාත්මකව සසඳා බැලීමත්ය.

මාස 12 ක් පුරා මසකට වරක් බැගින් සායනයට පැමිණීමට මට සිදුවනු ඇත. එම අවස්ථා වල දී මගේ සෞඛ්‍ය තත්වය පිළිබඳව පරීක්ෂා කෙරෙනු ඇති අතර, රුධිර පීඩනය සහ බර ද මැන බැලෙනු ඇත. වකුගඩු වල ක්‍රියාකාරීත්වය දැන ගැනීමට රුධිර සහ මුත්‍රා සාම්පල ලබාගනු ඇත. අවශ්‍ය වුවහොත් පමණක් අධික රුධිර පීඩනය සඳහා ප්‍රතිකාර ලබාදෙනු ඇත. එනලප්‍රිල් ඖෂධය ලබා ගන්නා කණ්ඩායමට මා අහඹු ලෙස ඇතුළත් වුවහොත් එම ඖෂධය සෑම උදෑසනකම හෝ රාත්‍රියකම ගැනීමට මට සිදුවනු ඇත. එම ඖෂධය දීර්ඝ කාලයක් ලොව පුරාම අධික රුධිර පීඩනය සහ වකුගඩු රෝග වලට ප්‍රතිකාර කිරීම සඳහා භාවිතා වේ. මෙම පර්යේෂණය සඳහා නව ඖෂධ කිසිවක් භාවිතා නොවේ.

මෙම පර්යේෂණයට සහභාගිවීමෙන් කිසිදු බරපතල අවදානමකට හෝ අපහසුතාවයකට මා ලක් නොවේ. මෙම පර්යේෂණයට සහභාගි වුවහොත් මගේ රුධිර පීඩනය සහ වකුගඩු ක්‍රියාකාරීත්වය පිළිබඳ නිසි වෛද්‍ය උපදෙස් ලබා ගැනීමේ වාසිය මට හිමි වේ. නිශ්චිත වකුගඩු රෝගය වලක්වා ගැනීම සඳහා කෙරෙන පර්යේෂණ කටයුත්තක් බැවින් සමාජමය වශයෙන් මෙහෙයක් ද මගෙන් සිදු වේ.

මගෙන් ලබා ගන්නා තොරතුරු වල රහස්‍යභාවය සුරැකෙනු ඇත. මෙම පර්යේෂණයට සහභාගි නොවීමට තීරණය කළත් මට හිමි නිසි වෛද්‍ය ප්‍රතිකාර නොනවත්වාම මට හිමි වේ.

ඉහත විස්තර කියවා බැලුවෙමි. / ඉහත විස්තර දැන ගැනීමට මට කියවන ලදි. ප්‍රශ්න විමසීමට මට අවස්ථාව ලැබිණි. නිසි පිළිතුරු මට සැහීමට පත් වීමට හැකි අයුරින් විස්තරාත්මකව පවසන ලදි.

මෙම පර්යේෂණය සඳහා මා ස්වකර්මතෝෂෙන් සහභාගි වන අතර ඕනෑම අවස්ථාවක මෙම පර්යේෂණයෙන් ඉවත්වීමට මට අයිතිය ඇත. එම ඉවත්වීමෙන් නිසි වෛද්‍ය ප්‍රතිකාර ලබා ගැනීම සඳහා මට හැකි අයිතියට කිසිදු බලපෑමක් ඇති නොවනු ඇත.

.....
සහභාගිවන්නාගේ සම්පූර්ණ නම

.....
සහභාගිවන්නාගේ අත්සන

.....
දිනය

ලිවීමට / කියවීමට නොදන්නා අයෙක් නම්

කියවීමට හා ලිවීමට හැකි ස්වාධීන සාක්ෂිකරුවෙකුගේ/සාක්ෂාකාරියකගේ නම යොදන්න.
(හැකි නම් සහභාගිවන්නාටම ස්වාධීන සාක්ෂිකරුවානෝරා ගැනීමට පහසුකම් සලසන්න. තෝරා ගන්නා සාක්ෂිකරුවා/සාක්ෂිකාරිය පර්යේෂණ කණ්ඩායම සමග සබඳතා ඇති අයෙකු නොවිය යුතුයි.)

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සාක්ෂිකරුගේ / සාක්ෂිකාරියගේ සම්පූර්ණ නම

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දිනය

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සාක්ෂිකරුගේ / සාක්ෂිකාරියගේ අත්සන

.....
පර්යේෂකයේ නම

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පර්යේෂකයේ අත්සන

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දිනය

Study on Renal Effects of ACEI in CKDu Patients

Information Sheet

මූල්‍යමය ප්‍රතිලාභ

මෙම පර්යේෂණයට සහභාගිවීමෙන් ඔබට කිසිදු මූල්‍යමය ප්‍රතිලාභයක් හිමි නොවේ. එහෙත් සායනයට පැමිණීම සඳහා අවශ්‍ය ප්‍රවාහන පහසුකම් සැපයෙනු ඇත.

තොරතුරු වල රහස්‍යභාවය

රැස්කර ගන්නා සියලු තොරතුරු වල රහස්‍යභාවය සුරැකෙනු ඇත. ඔබෙන් ලබා ගන්නා සියලු තොරතුරු ආරක්ෂාකාරීත්ව තැබෙනු ඇත්තේ නිර්නාමිකව සහ ඔබට හිමි අංකයට අදාළවයි. ඔබේ නම සහ අංකය සහිත ලිපිගොනු සුරැකිව තැබෙනු ඇත්තේ එම තොරතුරු වල රහස්‍යභාවය සුරැකෙනු පරිදිය. ඔබේ සෞඛ්‍ය නිලධාරියා වන වෛද්‍ය එස්. මතු, මහ රෝහල, අනුරාධපුර (දුරකථන අංකය 025-2226866) හරහා වෙනත් කිසිවෙකුට එම තොරතුරු දැන ගැනීමට ඉඩ නොලැබෙනු ඇත.

සහභාගිවීම ප්‍රතික්ෂේප කිරීමට හෝ ඉන් ඉවත් වීමට ඇති අයිතිය

ඔබ අකමැති නම් මෙම පර්යේෂණයට සහභාගි නොවී සිටීමට සම්පූර්ණ අයිතියක් ඇත. සහභාගි නොවී සිටීම නිසා ඔබට මෙම ස්ථානයෙන් සැපයෙන ප්‍රතිකාර වල කිසිදු අඩුවක් හෝ ඊට බලපෑමක් කිසිදු අයුරකින් සිදු නොවේ. සහභාගිවන්නන්ගේ ලැබෙන සියලුම වරප්‍රසාද සහභාගි නොවන්නන්ට ද එලෙසම හිමි වේ. ඔබට ඕනෑම අවස්ථාවක දී මෙම පර්යේෂණයට සහභාගි වීමෙන් ඉවත්වීමට අයිතියක් ඇත. ඔබට සැපයෙන ප්‍රතිකාර වලට ඉන් කිසිදු ආකාරයක බලපෑමක් සිදු නොවේ. මෙම පර්යේෂණයට සහභාගි නොවන්නන්ට ද හිසි ප්‍රතිකාර සාමාන්‍ය පරිදි මෙම සෞඛ්‍ය මධ්‍යස්ථානයෙන් ලැබෙනු ඇත.

දැන ගැනීමට යමක් ඇත්නම් පහත සඳහන් සෞඛ්‍ය නිලධාරියා අමතන්න.

වෛද්‍ය එස්. මතු, මහ රෝහල, අනුරාධපුර (දුරකථන අංකය 025-2226866)

මෙම පර්යේෂණ යෝජනාව ඊට අදාළ ආචාර ධර්ම කමිටුවේ නිසි අධීක්ෂණයට යොමු වී එම කමිටුව මගින් අනුමත කර ඇත. පර්යේෂණයට සහභාගි වන්නන්ගේ සුරක්ෂිතභාවය තහවුරු කිරීම එම කමිටුවේ කාර්යභාරය වේ. ඒ පිළිබඳ විස්තර දැන ගැනීමට අවශ්‍ය නම් වෛද්‍ය එස්. මතු, මහ රෝහල, අනුරාධපුර (දුරකථන අංකය 025-2226866) අමතන්න.

ஒப்புதல் சான்றிதழ்

இலங்கையில் காணப்படும் நோய் ஏது அறியப்படாத நீடித்த சிறுநீரக நோயை
மதிப்பிடுதலும் ஆய்வு செய்தலும்

பிரேதங்களில் நடாத்தப்படும் ஆய்வு

பிரேதங்களிலிருந்து பெறப்படும் மாதிரிகளை வேண்டிநிற்கும் இந்த ஆய்வானதுஇ சுகாதார அமைச்சினதும், உலக சுகாதார சுகாதார ஸ்தாபனத்தினத்தினதும் அனுசரணையுடன் நடாத்தப்படுகின்றது. இவ்வாய்வின் முழுமையான இலக்கானது இலங்கையின் சில பகுதிகளில் அதிகளவில் காணப்படுவதாக அறிவிக்கப்படும் நீடித்த சிறுநீரக நோயினை நிர்ணயம் செய்யும் காரணிகளையும் அடையாளம் கண்டு கொள்வதாகும்.

சிறுநீரகம், ஈரல் மற்றும் எலும்பு என்பவற்றிலிருந்து இழையங்கள் எடுக்கப்படவுள்ள இறந்த நபர் எனக்கு அறியப்பட்டவர். இறந்தவரிடமிருந்து இழையங்கள் எடுக்கப்படுவதற்கு ஒப்புதல் வழங்க எனக்கு சட்டரீதியான அதிகாரம் இருப்பதை உறுதி செய்கின்றேன். நான் எனது ஒப்புதலை வழங்குவதானது முற்றிலும் எனது சொந்த விருப்பிலாகும். ஒப்புதல் வழங்க மறுப்பதானது வைத்தியசாலையுடனோ அல்லது சுகாதார நிலையத்துடனோ எனக்குள்ள வருங்கால உறவைப் பாதிக்காது என்பதனை நான் அறிவேன்.

இறந்தவரிடமிருந்து இழையங்கள் ஆய்வாளர்களால் எடுக்கப்படுவதற்கு இடமளிப்பதானது எனக்கோ அல்லது இறந்தவரை அறிந்த வேறு யாருக்குமோ உடனடிப் பலன்களை வழங்காது என்பதை நான் அறிவேன். இருப்பினும், இந்த இழையங்களை ஆய்வு செய்வதனால் பெற்றுக் கொள்ளப்படும் தகவல்கள் இலங்கையின் சில பகுதிகளில் காணப்படும் ஒரு வகை சிறுநீரக நோய்க்கான காரணம் அல்லது காரணங்களை கண்டுபிடிக்கவும் அதன்மூலம் இச்சிறுநீரக நோயைத் தடுக்கவும் உதவுமாகையால், சமுதாயத்துக்கும் இதனால் பலனுண்டு என்பதனை நான் அறிவேன். .

எவருக்குமே எந்தவொரு அபாயமும், அசௌகரியமும் ஏற்படாது. எடுக்கப்படவுள்ள ஒவ்வொரு மாதிரியினதும் (சிறுநீரகம், ஈரல் மற்றும் எலும்பிலிருந்து) நிறையானது 100 கிராம்களுக்கு குறையாமலும் 500 கிராம்களுக்கு மேற்படாமலும் இருப்பதுடன், மாதிரிகளை எடுப்பதானது உடலையோ அதனது வெளித்தோற்றத்தையோ பாதிக்காது.

நான் முன்தரப்பட்ட தகவல்களை வாசித்தேன் அல்லது அவை எனக்கு வாசித்துக் காட்டப்பட்டது. இது பற்றி வினாக்கள் கேட்க எனக்கு சந்தர்ப்பம் தரப்பட்டதுடன்இ திருப்தியான முறையில் என்னால் கேட்கப்பட்ட வினாக்களுக்கு பதிலளிக்கப்பட்டது. எனது சுயவிருப்பில் இறந்தவரிலிருந்து மாதிரிகள் ஆய்வாளர்களால் எடுக்கப்படுவதற்கு ஒப்புதல் அளிக்கின்றேன்.

<p>இறந்தவரின் பெயர்</p> <p>இறந்தவருக்கும் ஒப்புதல் வழங்குபவருக்கும் இடையிலான உறவு முறையைக் கூறுக.</p>	<p>திகதி</p>	<p>ஒப்புதல் வழங்குபவரின் ஒப்பம்</p>
<p><i>ஒப்புதல் வழங்குபவர் படிப்பறிவு இல்லாதவர் எனின் (சாட்சியை பங்குபற்றுபவர் தெரிவு செய்ய வேண்டும்.. இந்நபருக்கு ஆய்வுக்குழுவுடன் தொடர்புகள் இருத்தலாகாது)</i></p>		
<p>படிப்பறிவுள்ள சுயாதீனமான சாட்சியின் பெயர்</p>	<p>திகதி</p>	<p>சாட்சியின் ஒப்பம்</p>
<p>ஆய்வாளரின் பெயர்</p>	<p>திகதி</p>	<p>ஆய்வாளரின் ஒப்பம்</p>

III. Socioeconomic and productivity impact of CKDu

Introduction / Background

Chronic Kidney Disease of unknown etiology (CKDu) is affecting thousands of people living in the North Central province and other areas of Sri Lanka. The number of those affected and dying has shown a progressive increase threatening the existence of whole communities living in these areas and repeatedly, North Central Province (NCP) has recorded the highest number of deaths due to chronic renal failure in the country. The disease is prevalent among farming communities and has devastated the economy of these areas in a number of ways. The loss of productivity from illness, the costs of care for those affected, and preventive action have taken a toll on the life of these communities, some of whom were anyway surviving in a subsistence economy.

Costs of care include seeking treatment for the disease (relating to consultation, drugs, dialysis and transplantation) and its complications (e.g. hypertension and anemia). Already the health services are burdened by the illness and there are indications that implicit rationing of healthcare provision is taking place. For example, older persons with chronic kidney disease are not being provided with dialysis. Villagers have taken different preventive actions which are also costly. Since Sri Lanka lacks a comprehensive formal social support system, the loss of productivity, the costs of care and prevention all have cumulative impacts and therefore have the potential to push families and communities towards poverty. Only a few publications describe the psycho-socio and economic impact on the household and the coping strategies adapted by the households. There are also no published intervention studies on social support for the affected families. This Socio-economic and productivity impact study was undertaken in this context as a part of the National Research programme for CKDu with the focus on understanding the disease burden at both local and national levels.

The Socio-economic and socio-economic and productivity study has two research components, i.e., the Community-based study and the Hospital-based study.

IIIa Community Based Study

IIIb Hospital Based Study

The community based study attempts to explore the Socio-economic and psychological impacts of chronic kidney disease on affected individuals, households and communities with identified methods of mitigating it.

The focus of the hospital based study is to estimate costs of care to the health system.

Scientific scope and objectives

The overall objective of Community-based study is to estimate the burden of CKDu at individual, household and community levels together with identifying methods of mitigating adverse effects of the disaster. Thus the study has the following specific objectives:

1. Estimate the costs of CKDu to the individuals, households and affected communities
2. To understand the psychosocial impact of CKDu on individual, households and affected communities
3. Describe modes of coping adapted by individuals, households and communities to mitigate adverse socio-economic and psychological impacts of CKDu
4. Evaluate the impact of existing coping mechanisms and modes of social support and recommend the best options for implementation on a wider scale

Research Questions:

The empirical investigation of the community-based study was focused on the following research questions.

1. How do the villagers recognise CKDu in their locality and their perceptions on illness?
2. How do patients and their families respond to the illness?
3. How does the illness impact on the economic activity of the patient and his/her family?
4. How does the illness affect children's education ?
5. How does the illness affect the psycho-social and economic well-being of the family?
6. How does the illness affect the everyday life of the patient and his/her family?
7. How does the illness affect the relationship of a family with other villagers?
8. What are the coping mechanisms adopted by a family in encountering the situation?
9. What are the social support mechanisms available at the community level to cope with the illness?
10. What are the problems encountered by the patients and their families while seeking treatment?
11. How does the community respond to the illness?

Materials and methods

The Setting and the Sample of the Study:

This socio-economic and productivity impact study, consisting of both community-based and hospital-based analysis was undertaken in the Anuradhapura district in the NCP. According to the patient registers, the highest number of patients in Anuradhapura district has been reported from Padaviya and Medawachchiya DS Divisions (CKDu Prevention Unit, NCP: 2011). The community-based study was conducted in the above two DS Divisions considering the high prevalence of disease.

The study sample included 200 CKD patients and their households, 100 from each DS Division. Initially, it was decided to adopt a random sampling method to select the study sample using the patient registers available to the researchers. However, the researchers faced some practical difficulties in finding patients from the existing registers as some of the patients in the list were physically not found in the relevant communities. Therefore, the snowball sampling method was adopted in order to find the required number of patients from each division for the study. The gender dimension was taken into consideration while selecting the sample as it was crucial in understanding various coping strategies adopted by the male and female patients. Accordingly, 65 male patients and 35 female patients were selected from Medawachchiya DS division and 66 male patients and 34 female patients from Padaviya DS division. Thus, altogether there were 131 male patients and 69 female patients in the selected sample.

In addition to the above sample, 13 households in Medawachchiya and 9 households in Padaviya where a death reported was due to CKDu were selected for the study as it could provide a comprehensive understanding of the illness burden from the beginning to the end of the tragedy. Information was also gathered from a number of other community members, village leaders and different service providers by conducting Focus Group Discussions (FGDs) and Key Informant Interviews (KII). Thus, a detailed account of the socio-economic and cultural background of the study locations will be provided in the second chapter of this report. The following section explains the investigation process with detailed accounts of the data collection methodology.

The Methodology of the Study:

The empirical investigation of the community-based study was conducted by two senior sociologists with a group of Research Assistants, Sociology graduates from the University of Colombo who had knowledge in the areas of Sociology, Social Work and Psychology. The group included two female and four male Research Assistants. They were trained prior to the commencement of the study.

Training Workshops for Research Assistants:

Although all the Research Assistants came from a sociology background and were well aware of how to use methods and techniques of data collection at individual, household and

community levels, two training workshops were organized for them prior to the commencement of the community-based study to enhance their knowledge, skills and sensitivity in order to investigate issues related to CKDu in the community. The first workshop focused on conceptual and methodological issues related to the study of Chronic Kidney Disease where ethical considerations were highlighted. This workshop was conducted at the University of Colombo by a multidisciplinary group of resource persons who came from Sociology, Economics and Medical backgrounds. The second workshop was organized at the RDHS office, Anuradhapura with the assistance of the Medical Officer, Health Education Officer and the two Research Assistants who were attached to the CKDu Prevention Unit in NCP. This interactive workshop was very significant as the research team was able to gain a thorough understanding of the issues related to CKDu while sharing experience from the local socio-cultural context before entering the concerned communities for empirical investigation.

Methods and Techniques of Data Collection:

The community-based study was conducted from a phenomenological perspective where multiple methods and techniques were adopted simultaneously with the objective of having a comprehensive insight of the illness burden at individual, household and community levels. Semi-structured questionnaire, in-depth interviews, Focus Group Discussions (FGDs), Key Informant Interviews, simple observations and participant observations were used in the study in order to collect both qualitative and quantitative data. The following table provides an overview of the study population covered using the different data collection tools.

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Study Population Covered by Using Different Data Collection Tools

Method of Data Collection	Medawachchiya	Padaviya	Total
Semi-structured questionnaire and Illness Narratives	100 patients and their households	100 patients and their households	200
Case studies in relation to dead persons due to CKDu	13 Households (in-depth interviews with the family members)	09 Households (in-depth interviews with the family members)	22
Focus Group Discussions (FGDs)	1 FGDs Male group -5 members Female group - 6 members	2 FGDs Male group - 5 members Female group -7 members	04
Key Informant Interviews	11 Key Informants	5 Key Informants	16

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(a) Semi-structured Questionnaire:

A semi-structured questionnaire was designed to gather information related to both patient and his/her household (See end of section for questionnaires). The local socio-cultural context was taken into consideration while preparing the relevant questionnaire which was pre-tested and finalized with necessary modifications. The pre-test was conducted in a location in proximity to the study community in Medawachchiya DS division.

As shown in above table the questionnaire was administered to 200 households with CKD patients. The questionnaire was administered through face-to-face interviews with the patient and/or his/her caregiver or any other family member/s. However, there were some instances where data were collected only from the caregiver or any other family member/s as the patient was in a critical condition and was unable to contribute his/her experience directly. The illness narrative of the patient was also collected during the time of administering the questionnaire.

(c) Focus Group Discussions

Four Focus Group Discussions, two in each location were conducted in order to collect information on community level impact of CKDu. Separate discussions were organized with male and female villagers while conducting FGDs. Historical background of the village, perceptions related to CKDu, the impact of CKDu and coping mechanisms were discussed in detail while conducting the FGDs.

(d) Key Informant Interviews

Key informant interviews were conducted with elderly villagers, office bearers of Community Based Organizations (CBOs), Priest at the village temple, service providers such as the Divisional Secretary, Development Officer, Grama Niladari, Medical Officers and Nurses at CKDu clinics. Socio-cultural background of the area, historical background of CKDu, their perception of illness and its impact on the community were discussed in detail.

(e) Observations

Observation technique was used as a data collection tool throughout the investigation process along with the other tools. The research team was able to gather and cross-check a lot of information with regard to the behavioral patterns of the patients and their families, interactions between patients and healthcare providers in the clinical setting, the role of CBOs, religious and ritual activities taking place in the locality etc. The team was also able to observe the patient profile through clinical records.

(f) Participant Observation

Participant observation was also used as a tool of data collection. Since the Research Assistants lived in the study community itself, while conducting fieldwork they were able to

engage in participant observation, an important research tool to collect qualitative data. In both communities they were able to participate in activities such as harvesting, ritual ceremonies after harvesting, funerals including CKDu patients, meetings of CBOs etc.

Field Investigation:

The field investigation relating to the community-based study was conducted from the first week of August to end of September 2011. The field work in both Padaviya and Medawachchiya DS Divisions were conducted in parallel where three research assistants were allocated to each community. The Research Assistants were located within the community throughout the investigation period. They were closely supervised by the two senior Sociologists who visited both communities once a week and even on some occasions they visited the field twice a week. The two sociologists facilitated the conducting of FGDs and Key Informant interviews and some of the in-depth interviews. They also participated in some of the events and activities taking place in both communities during the study period. The Medical Officer and two Research Assistants who were attached to the CKDu Prevention Unit in the NCP assisted the research team in field coordination.

Analytical Methodology:

As mentioned earlier, the community-based study was conducted from a phenomenological perspective. The subjective interpretations of patients and their families were analyzed by adopting the contextual analysis technique while locating their voices and experience at the center. Therefore, in each chapter we present their voice in boxes while evaluating the economic and psycho-social impact of CKDu on the patient, his/her family and the entire community.

Ethical Considerations:

The socio-economic impact and productivity study was undertaken as a part of the National Research programme on CKDu. The relevant research proposal and all the study materials including questionnaire and interview guidelines were approved by the Ethics Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka, prior to the commencement of the study. Permission was also obtained from the Provincial Health administration.

The consent of the patient, and/or the care-giver/ head of the households were obtained prior to enrolling them as subjects in this study. In all instances, the patients and/or the care-giver/ head of the household were given an introduction on the purpose of the study and their voluntary participation was accepted. The respondent or the household was given the freedom to opt out of the study at any time with no detrimental effect to any of the services provided prior to the beginning of the study. The consent was also obtained from all the participants who contributed to FGDs and Key Informant Interviews.

Confidentiality of all the information gathered from various methods and techniques will be ensured. The information will be kept for a period of 10 years after completion of the study and destroyed thereafter. Patient data will be secure and only available to the researchers, data entry operators, medical personnel and the policy makers.

Introduction to the Field Setting and the Profiles of Chronic Kidney Disease Patients:

As explained earlier, the present study was carried out in Medawachchiya and Padaviya Divisional Secretary Divisions (DS) in Anuradhapura District in the North Central Province of Sri Lanka. The first section will provide a brief description of the socio-economic background of the field setting which will be followed by the profiles of the Chronic Kidney Disease (CKDu) patients who were included in the sample of the present study. The socio-economic background of the study area is useful to locate the patients in their own social context to understand the impact the illness has on them and their families. Similarly an understanding of the demographic and socio-economic background of the patients is important.

Socio-economic Background of the Field Setting:

Anuradhapura District-

Sri Lanka is divided into nine provinces and the study was located in the North Central Province, one of the largest in the country. North Central Province has two districts, Anuradhapura and Polonnaruwa. Of the two districts, Anuradhapura is larger than Polonnaruwa and also is widely known as a CKD prevalent area.

Anuradhapura district has unique characteristics other than it being identified as a CKD prevalent area. It has a historical significance as the first ever ancient capital of the country. Even today it is a place of importance for Sri Lankans for its archaeological and religious significance. Anuradhapura as a district is the largest district among the 25 districts in the country. The total area of the district is sq. km. 9,741 which covers 68.5% of the whole province.

Sri Lanka's hydraulic civilization was based in Anuradhapura and even today the district has 2600 large, medium and small tanks irrigating large tracts of cultivable lands. Irrigation facilities are necessary as the district comes within the dry zone with little rain during certain months of the year. The annual rainfall for the district ranges from 1000 mm-1500 mm per year.

Anuradhapura district has 22 DS divisions, 694 Grama Niladari Divisions (GN) and 2715 villages. The number of local government units in the district is one Municipal Council, and 18 Pradeshiya Sabhas. The district has 7 electoral divisions. Anuradhapura is the capital city of the district. The district has a total population of 809000 and 251185 families (<http://www.statistics.gov.lk/DistrictStatHBook.asp?District=Anuradhapura&year=2011>).

According to the census statistics in 2001, the majority of the district population comprises of Sinhalese (90.7%). The next largest ethnic group is Sri Lankan Moors (8.3%) while Sri Lankan Tamils are a very small minority (0.1%). Similarly Buddhists are the majority religious community in the district and Islam is the next important religion as the second largest ethnic group in this area is Sri Lankan Moor (Economic and Social Statistics of Sri

Lanka 2011, Central bank of Sri Lanka, http://www.Cbsl.gov.lk/pics-n_docs/10_pul/_doc/statistics/other/econ_&_ss_2011.pdf).

The population in the district is mostly literate. However, there is a slight gender wise difference where males are more literate than females as shown in the following table.

Percentage Distribution of Population (10 Years and Over) by Literacy and Gender in the District of Anuradhapura

Literacy	Total%	Males %	Females %
Literate	90.5	92	88.8
Illiterate	09.5	08	11.2
Total	100.0	100.0	100.0

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Source: Sampath Pathi Kada, Medawachchiya DS Division 2010

Anuradhapura district is mainly rural and a majority of the population is engaged in cultivation. Paddy is a major crop in the area.

Medawachchiya Divisional Secretary Division -

Medawachchiya DS division which was selected for the study is located on the Anuradhapura- Vavuniya road. The boundaries of the division are Vavuniya district from the north, Rambewa DS division from the south, Kebitigollewa from the east and Central Nuwara Gam Palatha from the west. Medawachchiya DS division covers 507 sq. km. and it has 37 GN divisions and 112 villages. Within the local government it comes under the Medawachchiya Pradeshiya Sabha.

In 2010, the total population of the Medawachchiya DS division was 49,586. The sex distribution of the population showed that females were more than males as the statistics reveal- 25,222 females and 24,364 males. The total number of families in the DS division was 14,305. The ethnic composition in the division is given in the following table:

Distribution of Population by Ethnicity in Medawachchiya Divisional Division

Ethnicity	Number
Sinhalese	45,805
Moor	3,608
Tamil	173
Total	49,586

Source: Sampath Peti Kada, Medawachchiya DS Division 2010

It is very clear that Medawachchiya DS division is populated mostly by Sinhalese. Buddhism is the main religion in the area while there are a few who follow Islam, Christianity and Hinduism

Educational Level of the Village Population* in Medawachchiya DS Division

Village	No		Passed		Up to		Up to		Up to		Passed		Graduate		Total
	F	M	F	M	F	M	F	M	F	M	F	M	F	M	
Akkarawatte	1 4	2 6	9	13	1 4	18	39	35	18	14	20	13	1	1	235
Prabodagama	4 0	3 2	87	93	3 2	43	11	13	3	5	2	3	0	2	366
Phudivula	6	8	28	22	2 4	23	18	13	11	7	6	4	0	0	170
Attabagaskada	2 0	1 5	71	78	4 5	76	81	72	59	48	8	6	3	2	584
Paranahalmill ewa	1 2 3	1 0 2	16	12	1 8	11	6	4	4	2	2	1	0	1	302
Dutuwewa	2 5	1 1 3	87	37	1 7	8	5	3	2	1	2	0	2	0	302
Warakwewa	3 9	2 5	64	69	4 8	49	8	27	16	15	9	7	0	0	376
Mahakumbuk gollewa	3 6	1 2	13 6	13 9	8 0	74	69	65	39	31	20	19	2	3	725
Lunuphecyaw a	6 1	5 3	58	54	4 8	44	0	0	1	0	1	0	0	0	320
Kongollewa	7 3	8 2	17 8	15 7	4 3	36	21	17	12	10	2	0	1	0	660
Lolugaswewa	1 0	1 1	64	45	2 0	22	16	16	7	5	7	0	0	0	231
Attaweeragoll ewa	0	0	60	72	6 5	62	49	43	28	21	28	26	2	2	458
Mahadivulwe wa	0	0	10 2	10 7	8 6	78	26	30	36	42	8	12	1	1	529
Kodiyebandaw e	0	0	12	8	2 7	21	2	2	2	5	2	0	0	0	81
Gurukandega ma	6	3	69	51	3 2	27	2	5	0	1	0	1	0	0	197
Thammanaewa wak	2 1	2 2	45	47	2 8	30	29	30	22	20	11	11	1	1	318
Total	4 7 4	5 0 4	10 86	10 04	6 2 7	62 2	38 2	37 5	26 0	22 7	12 8	10 3	13	13	555 2

Note: *These are the villages from where the CKD patients were selected.

As per the previous explanation Medawachchiya DS division has 112 villages and the study covered 15 villages where CKDu patients were located. The educational level of the population in these villages is given above. According to the above table, 978 (17.6%) villagers who came under the present study have not received any formal education. Although national statistics on literacy shows that 90% are literate, in these villages it is not really the case. Thus it is important for the intervention mechanisms to take note of such situations. However, there are 26 university graduates. The majority has received education up to grade VIII. At present the DS division has one National School and 38 other schools.

Economic Activities of the Villagers* in Medawachchiya DS Division

Village	Teaching	Clerical	Driving	Office Labourer	Laborers	Security Service	Agriculture	Fishing	Casual Labour	Other	Total
Akkarawatte	6	28	8	14	50	67	90	0	12	32	307
Prabodagama	6	17	2	11	20	39	128	0	31	21	275
Phudivula	3	0	2	0	0	32	78	0	34	18	167
Attabagaskada	11	5	3	0	0	93	258	0	38	31	439
Paranahalmillewa	2	2	1	2	5	86	78	0	17	15	208
Dutuwewa	2	1	1	0	2	65	85	0	14	10	180
Warakwewa	4	4	7	1	16	32	45	0	73	19	197
Mahakumbukgollewa	5	25	3	2	49	66	125	0	46	17	338
Lunuphecyawa	0	0	0	0	0	61	260	0	20	5	346
Attaweeragollewa	11	9	2	1	13	69	86	0	19	11	221
Mahadivulwewa	11	11	4	0	0	46	122	0	14	28	236
Kodiyebandawe	0	0	0	0	0	10	21	0	5	4	40
Gurukandegama	0	0	0	0	0	38	70	0	17	5	130
Thammanaelawaka	5	1	0	0	0	71	128	0	54	6	265
Total	66	103	33	31	155	775	1574	0	394	222	3349

*These are the villages from where the CKD patients were selected

Source: Sampath PetiKada, Medawachchiya DS Division 2010

Agriculture is the most important economic activity of the villagers. 47% of villagers are engaged in cultivation. However, due to the prolonged war, a number of villagers (23%) have received employment in the security services (mostly in the Civil Security Department) as shown in the above table.

According to the DS Division records 134 deaths due to CKD have been reported. In addition to this, 192 have been diagnosed as CKD patients. Presently the DS division has one District hospital and two rural hospitals.

Padaviya Divisional Secretary Division -

Padaviya DS division is surrounded by a number of GN divisions. The boundaries of Padaviya DS division are Alikbulaga and Abayapura GN division from north, Bogaswewa GN division from south, Urewa GN division from east, Biso Kotuwa GN division from west Mahasenpura DS division from north east and Budangala GN division from north west.

The community study was carried out in five GN divisions – Sudrshana Gama, D 10, 18 Post, B Yaya and Budangala in the Padaviya DS division. The DS division has a total population of 22,880 and the population in the studied GN divisions is given below:

Population Distribution by Sex in GN Divisions* of Padaviya DS Division

GN Division	Males	Females	Total
Sudarshana Gama	1109	1121	2230
D10	735	718	1453
18 Post	957	1017	1974
B Yaya	929	870	1799

*These are the GN divisions that were selected for the study. However data is not available for Budangala GN division

Source: Padaviya DS division Records 2010

Similar to the villages in Medawachchiya, Sinhalese are the dominant ethnic group and Buddhism is the main religion in the GN divisions that came under the community study. In all GN divisions majority have permanent houses. However there are 170 families living in temporary houses and 133 families are not having housing. This is more to be seen in D10 and B Yaya as shown in the following table:

The table below highlights that even basic needs are not being met for some families in these GN divisions. Available statistics for Sudarshana Gama, Buddhangala and B Yaya GN divisions reveal that there are many households that receive Samurdhi benefit from the Government.

Housing Conditions of Selected GN Divisions for the Study in Padaviya DS Division

Type of Housing	Sudarshana Gama	D10	18 Post	Buddhangala	B Yaya	Total	%
Permanent	399	296	442	244	300	1681	67.5
Semi-permanent	94	36	78	102	195	505	20.3
Temporary	59	10	-	46	55	170	06.8
No housing	-	74	04	-	55	133	05.4
Total	552	416	524	392	550	2489	100.0

Source: Padaviya DS division Records 2010

Samurdhi Beneficiaries by GN Divisions in Padaviya DS Division

GN Division	Number of Samurdhi Beneficiaries
darshana Gama	184
Buddhangala	144
B Yaya	140

Source: Padaviya DS Division Records 2010

Chronic Kidney Disease patients received Government assistance of Rs. 500 per month at the time of the survey. Available statistics for Buddhangala GN division show that 09 patients receive such assistance and in B Yaya GN division 20 patients receive the same. Data are not available for the other GN divisions.

Profiles of Identified Patients:

Demographic Characteristics -

As shown in the demographic profile of patients, a clear differentiation between the sexes was identified where male dominance is apparent in the identified CKD patients in both the DS divisions. However, there are a significant number of female patients as shown in the following table.

Sex distribution of patients by DS divisions

DS Division	Male	%	Female	%	Total
Medawachchiya	65	65.0	35	35.0	100
Padaviya	66	66.0	34	34.0	100
Total	131	65.5	69	34.5	200

A majority of the patients belong to the age group between 51 and, 60 and above 60 years. There are two important implications; one is the implication on the labor force and the loss of the main income to the family. Second the burden on the family in the lack of any social security schemes for old age. There are also a few patients of younger ages as given in the following table.

Age Distribution of Patients by DS Divisions

	Medawachchiya	%	Padaviya	%	Total	%
<40	9	9.0	7	7.0	16	8.0
41-50	16	16.0	23	23.0	39	19.5
51-60	40	40.0	33	33.0	73	36.5
>60	35	35.0	37	37.0	72	36.0
Total	100	100.0	100	100.0	200	100.0

Marital Status of Patients by Gender and DS Division

Gender	D.S.Division	Unmarried	%	Married	%	Divorced	%	Widow	%	Total	%
Male	Medawachchiya	2	3.1	61	93.8		0.0	2	3.1	65	100
	Padaviya	1	1.5	63	95.5			2	3.0	66	100
	Total	3	2.3	124	94.7			4	3.1	131	100
Fe-male	Medawachchiya	1	2.9	17	48.6	0	0.0	17	48.6	35	100
	Padaviya	0	0.0	20	58.8	1	2.9	13	38.2	34	100
	Total	1	1.4	37	53.6	1	1.4	30	43.5	69	100
Total	Male	3	2.3	124	94.7		0.0	4	3.1	131	100
	Female	1	1.4	37	53.6	1	1.4	30	43.5	69	100
	Total	4	2.0	161	80.5	1	0.5	34	17.0	200	100

Looking at the marital status of the patient, there is an important gender difference. While a majority of male patients are married, a significant number of female patients are widows. This shows that females can be more vulnerable by not having the care of spouse and having to depend on children. However, area wise there is not much of a difference, except the number of female widows in Padaviya is higher than Medawachchiya.

This brings out an important issue in times of intervention and providing assistance to patients and their households. While there needs to be uniformity in providing assistance to patients as all are equally suffering from the illness, specific differences also should be given consideration.

A majority of the patients in both DS divisions are heads of households making the whole household vulnerable both economically and socially.

Patient's Relationship to Head of the Household by DS Divisions

Relationship to Household Head	Medawachchiya	%	Padaviya	%	Total	%
Household Head	67	67.0	71	71.0	138	69.0
Spouse	15	15.0	16	16.0	31	15.5
Son/daughter	2	2.0	1	1.0	3	1.5
Parents	9	9.0	9	9.0	18	9.0
Brother/sister	1	1.0	1	1.0	2	1.0
Uncle/Aunt	6	6.0	2	2.0	8	4.0
Total	100	100.0	100	100.0	200	100.0

Looking at the residential status there is a clear difference in the two DS divisions, where Padaviya being a settlement a majority had migrated to the area receiving state land. However, the majority have been living in the area for more than thirty years.

Residential Status of Patients by DS Division

Duration	Medawachchiya	%	Padaviya	%	Total	%
From Birth	72	72.0	18	18.0	90	45.0
Migrated	28	28.0	82	82.0	110	55.0
Total	100	100.0	100	100.0	200	100.0

Educational Status -

The following table shows the level of education by division

Educational Level of Patients by DS Division

Educational Level	Medawachchiya	%	Padaviya	%	Total	%
No schooling	7	7.0	4	4.0	11	5.5
Primary	36	36.0	54	54.0	90	45.0
Secondary	40	40.0	34	34.0	74	37.0
Passed GCE O/L	11	11.0	5	5.0	16	8.0
Up to GCE A/L	2	2.0	1	1.0	3	1.5
Passed GCE A/L	2	2.0	0	0.0	2	1.0
Degree /Professional qualification	1	1.0	1	1.0	2	1.0
Other	1	1.0	1	1.0	2	1.0
Total	100	100.0	100	100.0	200	100.0

Looking at the educational level of the patients, in Medawachchiya 40% have secondary level and 36% primary level education. However in Padaviya the educational level of the patients is lower where 54% have just primary level education. It is also important to note that while 7% of patients in Medawachchiya and 4% of patients have not received any formal education.

Economic Background-

While a majority of patients are unable to engage in any activity due to their illness, there are still some who are engaged in economic activities. However, due to their illness they have less capacity in fulfilling their economic responsibilities.

Activity Status of Patients by DS Divisions

Activity	Medawachchiya	%	Padaviya	%	Total	%
Household work	10	10.0	7	7.0	17	8.5
Employed	43	43.0	27	27.0	70	35
Unemployed	1	1.0	0	0.0	1	0.5
Retired	1	1.0	1	1.0	2	1
Elderly	4	4.0	10	10.0	14	7
Sick	41	41.0	54	54.0	95	47.5
Helping for the family business	0	0.0	1	1.0	1	0.5
Total	100	100.0	100	100.0	200	100

Main Occupation of Patients by DS Divisions

Occupation	Medawachchiya	%	Padaviya	%	Total	%
Executive / Administrative	1	2.0	0	0.0	1	1.0
Clerical	1	2.0	0	0.0	1	1.0
Teaching	0	0.0	2	4.2	2	2.0
Cultivation	22	43.1	31	64.6	53	53.5
Casual labour	2	3.9	0	0.0	2	2.0
Blue-collar work	1	2.0	4	8.3	5	5.1
Security force	0	0.0	3	6.3	3	3.0
Civil Security Department	16	31.4	3	6.3	19	19.2
Technical work/ Skill work	1	2.0	3	6.3	4	4.0
Transport Sector	1	2.0	0	0.0	1	1.0
Other	6	11.8	2	4.2	8	8.1
Total	51	100.0	48	100.0	99	100.0

In both Medawachchiya and Padaviya, a majority of patients are engaged in cultivation. This is more ostensible in Padaviya as it is an irrigated settlement area where cultivation is the main economic activity for the many. The next important economic activity in both the areas is civil security service where many received employment due to the war in the north and east in the country. This is more apparent in Medawachchiya.

As per the aforesaid explanation, since a number of patients in Medawachchiya are engaged in civil security service, their income level is better than the patients in Padaviya. However, in both DS divisions there are not many patients who receive a monthly income between Rs. 15001 and Rs. 30000. It is important to note that there are patients in both

Medawachchiya and Padaviya DS divisions who receive less than Rs 2500 as monthly income as shown in the following table.

Monthly Income of Patients by DS Divisions

Income (Rs.)	Medawachchiya	%	Padaviya	%	Total	%
<2500	8	14.5	10	17.5	18	16.1
2501-7500	16	29.1	30	52.6	46	41.1
7501-15000	17	30.9	11	19.3	28	25.0
15001-30000	14	25.5	6	10.5	20	17.9
Total	55	100.0	57	100.0	112	100.0

The total family income of patients is once again better in Medawachchiya compared to Padaviya as shown in the table below. The reason would be because cultivation is the main source of income of the majority, whereas in Medawachchiya, there are those who are engaged in more regular work other than cultivation.

Total Family Income of Patients by DS Divisions

Income (Rs.)	Medawachchiya	%	Padaviya	%	Total	%
<5000	10	10.0	19	19.0	29	14.5
5001-15000	19	19.0	30	30.0	49	24.5
15001-25000	20	20.0	23	23.0	43	21.5
25001-50000	38	38.0	22	22.0	60	30.0
>50000	7	7.0	2	2.0	9	4.5
No Income	6	6.0	4	4.0	10	5.0
Total	100	100.0	100	100.0	200	100.0

Although the income level of the patients' families in Medawachchiya is better than Padaviya, the number of families receiving Samurdhi in Medawachchiya is more as against Padaviya. In Padaviya 80% of families do not receive Samurdhi whereas in Medawachchiya it is only 48%. This shows the need to provide special assistance to these families as they are economically vulnerable.

Samurdhi Beneficiaries by DS Divisions

Receiving Samurdhi	Medawachchiya	%	Padaviya	%	Total	%
Receiving	52	52.0	20	20.0	72	36.0
Not receiving	48	48.0	80	80.0	128	64.0
Total	100	100.0	100	100.0	200	100.0

A majority of patients live in permanent houses while a very few live in temporary houses as shown in the following table.

Housing Conditions of patients by DS Divisions

Housing Condition	Medawachchiya	%	Padaviya	%	Total	%
Permanent	68	68.0	74	74.0	142	71.0
Semi-permanent	30	30.0	23	23.0	53	26.5
Temporary	2	2.0	3	3.0	5	2.5
Total	100	100.0	100	100.0	200	100.0

A majority of patients live in a land of their own. However, there are a few who have either joint ownership to land or not owning land and live as squatters.

Patients Ownership to Land by DS Division

Type of Ownership	Medawachchiya	%	Padaviya	%	Total	%
Owned	94	94.0	71	71.0	165	82.5
Joint	5	5.0	15	15.0	20	10.0
Squatter	1	1.0	0	0.0	1	0.5
Other	0	0.0	14	14.0	14	7.0
Total	100	100.0	100	100.0	200	100.0

Time Duration of Identified as a Patient -

Looking at the illness profiles of the patients it is clear that while some have been identified as patients for a long time the others are not. However, in Padaviya most of the patients do not have a long record of the sickness.

Time Duration of Identified as a Patient by DS Division

Time duration of identified as a patient by DS division

Duration	Medawachchiya	%	Padaviya	%	Total	%
Less than 2 years	22	22.0	18	18.0	40	20.0
Between 2-4 years	8	8.0	31	31.0	39	19.5
Between 4-6 years	26	26.0	24	24.0	50	25.0
Between 6-8 years	27	27.0	21	21.0	48	24.0
Between 8-10 years	14	14.0	5	5.0	19	9.5
More than 10 years	3	3.0	1	1.0	4	2.0
Total	100	100.0	100	100.0	200	100.0

The above discussion clearly reveals that CKD patients are not a homogeneous group although they could be identified as a particular group suffering from one sickness. Therefore the impact, resilience and coping to the situation of patients and their families may differ, which could also have a different impact on them. Thus the patients' profiles as given above would be used in the analysis in the following chapters. The socio-economic characteristics of the DS divisions would be also useful in the analysis.

Results/outputs

Community Discourse on CKDu and Treatment Seeking Behaviour:

The community perception of CKDu is significant in evaluating its impact on the individual patients, their households and the communities concerned. In both Medawachchiya and Padaviya, CKDu is considered as the most sensitive issue of everyday life of villagers and it is articulated as a tragedy and a struggle between 'life and death' of a human being. The villagers, based on their experience have developed a discourse with regard to the prevalence of CKDu in their locality, the cause of illness and its adverse effects on their everyday life. The focus of this chapter is to explore the above discourse with particular attention to lay perceptions of CKDu and the relevant treatment seeking behavior. The economic and psychosocial impact of CKDu and coping strategies adopted by villagers will be thoroughly analyzed in the following chapters of this report.

(a) The Community Discourse on CKDu:

The community discourse on CKDu in both Medawachchiya and Padaviya has been emerging since late 1990s after identification of CKD with unknown etiology as one of the main health problems in the localities by healthcare providers. Initially, in the late 1990s and early 2000, the problem was identified by local healthcare providers after investigating

a considerable number of patients who visited them seeking treatment for symptoms such as continuing fever, back pain, swollen legs, headache, body-ache, kidney stones, urine infections and loss of appetite. While investigating patients with the above symptoms, the local healthcare providers were able to diagnose the disease as CKD but the etiology is yet to be determined as it goes beyond all existing knowledge systems and explanatory models with regard to renal failure. The local healthcare providers also noticed that the number of patients visiting them with the above symptoms was gradually increasing. In this context, the local practitioners gave more attention to this issue and conducted a number of screening programmes at grass root levels with the objective of identifying CKD patients. As a result, they were able to identify a large number of patients with CKDu in the North Central Province and by now it has become one of the main causes of death in the North Central Province. Within the province there is a high prevalence in Medawachchiya and Padaviya DS Divisions (CKDu Prevention Unit, North Central Province: 2011). Within the community discourse, there is a dilemma whether CKDu is a new phenomenon or an old issue in their locality.

Is CKDu a Recent Phenomenon in the Local Context?

The village discourse with regard to the history of the prevalence of CKDu and its etiology is quite complicated and contradictory. Both in Medawachchiya and Padaviya, the community discourse suggest that the people were aware of patients with similar symptoms in the area as far back as the 1960s, though the numbers were small, and diagnosis was not known to be CKD. According to the narratives of villagers, symptoms of body swelling, anemia and disfigurement of face were identified locally as “pipihaluwa” in Medawachchiya and “pitthapanduwa” in Padaviya. Some of the villagers believe that pipihaluwa/pitthapanduwa would be a similar condition to that of CKDu and believe that it was closely associated with a severe condition of anemia (enga sudumeli weema- weakness of the body due to lack of sufficient blood in the body). The experience of villagers further verified the fact that patients who suffered from pipihaluwa/pitthapanduwa were all treated with more nutritious food such as different kinds of meat (etikukul mas, talagoi mas, kiri-ibi-mas), milk and some of the green leaves available in their local environment as the cause of illness was believed to be a condition of anemia. Complementary to providing nutritious food, herbal medicine was used as a treatment along with various types of religious and ritual practices simultaneously.

The community discourse with regard to the history of CKDu in the local context creates a dilemma as some of the villagers connect their past experience with regard to pipihaluwa/pitthapanduwa along with the symptoms of CKDu and view that the same has been prevailing in their locality for a long time, even though it was not recognized as CKDu and the numbers were relatively less. As against this view, most of the villagers view CKD as a recent phenomenon in their locality due to adverse effects of contemporary transformations that have been taken place in their social and natural environments since 1970s after the introduction of agricultural modernization process to the local context. The following section further explores their views on the causes of illness.

Lay Perception on the Causes of CKDu

In parallel to the process of identification of CKDu patients by local healthcare providers, a number of studies were also conducted at village level to discover the etiology of CKD by various researchers who came from different disciplines. These studies have focused on various dimensions including both clinical investigations as well as the risk factor that were associated with the surrounding environments of the concerned patients. However, the community discourse suggests that the villagers were marginalized throughout the process of discovering the etiology CKD by limiting their participation only to giving necessary items for scientific investigation (some of the body parts of patients such as part of kidney, hair, nails and material objects such as water samples from different sources, soil samples, some of the food items, plants etc.) and hardly ever taken their illness experience and risk behavioral patterns into account while investigating the etiology.

The present empirical study also uncovers that most of the interventions related to both identification of CKDu patients and discovering the etiology have been implemented in an ad-hoc manner rather than an organized programme in the rural context. Thus, the outcomes of these investigations too have created a rather complicated situation at village level not just because of quite contradictory explanations by different experts but also due to their varying conclusions. Under these circumstances, the villagers are confused on the one hand and are very critical about what is happening in their locality on the other. However, their discourse related to the etiology of CKD has been shaped by the above process.

The villagers have different interpretations with regard to the cause of CKD based on their own experience as well as the awareness that they gained from various experts who came to their locality in order to investigate the etiology of CKD. According to the community discourse, unhygienic drinking water, heavy usage of pesticides and chemical fertilizers, dehydration due to hot weather in dry zone, snake bites, genetic factors, due to some other ailments such as hypertension, diabetes, body pains etc., heavy use of alcohol, long term use of medicines and hard work associated with their livelihood activities are some of the causes for CKD. In addition to the above factors some of the edible stuffs that are available in the locality such as *thala-kola* (one of the leaves commonly used by the villagers as a betel replacement in this particular locality) were also considered as a possible cause for CKD as many villagers commonly use it as a habitual practice. Even though the villagers have identified many possible causes for CKD, they consider the poor quality of locally available drinking water as a main cause of CKD and therefore they are in search of potable water from the optional sources that they believe are not contaminated, even at a very high cost.

It is significant to note that a Sociological study on behavioral factors related to CKDu was carried out in Medawachchiya and Padaviya DS Divisions (2009) reflecting the fact that there were no CKD patients reported in the control village namely Gonamariyawa, in Medawachchiya DS Division where people have access to spring water for drinking. The above comparative study also highlighted the fact that livelihood activities and most of the other behavioral patterns were very similar in both study villages and in the control village-Gonamariyawa except the source of drinking water which further highlighted the necessity

of investigating the correlation between drinking water from spring well and the prevalence of CKD by conducting a screening test for CKD in Gonamariyawa where people have had access to spring water for a long time (Liyanage, C. and Jayatilaka, R., 2009).

The present study too, highlights the importance of conducting such a thorough scientific investigation to observe the correlation between CKD and the potable water as many people walk several miles in search of spring wells. They strongly believe and are aware that CKD does not prevail in villages where there are spring wells in the locality such as Gonamariyawa, Singhaya Ulpata etc.(this factor will be elaborated in chapter six under coping mechanisms). The following section focuses only on the lay perception on the articulation of CKDu in the local context.

The Articulation of CKDu within the Community Discourse

As mentioned earlier, the villagers perceive CKDu as a struggle between “life and death” in their everyday life. As an outcome of this health hazard, the wellbeing of the patient and his/her family as well as the wellbeing of the entire community gradually deteriorates. In this scenario, CKDu is articulated within the community discourse as not only ‘life threatening’ and ‘incurable’ but also as an illness that associated with a lot of “injustice”(asadharana ledak). The villagers are very critical on several issues related to the prevalence of CKDu in their locality. As the villagers raised in their focus group discussions, key informant and in-depth interviews “why is only this particular geographical location vulnerable to this health hazard and why does it not prevail in Colombo or other areas of the country”, “why now and not in the past”, “why only some members of the family/community get affected while others who are in the similar condition are not affected” etc. While reviewing more than two decades of their experience, the villagers correlate the cause of illness with Karma in order to confirm the above issues. As one of the members who contributed at a FGD pointed out “mekka merenna lan wenakota hedena karma ledak” (this is an illness that a person can get when his/her life expectancy is almost over for the present birth due to karma).

The empirical evidence clearly suggests that there is a fear with regard to the illness and stigma is gradually developing with CKDu. There is also an emerging trend of hiding the illness even from their close relatives and the neighborhood. The empirical evidence shows that on the one hand, the patient who wishes to keep CKDu as a secret attempts to hide it from fellow villagers by saying that they attend another clinic (hypertension or diabetic clinics) and not the CKDu clinic at the hospital. On the other hand, there is a trend of labeling people as CKDu patients by others even if they attend other clinics at the nearest hospital and not the CKDu clinic. The empirical evidence also shows that there is a trend among patients to bypass the nearest healthcare facility and visit faraway places even with lots of difficulties just to maintain the confidentiality of their disease identity (these issues will be explained further in chapter 5 under psychosocial impacts of CKDu).

The lay perception and the community discourse on CKDu have been further influenced through responses and interventions by healthcare providers with regard to the identification of CKD patients and treating their ill-health. However, the community discourse has its own culture bound interpretations that go beyond the biomedical

explanatory model with regard to the prevalence of CKD, its etiology and also its treatment. Kleinman's explanatory model would be useful in looking at the process by which illness is patterned, interpreted and treated in the local context by both the experts and the lay people who live in their relevant social-cultural and ecological context. According to Kleinman's explanatory model, basically there are five aspects of illness, the etiology or cause of the illness; the timing and mode of the onset of symptoms; the patho-physiological process; the natural history and severity of the illness and appropriate treatment for the condition which are significant in understanding different perspectives, knowledge and attitudes towards CKDu from both user and the provider perspectives. Thus, there are three overlapping and interrelated sectors of healthcare that include the popular sector, the folk sector and the professional sector, where each sector has its own way of explaining and treating (Kleinman 1980).

The identified CKD patients have been categorized into stages while considering the severity or the progress of disease and level of the function of kidneys by healthcare providers based on their biomedical model of renal failure. Even though the community discourse on CKDu is overlapping and interrelated to a certain extent with the above biomedical explanatory model, the lay people also have their own culture specific interpretations in this regard. Accordingly, both communities in Medawachchiya and Padaviya have recognized three categories of CKDu which are based on their illness experience over the past two decades. The categorization has an impact on their treatment seeking behavior with regard to CKDu. The three categories of CKDu identified by the lay people are as follows:

- **Vakugadu ekilenawa** (the kidneys shrink, or the shrinking of kidneys)
- **Vakugadu diyawenawa** (the kidneys dissolve, or the dissolving of kidneys)
- **Vakugadu idimenawa** (the kidneys swell, or the swelling of kidneys)

Shrinking of kidneys- As verified by the villagers in both communities, each category of CKDu can be identified based on its symptoms. The cause/s of illness may vary depending upon the illness category. According to village narratives, physical appearance of people who suffer from "shrinking of kidneys" looks like they are very healthy and no visible symptoms are generally found except for passing protein with urine for which they believe medicine is not required. According to their experience, urine infections are very common in their locality due to dry climatic conditions. They believe that this type of illness can be controlled by increasing daily water consumption. Most of these patients are identified as CKDu patients due to screening tests conducted at grassroots level. Even though these people are labeled as CKD patients they are not given any medication and not requested to attend regular clinics for CKDu. However, they are instructed to go for a checkup once a year.

Dissolving of kidneys- The villagers believe that kidneys can gradually dissolve due to various reasons. Breathing difficulties, back pain and headache are some of the symptoms of dissolving of kidneys. They also believe that it is impossible to recover completely even though such symptoms can be controlled by taking medicine. Most of the patients who

attend CKD clinic are relating their problem either to dissolving of kidneys or swelling of kidneys.

Swelling of kidneys- This is considered as the worst category of CKDu by the villagers. According to their illness narratives “it is a matter of life and death”. Swollen body, severe breathing difficulties, loss of appetite is some of the symptoms of this type of problem. The patients who are recommended for dialysis are easily put into this category by the villagers. The empirical evidence suggest that there is a fear amongst the villagers to go through dialysis as it symbolically suggests the imminent death of the patient by the third time of his/her dialysis. The illness narratives of this category indicate that there is an emerging trend of avoiding dialysis as a treatment for CKDu by the concerned communities. There are some cases where patients have completely stopped visiting the regular clinic when they are referred for dialysis.

An unpleasant and a painful death are expected due to swelling of kidneys by the villagers. They believe that this type of experience in the life of a person is mainly due to karma (cankers associated with the realm of transmigration of a person). Thus, the self and the identity of relevant patients are reviewed by the villagers. The study team was able to further verify the fact with an insight from a case study of a 40 year old woman who died due to swelling of kidney in Medawachciya during our investigation period. The relatives of the patient and villagers strongly believed that the death was due to bad Karma. The patient’s condition became very critical just before her death where she badly suffered from severe breathing difficulty for two weeks. The incident was interpreted by the relatives and the neighbors as an outcome of her bad karma not only in the previous birth but also with the present birth as well. The patient’s mother pointed out

“She is an unlucky child and I am so sorry for her. As far as I can remember, she hardly went to a temple and never offered at least a single flower by her hands to the Lord Buddha”.

The funeral took place after two days of her death. The study team was able to observe that her profile with diagnosis card and related reports were kept on the coffin until the end of her funeral which symbolically expresses the view of the relatives that they were not responsible for the death of their relative as evident but it was due to her own karma. The Buddhist perspective of life and physical body gives a consolation to relatives and the neighborhood (the physical body is not permanent; mind should be developed etc.).

The above lay explanatory model that emerges through community discourse on CKDu has been shaped by day-to-day interactions between healthcare practitioners and the patients in the clinical setting. While the practitioners are compelled to categorize the patients into different stages by using their medical gaze with standard measurements, the lay people too react by replying not as passive patients but also as active agents. Therefore, the community discourse is equally important as that of the medical discourse and the health hazard should be located within the relevant sociocultural context. The community discourse on CKDu is also useful in exploring economic and psychosocial impacts of illness on patients, their household and the community which will be dealt with in chapters four and five. The following section explores the treatment seeking behaviour of CKDu patients in the light of the above community discourse in this regard.

(b) Treatment Seeking Behaviour:

As mentioned earlier, the present study includes a sample of 200 CKD patients and their households in Medawachciya and Padaviya DS Divisions. The following table provides an account of the ways in which people were diagnosed as CKD patients.

Diagnosis as CKDu patient

The mode of diagnosis as CKDu patient	Medawachciya No	%	Padaviy No	%	Total	%
When visited a doctor/ hospital seeking treatment for symptoms/ ailment	71	71.0	91	91.0	162	81.0
Mobile clinic for screening CKDu at grass root level	29	29.0	09	9.0	38	19.0
Total	100	100.0	100	100.0	200	100.0

It is significant to take into account that 81 % of patients in the study sample were diagnosed as CKDu patients when they visited a doctor/ hospital seeking treatment for symptoms such as back pain, stomachache, muscle pain, swollen body, urine infections, fever etc. As mentioned earlier, a number of mobile clinics were conducted at grassroots level by the local healthcare providers in order to identify patients with CKDu. As a result, 19% of the study population was identified as CKDu patients through these screening programmes. Thus, the above findings highlight the fact that people associate this illness with symptoms only when they are diagnosed at the acute stage and one can hardly see any trend of self screening for CKDu by the villagers even though it is considered as the most sensitive issue in their local context. However, villagers are keen on mobile clinics for screening. The findings clearly suggest that there is a need for better health education regarding the need for self-screening, knowledge on early screening and the villagers have requested related services, through mobile clinics if possible. The evidence of this study suggest that the importance of maintaining patients' confidentiality while conducting such screening tests for CKDu at village level as the disease has been already associated with stigma in the local context.

The First Communication between Doctor and Patient at Clinical Setting;

As mentioned earlier, many of the patients came to know that they were suffering from CKDu when they went to clinic/hospital with different symptoms where the doctor had directly communicated to the patients about the sickness. The first experience had been very hard on all. However, the patients are not homogeneous, they react differently even to similar situations depending upon his/her personal characteristics as well as the strength

and limitations of his/her immediate networks. As evident from narratives of patients, their reactions have been different from one patient to another. Some were unable to accept the doctors' diagnosis as such thing could not happen to them as CKDu is associated with the struggle between life and death in the local context. While some patients did cry loudly, shouted at doctors without being able to control their emotions, some others could control their emotions in front of the doctor but reacted in different ways such as crying later, discussing with family members, keeping it as a secret from all the family members or sharing with only some members of the family. However, there were also some patients who were able to accept the doctors' diagnosis but went for second opinion to private medical practitioners to confirm the sickness. Some of the voices of patients are as follows:

Box 3.1: Immediate Response by Patient when he/she was diagnosed as CKDu

"The doctor said that there is 8 ½ cm stone in the upper part of one of my kidneys. When I heard this I cried and fainted." (Male patient)

"When the doctor told me that there is a problem in my kidneys, I could not bear it. I felt extremely sad. I shouted at the doctor saying that I cannot agree and that the doctor had made a mistake" (Male Patient)

"I came to know that I'm suffering from CKDu at a mobile clinic conducted in our village. However, I kept it as a top secret from my children as I didn't want them to suffer because of my illness. When they asked as to why I go to monthly clinic I told them a white lie connecting it with one of the side effects of a previous surgery that I had undergone. Somehow after a year or so my children came to know about this from some other sources and later they came to me for confirmation. Then I slowly explained it to them, consoling them not to worry and it's under my control and the nature of life is like this" (Widow Patient)

The above experience of patients elucidates the importance of understanding different behavioral patterns of patients rather than considering them as mere objects for scientific investigation without any subjective feelings. In the local context, it remains a dilemma as to whether the healthcare practitioner should convey his/her observation with regard to diagnosis of CKDu directly to the concerned patient. The patients' narratives clarify that most of the patients and their family members were unhappy when the practitioner conveyed the diagnosis directly to the concerned patient as the illness is associated with a grave symbolic meaning in the local context. As villagers pointed out in their FGDs "if a person is diagnosed as CKDu, not only the psychology of that particular patient but also the mental well-being of the whole family starts to rapidly deteriorate where all of them suffer together". The above evidence clearly suggests that the importance of considering family as a unit even in the clinical setting when dealing with ill-health of an individual. The evidence also highlights the necessity of integrating clinical social workers into local healthcare delivery system as those professionals are qualified with required knowledge, skills and competency in order to mediate such situation and also to overcome most of the gaps arising in interaction between the user and the healthcare provider within the clinical setting. This is one of the urgent needs in the local context where the health hazard has already become a tragedy.

Patterns of Help/Health Seeking Behaviour:

As mentioned earlier, 200 CKDu patients and their family members were interviewed for the present study. In addition to the above sample, the community based study was able to conduct 22 case-studies, 13 case-studies in Madawachciya and 9 case-studies in Padaviya DS Divisions in relation to the patients who died due to CKDu in the recent past. The relevant data were gathered through interviews with the close relative of the above patient while reviewing their relevant available records. While revealing illness narratives of both the above 200 CKDu patients and the 22 case-studies of dead patients due to CKDu, different patterns of help/health seeking behavior can be identified.

Treatment Seeking Behaviour of Dead Patients due to CKDu;

As revealed through illness narratives of most of the dead patients, there was no clear-cut pattern of help/health seeking behavior with regard to CKDu. Most of them were diagnosed as CKDu patient while they were seeking treatment from government hospitals for different ailments and some of the CKD related symptoms. However, the empirical evidence suggests that those patients have not followed any regular treatment for CKDu as they have shifted from one healing practice to another in an ad-hoc manner. Accordingly, most of dead patients had resorted to indigenous medicine (this includes both Ayurveda and desiya chikithsha) and various types of religious/ritual healing practices as their main therapeutic options while attending the government hospitals for western medicine when the illness became quite serious. The evidence also reflects that some of these patients had even visited remote places seeking religious and ritual healing practices in this regard. As some of the relatives of patients concerned have pointed out the prayer meeting held at Koswatta (commonly known as Koswatta-deva-yakgawa) was a very popular event among the CKDu patients from 2007-2009. There was an organized transport service for this purpose every Saturday from Padaviya to Koswatta, in order to take patients for the prayer meeting. They also had visited many distant places in search of indigenous medicine for CKDu. All the above case-studies further verify the fact that patients had not attended the regular clinic for CKDu in the hospitals. However, most of the above patients had from time to time visited western treatment when they were in a critical condition while experiencing all the above therapeutic options as a backup healing system. Most of the above patients had visited Anuradhapura and Kandy hospitals for treatment when the problem became serious.

Patterns of Help/Health Seeking Behaviour of Current Patients;

A clear pattern of treatment seeking behavior can be identified within the sample of 200 CKDu patients who seek treatment at present in both Medawachchiya and Padaviya DS Divisions. The following table provides a distribution of patients based on the stage of their renal failure by DS Divisions. The stage of renal failure of each patient was identified by observing the relevant diagnosis card where the research team did not ask any question from patient in this regard.

The Stages of Renal Failure by Division

Stage of Renal Failure	Medawachchiya No	%	Padaviya No	%	Total	%
Stage 1	6	6.0	3	3.0	9	4.5
Stage 2	74	74.0	95	95.0	169	84.5
Stage 3	20	20.0	2	2.0	22	11.0
Total	100	100	100	100	200	100

As mentioned earlier, 81% of patients in the sample were diagnosed as CKDu only when they visited a doctor/hospital seeking treatment for relevant symptoms or other ailments. The above table clearly shows that 84.5 % of patients are in the 2nd stage of the Renal Failure. The data further reveal that DS division wise there are some discrepancies. The rate of those who are in the 3rd stage of Renal Failure is quite high in Medawachchiya as the percentage is 20 while it is only 2 % in Padaviya where the vast majority are in the 2nd stage of Renal Failure. The following table indicates whether the CKDu patients receive any regular treatment for their sickness.

Regular Treatment for CKDu by Gender

Gender	Receive Regular Treatment	Medawachchiya No.	%	Padaviya No.	%	Total	%
Male	Yes	58	89.2	61	92.4	119	90.8
	No	7	10.8	5	7.6	12	9.2
	Total	65	100.0	66	100.0	131	100.0
Female	Yes	35	100.0	33	97.1	68	98.6
	No	0	0.0	1	2.9	1	1.4
	Total	35	100.0	34	100.0	69	100.0
Total	Yes	93	93.0	94	94.0	187	93.5
	No	7	7.0	6	6.0	13	6.5
	Total	100	100.0	100	100.0	200	100.0

As shown in the above table, more than 90% of CKDu patients in both locations utilize regular treatment for their ailment. However, it was evident that there were some gender wise discrepancies in this regard. Comparatively the percentage of female patients who receive regular treatment is higher than that of their male counterparts. As evident from the above data, 10.8 % of male patients in Medawachchiya and 7.6 % of male patients in Padaviya have not gained regular treatment for CKDu. The main reason was that some of the male patients face some practical difficulties in getting leave from their workplace to attend the monthly regular clinic. Only a few patients have mentioned that they are compelled not to use regular treatment due to side effects of medicine and only two patients pointed out that there is no use of medicine as it is an incurable illness. There was only one female patient who does not take regular treatment. She has stopped attending the clinic since she was asked to go for dialysis.

Nearest Government Hospital as the Regular Treatment for CKDu:

Most of the patients who receive regular treatment attend the CKD clinics at the nearest government hospitals while only a few patients have to cover some distance for this purpose. This shows that patients believe that the government hospitals/clinics are the best source of medical attention. Most of the patients have a well maintained file with their diagnosis card and reports of various tests that they have undergone. The file is kept in a safe place at home and it was observed that some patients had even pasted a picture of Lord Buddha on their files. The empirical evidence strongly suggests the importance of strengthening the nearest hospitals for CKDu treatment in the CKDu prone areas.

Private Sector Only for Certain Health Care Services:

However, some patients are pushed to obtain healthcare facilities for certain service from the private sector due to some practical problems that exist in the government hospitals/clinics. They generally seek medical testing, interaction with doctors to get better explanation on the sickness, confirming about the illness etc. from the private sector. The experience of patients suggests that most of the patients had visited private hospitals in Anuradhapura, Kandy and Colombo at the initial stage of their diagnosis of CKDu, seeking further confirmation. However, there is hardly any patient who totally depends on private sector for CKDu treatment other than visit the same only for medical checkups and/or testing when and where necessary.

Indigenous Medical Practitioners for Health Promotion:

The empirical evidence shows that there only a few patients have obtained Ayurvedic medicine or Desiya Chikitsa as a major treatment for CKDu. Thus, there are some patients who have utilized indigenous medical systems as a complementary to western medicine. However, it is significant to note the contribution made by indigenous medical practitioners in this regard as they implement various programmes at grass root level to raise an awareness on best practices related to management of ill-health and health promotion through different interventions such as promoting home gardening, distributing clay pots, providing information with regard to dietary, healthy lifestyle etc. through brochures and workshops at village level etc. The villagers highly appreciate the contribution of indigenous practitioners and their frequent visits to the villages.

Religious/Ritual Healing Practices to Enhance Mental Well-being;

The illness narratives in both Medawachchiya and Padaviya clearly reveal that the psychological well-being of the patients and their families have been totally neglected by the above service providers as there are no formally organized mechanisms at clinical or community levels to address the emotional dimension of CKDu. Therefore, many have been attracted to observe religious and ritual practices to overcome their sufferings. Identified religious and ritual practices in the two local settings are chanting *prith* at temples by priests, at homes by lay devotees and by family members, *bodhi-pujas*, and meditation programmes at temples, reading horoscopes and tying talismans to get protection. While

some of these practices are performed at individual family levels, the others are done at group/community levels.

However, what is important is that these practices have become more regular and a part of villagers' everyday life. At the same time most of these activities are institutionalized due to the huge demand by villagers. Study team was able to observe a Buddhist temple in Padaviya with monks given specific tasks such as the in-charge for *bodhi-puja*, in-charge for public dealings such as giving appointments for various activities, and the in-charge of horoscope reading etc. It is also important to see the transformation of these ritual practices getting institutionalized within the local settings where as earlier people went outside their villages to receive such services. An earlier sociological study on CKD indicates the villagers going in search of outside ritual healers (Liyanage, C., Jayathilake, R., 2009).

(c) Economic Impact of Chronic Kidney Disease with Unknown Etiology:

Analyzing the Economic Burden

From an economic perspective the burden of CKDu falls on both households and the nation. This chapter focuses only on the household burden of CKDu. It attempts to quantify the following aspects:

- Direct cost burden on households due to CKDu
 - o Cost of treatment
 - o Cost of transport for treatment
- Indirect cost burden in terms of lost earnings of CKDu
- Lost earnings of patient/care giver
- Economic impact of alternative coping strategies adopted by the household
 - o in financing the costs of the illness
 - o in re-allocating household resources

In assessing the economic burden of CKDu it is important to keep in mind the profile of the patients and their households provided in chapter 2. In particular we focus on the gender distribution of patients and the economic impacts this could engender such as

- Do gender differences affect expenditure on treatment and source of funding?
- Do gender differences affect cost of caring for the patient and burden on household?

These issues will be focused on, though the main emphasis of this study will be the overall economic impact of CKDu on the community.

Economic Profile of CKD Households -

Family Structure-

All patients under consideration are of the same ethnicity and religion: Sinhala and Buddhist as mentioned in Chapter 2. The modal household size in Medawachchiya was 4 members while it was 5 in Padaviya. In Madawachchiya and Padaviya 51% and 53% of households only encompass nuclear families. The households are long term residents in the area, either from birth or migration in the distant past: with only 7.1% in Medawachchiya and 1.2% from Padaviya having migrated more recently, that is within the last 10 years. Considering marital status by gender of the 35 females in Medawachchiya 17 were married and 17 were widowed; while in Padaviya of the 34 female patients 20 were married and 13 were widowed. Likewise among the 65 males in Medawachchiya 61 are married, 2 are widowed and 2 never married and in Padaviya among 66 males the numbers are 63 married, 2 widowed and 1 never married. Dependency is likely to be a greater issue in the case of females, given the large number of widows despite their not being a significant difference in age between male and female patients in the sample.

Average Age of Patients

Division	Male	Female
Madawachchiya	56.6	56.9
Padaviya	58.9	55.4

The number of potential dependents given age as a factor is quite high: 26.5% in Madawachchiya and 25.8% in Padaviya are aged 18 and under; 21.2% and 23.7% as 55 and over compared to 52.3 and 50.2 aged 19 to 54. This view is further confirmed by Table 2,14 where only 34.0% and 25.5% of the households are classified as employed in Medawachchiya and Padaviya respectively.

Housing-

The majority, 94% in Medawachchiya and 71% in Padaviya owned land. In Medawachchiya and Padaviya, the majority of patient households have permanent housing (68% and 74% respectively) but the numbers living in semi-permanent housing is still significant at 30% and 23% with 2% and 3% living in temporary shelters. In Medawachchiya 94% own their dwellings while in Padaviya this percentage is only 71%: of the others 5% in Medawachchiya and 15% in Padaviya live in shared housing. Economically such land holding and housing denotes stability and limits the burden of regular housing expenditure.

Education-

The level of education among residents in the sample households is relatively low compared to national standards with the modal category in both areas given as secondary education. The percentage with education levels of passed G.C.E. O/L and above is only 26.5% in Medawachchiya and 18.1% in Padaviya. This observation has a bearing on the earning potential of households, which in turn has a major link to the burden of illness and

coping strategies of these households. Level of education is even lower among patients with the modal category being secondary education in Medawachchiya (40%) and only primary education in Padaviya (54%). In addition 7% and 4% reported no education in Medawachchiya and Padaviya. Only 17% and 8% of the patients had educational levels of G.C.E O/L and above in the two locations.

Employment-

The majority of patients: 67% in Medawachchiya and 71% in Padaviya were the household heads. This is likely to have a major bearing on the economic status of the family, since CKDu has a chronic debilitating impact on the health of individuals that is likely to affect the productivity of workers even in the early stages, culminating in withdrawal from the workforce and death.

Table shows that only 9% and 7% of the patients in the two areas are below the age of 40. The age range of the modal group is 51-60 in Medawachchiya (40%) and over 60 in Padaviya (37%). The high percentage of patients in the age range 41 to 60, 56% in Medawachchiya and Padaviya, has a major bearing on the economy: both at household and national level, since these patients are within the working age group and the loss of their incomes likely to have a significant impact on household budgets, resulting in inter-generational impacts of CKDu, and loss of output and an adverse impact on growth in the national economy.

Considering family members of patients, 34% of the study group was employed in Medawachchiya, compared to 25.5% in Padaviya, reflecting a large dependent population. The fact that the percentage employed is relatively low, means that loss of employment for the patient is likely to have a significant impact on the household budget.

Data relating to household members show the major categories of employment to be cultivation (25.9 in Medawachchiya and 43.6 in Padaviya); armed forces (18.4% and 22.8%) and home guards (15.5% and 7.4%). Of the household members in both locations 13% report a secondary occupation that is cultivation in the case of the majority (84.3 and 44.1 of the secondary occupations in Medawachchiya and Padaviya respectively).

In the case of patients only 43% were employed in Medawachchiya and 27% in Padaviya as 41% and 54% respectively reported that they were too sick to work. The severity of the CKDu burden is reflected in these statistics. Of those employed the majority were once again into cultivation (43.1% and 64.6% in Medawachchiya and Padaviya respectively). Of those reporting secondary employment 90.5% and 42.9% were into cultivation as well. Cultivation is an inherently unstable occupation, being dependent on the weather and at risk from environmental factors and crop pests as well as fluctuating market prices. It also involves hard physical labour that makes it challenging for those even in the early stages of CKDu to remain productive. Both these factors have repercussions on the economic burden of CKDu.

In this context, it is important to note the case of Padaviya where 82% of patients are migrants as opposed to being born in the area though migration has happened in the

majority of cases in the distant past (86.5% have migrated more than 30 years ago). Migration to the area however has been from within and without the district (43.9% within the district and 45.1% from outside the district, with 11% merely moving within the DS division). Migration in a majority of cases has been tied to receiving land (54.9%) and cultivation (14.6%). This feature has characterized livelihoods in that study site.

Income –

The chosen areas in the North Central Province are relatively low income areas. The patient's family incomes are given in the table below. The income range of the modal group is 2,502-7,500 (40.2%) in Padaviya and 15,001-30,000 in Medawachchiya (40.8%).

It should be noted that the poverty line (minimum expenditure per person per month to fulfill basic needs) in the Anuradhapura district for December 2011 was Rs 3241. Assuming a four member household, then the household poverty line would be 12964. In Medawachchiya 29.1% and in Padaviya 48.7% of households earn less than Rs 7500 with another 25.1% and 25.0% earning between 7501 and 15000. Considering total household income 29% in Madawahchiya and 49% in Padaviya gain less than 15,000 rupees per month. Poverty clearly is a major issue among these households. Of the patient's families 52% in Medawachchiya were Samurdhi recipients, while only 20% were so in Padaviya, though earnings were lower and household size larger in most cases.

Considering patient incomes separately is important, for future work on lost earnings. Table below presents information on the monthly income of patients in the two DS divisions.

Patients Income as Percentage of Family Income on Average

	Male	Female
Madawachchiya		
Number of patients	44	56
Number reporting income	31	24
Average % patient income to household income	56.9	52.3
Padaviya		
Number of patients	61	39
Number reporting income	44	13
Average % patient income to household income	59.2	46.9

Source: Calculations based on CKDu S-E Survey

The table above shows that while many patients do not report current earnings, particularly among the females, that where earnings are reported they are a significant share of household income. This suggests that the loss of such an income as the disease progresses will be a heavy blow for the household economy.

Progression of the Illness-

The economic burden of CKDu depends on the progression of the disease and partly on the treatment options selected by the patient, as discussed in the next section.

The duration of illness has a major bearing on the economic impact of the disease: on the one hand it is a chronic illness, associated with increasing disability; secondly over time individual's coping strategies could change: evolve and diversify; or shrink given binding economic conditions, depending on the illness and degree of external support.

As table shows the majority (70%) in Medawachchiya has been diagnosed four years or more ago and in Padaviya this percentage is 51%. The modal category in Medawachchiya is 6 to 8 years, followed by 4 to 6 years and less than two years. In Padaviya on the other hand the modal category is 2 to 4 years, followed by 4 to 6 and 6 to 8 years.

The diagnosis in a majority of cases sampled has been the result of illness, and not screening. In the past, CKD has been diagnosed mainly as a result of investigations carried out in the context of another disease. Mobile clinics seem an important source of diagnosis in Medawachchiya. Early diagnosis of the disease has two benefits: better monitoring and control of the disease and the chance of rationalizing economic decisions in line with future uncertainty.

In the case of females, illness prior to CKD diagnosis is more common. In Medawachchiya the percentage reporting such illness is 60% (male 41.5%) and in Padaviya 50% (male 31.8%) so such families would have faced the economic burden of illness even prior to the diagnosis of CKD. The main diseases reported in this context are hypertension (51.9% of females, 31% of males in Medawachchiya and 7.7 and 25% in Padaviya) and Diabetes (18.5% of females and 6.9% of males in Medawachchiya and 38.5% and 20.8% in Padaviya respectively). This raises the issue that what is being captured could be the economic burden of CKD rather than CKDu in certain cases.

Severity of Illness and Number on Treatment

	Medawachchiya		Padaviya		Total	
	Male	Female	Male	Female	Male	Female
Stage 1	1 (0)	5 (4)	1 (0)	2 (1)	2 (0)	7 (5)
Stage 2	35 (32)	39 (37)	58 (54)	37 (37)	93 (86)	76 (74)
Stage 3	8 (8)	12 (12)	2 (2)	0	10 (10)	12 (12)
Total	44 (40)	56 (53)	61 (56)	39 (38)	105 (96)	95 (91)

Note: Number on medication given in brackets.

The majority of patients in this sample are in stage 2. The data does not show a correlation between year of diagnosis and stage of illness, suggesting that progression depends on other factors, apart from time.

Relating stage of illness to currently being on medication we find that all those at stage 3, and almost all in stage 2 are on medication (95%). By gender 96% of females are on

treatment as compared to only 91% of males. The majority who are not on treatment report that this is on medical advice. Only 2 respondents mention economic difficulties, and another, also male, the difficulty of gaining leave as the reason for not being on medication. These findings suggest that economic factors are not hampering the treatment process for most patients, though the later sections of this chapter show that a sizeable economic burden is imposed in terms of treatment costs for some.

Treatment of CKDu-

Healthcare in the Current Period

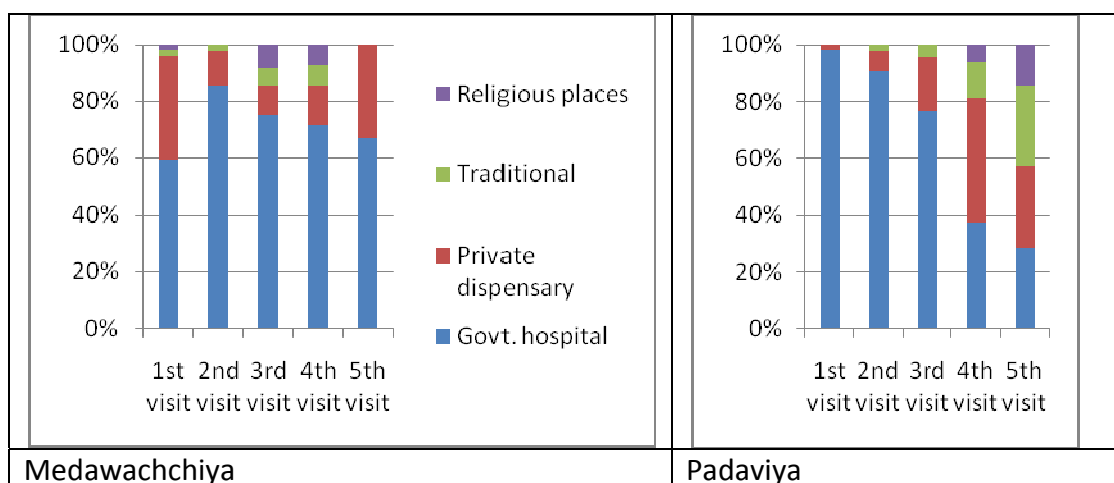
Clinical treatment from the government hospital is the source of treatment for 94% of patients in each sample. Given the socio-economic profile of patients' households this would be the expected source of treatment, and the free care reduces the burden of the illness to an extent.

Source of Current Treatment

Treatment	Madawachchiya	%	Padaviya	%	Total	%
Government hospital	89	93.7	90	94.7	179	94.2
Private hospital	2	2.1	2	2.1	4	2.1
Buy medicine using clinic card	3	3.2	1	1.1	4	2.1
Medication	1	1.1	0	0.0	1	0.5
Inpatient Govt. Hospital	0	0.0	1	1.1	1	0.5
Home based medicine	0	0.0	1	1.1	1	0.5
Total	95	100.0	95	100.0	190	100.0

Post Diagnosis Treatment Profile

The number of patients, accessing care, diminishes as the number of visits considered increases: while all 200 have sought care in the first instance, the number reported diminishes to 166 (2nd visit), 96 (3rd visit), 31(fourth visit), 13 (fifth visit), 4 (sixth visit), 2 (seventh visit), and 1 (8th visit). The reason for most early visits is further testing for verification of the diagnosis, as well as gaining clinical care. The question sought to establish treatment profile from diagnosis up to the point of the survey.



Source: CKDu S-E Survey

The patterns of treatment, as reflected by choice of location per visit, seem to differ by location: for every visit clearly the government hospital is the major option in Medawachchiya but in Padaviya the importance of this source diminishes systematically over the visits. The private sector plays an important role as a source of treatment in both survey sites, increasing in importance in Padaviya as the number of visits progresses. Traditional care including Ayurveda care also seems to become more important as the number of visits progresses, in Padaviya, as do religious observances. The choice of treatment source will have a major bearing on the cost of care of CKDu.

It should be noted that many of these patients have co-morbidities: 62% of males at both locations, 68% of females in Medawachchiya and 82% in Padaviya report having another illness concurrently. Most common disease are hypertension (49% raising the issue of whether some in the sample are actually CKD rather than CKDu, as many have reported having hypertension even prior to diagnosis of CKD), Diabetes (16.6% - also strongly correlated in the literature with CKD), Cholesterol (13.5%) and Asthma (4.7%). The need for better NCD care to be targeted to these locations and to be provided 'close to client' should be noted, since control of these co-morbidities could be important to the prognosis of CKD, and patient welfare in general.

Utilization of Healthcare Facilities-

Medawachchiya sample

In response to the query have you ever used the named facility it was found that 94% had accessed the Medawachchiya hospital, 54% the Anuradhapura Hospital, 21% the Kandy Hospital and 13% the Vavuniya Hospital. The Anuradhapura and Kandy Hospitals are large well equipped teaching hospitals. The number of visits to small hospitals is very limited. Only 13% had accessed the mobile clinic.

Of the sample 41% had visited private Western practitioners. Only 1% had visited the Ayurveda hospital and 6% traditional practitioners suggesting that CKD is perceived to need treatment from allopathic sources. Of the sample 38% had visited the pharmacy suggesting that even where free health consultations are provided that the cost of drugs is sometimes shifted on to the patients due to drug scarcities.

Of the 96 patients who accessed Medawachchiya hospital, the majority 91.7% visit this hospital once a month, probably as a clinic visit. In the case of the 54 who have visited the Anuradhapura hospital 25.9% do so once a month; 27.8% have only visited it once, while another 29.6% report visiting Anuradhapura hospital when needed. Kandy Teaching Hospital, has only been visited by 20 patients, of whom 65% respond that they visited this hospital once. A similar pattern exists in the case of private sector practitioners, where the 38 who visited this source 55.3% report only one visit. Only 8 patients have accessed traditional practitioners and 62.5% respond that they only visit this source when needed.

From a cost perspective the above discussion suggests that regular expenses are incurred on travel to access Medawachchiya Hospital in the case of the majority, and in the case of some patients to visit Anuradhapura hospital as well. Most visits to Anuradhapura and Kandy, as well as to the private sector, along with anecdotal evidence suggest that such visits were for confirmation of original diagnosis and are likely to be one off cost items. Currently, not many have had to access private sector care and pharmacies in treating CKD, which is likely to have limited the costs borne by the household.

Padaviya Sample

Responding to the same query, 99% cited having accessed the Padaviya hospital at least once. Of the sample 62% had also accessed the Medawachchiya Hospital that has better facilities as has Anuradhapura Hospital, utilized at least once by 48%. Only 3% accessed the Kandy Teaching Hospital.

Less utilization of the private sector is shown in Padaviya, with only 29% accessing private Western Practitioners, and 19% pharmacies. Only 5% accessed the Ayurvedha hospital and traditional Practitioners, confirming that CKD is viewed mainly as needing allopathic care.

Padaviya hospital is accessed by 99 patients 91.9% of whom report that they visit the hospital once a month. Of the 62 visiting Medawachchiya hospital 21% visit the hospital once a month but another 40.3% access it only when needed while 37.1% have only visited it once.. Anuradhapura hospital likewise has been accessed by 37.5% patients only once, and by another 52.1% only when needed (48 patients have accessed this hospital at least once). Similarly of 27 patients accessing private practitioner care 55.6% have only done so when needed and 25.9% only once.

From a cost of care perspective, three issues emerge-

- the issue of travel costs are important since many in the sample are accessing regular clinic care, sometimes at more than one location.
- The need for clinic visits to two sites (Padaviya and Medawachchiya in this case, and Medawachchiya and Anuradhapura in the previous section) should be examined, as it may be resulting in a wastage of resources, both to the health system and the household
- What type of care is classified 'as care when needed' that results in patients accessing further off hospitals/private sector should be examined, to see if the

closest hospital could not be equipped to cope with such contingencies, as this would reduce the burden to households of travel, consultation and treatment costs.

Treatment Expenditure-

Treatment Costs

Table provides information on the percentage distribution by stage of renal failure. The sample in Madawachchiya has 20% in stage 3 that is considered the acute phase of the illness but in Padaviya only 2% that fall into this category. The fact that some of the patients interviewed are in the early stages explains why only 93% in Madawachchiya and 94% in Padaviya are currently gaining treatment for CKDu.

Source of Current Treatment

Treatment	Medawachchiya	Padaviya	Total
Treatment from Govt. hospital	93.7	94.7	94.2
Private hospital	2.1	2.1	2.1
Buying medicine using clinic card	3.2	1.1	2.1
Meditation	1.1	0.0	0.5
Govt. Hospital inpatient care	0.0	1.1	0.5
Home based medicine	0.0	1.1	0.5
Total	100.0	100.0	100.0

The percentage of females currently receiving CKDu care is higher than males (95.8 to 91.4). All those not receiving care are in stages 1 or 2. The reasons for not receiving care are recorded by the four females, as two mentioning that this is according to medical advice, one cites difficulty in getting leave, and the fourth that she does not feel any treatment is necessary, while the nine males give the following responses: three that it is in accordance with medical advice, two that it is due to economic difficulties, three that it is due to difficulties in getting leave and one giving the reason as other. Most noteworthy among these findings is that four mention difficulties in getting leave. Greater education of employees regarding the importance of regular treatment and screening is highlighted by this finding.

The number undergoing dialysis is very small at present: only one male and one female in the Medawachchiya sample. This is due to the number of patients in stage 3 being small in these samples as yet.

Drug Costs

Though the patients mainly access public sector care, and should be receiving their drugs at no cost through such a health system, the majority do report monthly drug costs with the costs varying by source of treatment: higher in the larger hospitals and the private sector.

Expenditure on Drugs

Hospital	No expenditure	<100	101-500	501-1000	>1000	Total
Medawachchiya	17	5	24	2		48
	35.4	10.4	50.0	4.2	0.0	100.0
Padaviya	26	1	14	4	1	46
	56.5	2.2	30.4	8.7	2.2	100.0
Anuradhapura	1	2	3			6
	16.7	33.3	50.0	0.0	0.0	100.0
Private Sector	1	7	4	2	2	16
	6.3	43.8	25.0	12.5	12.5	100.0

Rationalizing drug provision to state hospitals to avoid shortages and putting systems in place for forecasting the increased demand of CKD drugs is of immense importance in this regard, when we note the cost of these drugs is high in relation to household incomes in these areas.

Diagnostic Investigation Costs

The number undergoing urine, blood and other testing with regard to CKD is as follows: 77% of males in Medawachchiya and 74% among those from Padaviya; 91.4% females in Medawachchiya and 74% in Padaviya. The numbers suggest that patients are being monitored using at least some of the necessary diagnostic tests. The high number of females reporting testing in Medawachchiya is noteworthy in this context and tallies with the fact that the largest number of stage 3 patients (12 persons) is among this sub-sample.

Cost on Medical Investigations

Hospital	No expenditure	<100	101-500	501-1000	>1000	Total
Medawachchiya	28	1	5	2		36
	77.8	2.8	13.9	5.6		100.0
Padaviya	15	8	15	4		42
	35.7	19.0	35.7	9.5		100.0
Anuradhapura	2	2	1	1		6
	33.3	33.3	16.7	16.7		100.0
Private Sector		1	4	2	4	11
	0.0	9.1	36.4	18.2	36.4	100.0

The majority is undergoing diagnostic testing at no expenditure to households accessing Medawachchiya Hospital, though for those accessing Padaviya Hospital and Anuradhapura Hospital costs are borne by households suggesting that they are accessing private sector diagnostic facilities. It should however be noted that sometimes even when accessing public sector care, that travel and other costs have to be borne in accessing state diagnostic

services, since the tests and the giving of reports occurs in some instances on days other than the clinic visit days.

Travel Cost

The majority travel alone for treatment: in the case of males in Medawachchiya and Padaviya 77.4% and 77.8% do so while in the case of females the numbers are lower 57.1% and 42.4%. These patients are at present accessing clinic care and are therefore able to travel alone. The situation is likely to be different as the disease progresses: both the need for patients to be accompanied and the mode of transport change with severity of illness.

Patients are accompanied by relatives: mainly the spouse, children or parents. Currently there is no trend of paying outsiders to perform this service. Unlike in urban settings, often family members are unemployed and are therefore available to accompany the patient.

Those in the Medawachchiya sample, accessing Medawachchiya had the majority (89.2%) spending less than 100 rupees; of the 8 accessing Anuradhapura Hospital 5 had spent between 101 and 500 rupees. Of the Padaviya sample, 33 spent less than Rs 100, and 17 between Rs 101-500, in accessing Padaviya Hospital. Accessing private sector care, apart from consultant charges seems expensive even for travel, with 6 persons in Medawachchiya and 3 in Padaviya spending between Rs 101-500 per visit on travel.

Time Costs of Accessing Treatment

This involves travel time and treatment time, as well as time spent for consultation and drug dispensation.

Medawachchiya Sample

Given that the majority in this sample access the Medawachchiya hospital, it is noteworthy that 88.5% report spending between 6 and 12 hours in accessing care in this hospital; with the situation in Anuradhapura even more severe: 57.4% mention 6 to 12 hours and a further 37% that they spend between 12 and 24 hours in accessing care. In responding to problems faced in accessing care at the Medawachchiya Hospital difficulty of bearing time cost is reported by 14.4% of respondents. Such long time durations imposes two costs on the household: firstly an economic burden, since it is likely to have a major impact on the earnings of daily income earners and those who are in self employment, as well as those who need to hire replacements; secondly it is a major psychic cost to the patient and his/her family.

Padaviya Sample

Accessing care in the Medawachchiya Hospital is even more time consuming for these respondents as 80.6% report spending between 12 and 24 hours on this process, while of those accessing Anuradhapura hospital 70.8% spend 12 to 24 hours, and another 18.8% 24 to 48 hours. Padaviya Hospital that is accessed by over 90% of the sample on a monthly basis had

82% of the sample reporting spending 4 to 6 hours on seeking care. Time costs clearly are a major component of the costs of CKD care and the fact that it is a burden is established when 10.9% report this as a major problem in accessing care (with another 14.1% responses relating to difficulties in transport and 16.7% to distance to health care facilities in the case of Medawachchiya Hospital and with 50% and 25% giving the same responses in the context of Anuradhapura Hospital).

These responses clearly support the view that more CKD care activities should be provided at lower level hospitals, so as to limit the time costs imposed by congestion at higher level health care facilities. Respondents also noted that the number of doctors should be increased and that doctors in Padaviya should be designated to specifically cover CKD care. Rationalizing consultation and drug dispensing practices through hospital level audits is important. Likewise more attention could be paid to the transport system to assist patients to reach the hospitals in less time and with greater ease.

Financial Cost of Accessing Care

The table below presents cost of accessing care by DS division (sample site).

Total Cost in Accessing Care

DS Division		No expenditure	<100	101-500	501-1000	>1000	Total
Madawachchiya	Transport	1	59	24	4	5	93
		1.1	63.4	25.8	4.3	5.4	100.0
	Drugs	15	20	39	8	1	83
		18.1	24.1	47.0	9.6	1.2	100.0
	Medical testing	30	1	8	5	3	47
		63.8	2.1	17.0	10.6	6.4	100.0
	Foods	3	52	24	3	1	83
		3.6	62.7	28.9	3.6	1.2	100.0
	Other	39	1	2		3	45
Padaviya		86.7	2.2	4.4	0.0	6.7	100.0
	Transport	8	40	24	4	1	77
		10.4	51.9	31.2	5.2	1.3	100.0
	Drugs	7	8	39	10	5	69
		10.1	11.6	56.5	14.5	7.2	100.0
	Medical testing	16	12	20	8	2	58
		27.6	20.7	34.5	13.8	3.4	100.0
	Foods	6	48	17	2	1	74
		8.1	64.9	23.0	2.7	1.4	100.0
	Other	24	4	3	2	2	35
		68.6	11.4	8.6	5.7	5.7	100.0

The modal category with regard to transport for both sample sites is less than Rs 100; for drugs it is between Rs 101 and 500; for medical investigations it is no cost in Medawachiya but between Rs 101 and 500 in Padaviya; cost on food during the time of seeking outpatient medical care is less than Rs 100 and the majority bear no other costs in accessing care.

In order to get a very rough approximation on the cost of an outpatient visit, we can use the mid-point values for a modal patient

Cost of Outpatient Visits by Modal Patient Considering the Two Sample Sites

	Medawachchiya	Padaviya
Transport	50	50
Drugs	250	250
Medial Investigations	0	250
Food	50	50
Other	0	0
Total	350	600

Cost of Outpatient Visit to Given Hospital by Sample's Modal Patients

	Medawachiya sample Medawachchiya Hosptial	Padaviya Sample Padaviya Hospital
Transport	50	50
Drugs	250	0
Medial Investigations	0	250
Food	50	50
Other	0	0
Total	350	350

Source: Calculation based on CKDu S-E Survey data

The mean cost of an OPD visit across all sources of care is Rs 350 in the case of a Medawachchiya respondent and Rs 600 for a Padaviya respondent, the difference arising from the need of those in Padaviya to spend on medical investigations. When we analyze by hospital we find that an OPD visit to Medawachchiya Hospital by those in the Medawachchiya sample and by a Padaviya patient to Padaviya Hospital both cost Rs 350, though in the first case Rs 250 is on drugs, and in the latter case the Rs 250 is on medical investigations. This highlights the need for cost curtailment strategies to be determined by the state by locality,

Major Cost items Post Diagnosis

The survey posed the following question: “In addition to the above cost, did you have to bear any other cost of more than Rs. 1000 after identification of CKD?” The question sought to identify unusual cost items that apart from the regular treatment regime had been a burden to the household.

Three major categories of cost exist:

- costs of channeling specialists, blood tests and scans that are particularly aligned to confirming the original diagnosis of CKD
- Cost of treatment, drugs, special appliances and special food targeted at improving health and wellbeing post diagnosis
- Alternative medicine, rituals and religious functions including pirith, bodhi puja, yantra dameema – costs borne alongside or rarely as alternatives to costs of allopathic care.

Such costs contribute to the economic burden, being much larger costs than can be accommodated given regular household income levels in this sample, often resulting in indebtedness including pawning or sale of assets.

Cost of Traditional/religious Practices

While the costs of traditional/religious practices were not collected, these are likely to be quite significant. Of the patients in Medawachchiya 55.4% and 57.1% of males and females report undertaking religious ceremonies in relation to their illness, in Padaviya the percentages are 36.4 and 35.3%. The difference between the two sub-samples may be linked to severity of the illness, as observations in the field suggest that patients turn to traditional/religious activities as the disease progresses, some even losing faith in allopathic care at this point and concentrating on religion as the means of salvation or focusing more on the afterlife, since the community sees this disease clearly as a catastrophe.

Of the religious practices Bodhi Puja (ceremony centered around the Bo-tree, the Bo-tree having been revered by the Buddha for having given shade at the time of enlightenment) seems the most common (20% of entire sample), followed by the wearing of a blessed amulets (17%), Bara (promises to the gods) are reported by 11% and Pirith chanting (chanting of holy scripture) by 10%.

Impact on Household Activities

Currently the majority respond that they are engaged in activities in their households. However it should be noted that those not engaging in any activity are far greater than those in stage 3, suggesting that better treatment options and motivation could increase the involvement in household activities of patients in stages 1 and 2.

Severity of Illness and not Engaging in Activities of Household

	Medawachchiya		Padaviya	
	% not engaged in any activity in household	% in stage 3	% not engaged in any activity in household	% in stage 3
Male	33.8	18.2	36.4	3.3
Female	25.7	21.4	44.1	0

Inability of the patient to attend to household activities either increases the workload of other household members, necessitates hiring out activities that were previously done at home such as replacing home cooked food with that bought in boutiques or sending washing to the laundry or hiring labour. In addition to changes in the patient's provision of labour, reduction in family labour could also result from the responsibilities of patient care.

In the Medawachchiya sample 48% respond that their contribution to household chores is less, while 41% do so in Padaviya; more striking is the fact that 16% and 25% in the two samples mention stopping household chores entirely. The effect of withdrawal from household work by the patient, on other household members' time, affects household income or output, assuming that the family member was already working full time: given the agricultural community that is under study, this impact is minimal at present as there is evidence of unemployment and underemployment within the family. Where paid services substitute for family labour household expenditure and savings are adversely affected.

Impact on Livelihoods -

Current Period

The financial implications of the illness are striking, even though many are still in the early stages of the disease, since only 23% in Medawachchiya and 20% in Padaviya report no impact. The majority: 45% and 48% respectively note a decrease in income, while another 32% in each location report having totally lost their income due to this illness. Such outcomes are inevitable given that the 90.5% in Medawachchiya and 42.9% in Padaviya are into cultivation, with many others are involved in manual work as casual labourers.

Prior to diagnosis of CKD 95% and 92% of males in Medawachchiya and Padaviya were working as were 66% and 65% of females in the two sub-samples. The types of employment undertaken prior to diagnosis are given below. These are very similar to the current employment patterns in these areas with the majority being employed as farmers followed by home guards. Post diagnosis impacts on livelihood are reported by 88% and 92% of males in Medawachchiya and Padaviya and 78% and 96% of females: though the illness severity distribution is more severe in Medawachchiya given the larger number in stage III, the livelihood impacts are felt more in Padaviya.

The main responses to the diagnosis of CKD with regard to livelihood were stopping work (Medawachchiya male 38% and female 50% and Padaviya 34% and 81% respectively) reducing working time (49% male Medawachchiya, 48% among males in Padaviya and 39%

and 19% for females in Medawachchiya and Padaviya respectively). Only five persons in the whole sample mention getting medical leave, and clearly given the employment structure this is not a common option given that most are self-employed or employed in the informal sector. This has a major bearing on household income: measures to limit this impact would involve appropriate timely treatment to safeguard patient health, motivating patient to continue in labour force, training for other family members to continue in trade and social awareness creation to encourage the informal sector to provide leave and the option of part time or flexible work to such patients and their households.

The support of family members has been used as the major coping strategy in maintaining livelihoods post diagnosis. However 11% of livelihood opportunities have had to be foregone due to CKD.

Livelihood Prior to CKD Diagnosis

Occupation	Madawachchiya	%	Padaviya	%	Total	%
Farmer	55	64.7	67	64.7	122	64.7
Govt. Servant	3	3.5	2	3.5	5	3.5
Labour	5	5.9	4	5.9	9	5.9
Home Guard	15	17.6	3	17.6	18	17.6
Carpenter	3	3.5	1	3.5	4	3.5
Business	2	2.4	2	2.4	4	2.4
Livestock	0	0.0	2	0.0	2	0.0
Other	2	2.4	2	2.4	4	2.4
Total	85	100.0	83	100.0	168	100.0

The magnitude of monthly income lost per worker who is laid off due to illness can be approximated based on the earnings of the others in the sample: in Medawachchiya the modal monthly earning category of patients is between 7501-15000, while for Padaviya it is 2501-7500.

The major factor that influences if livelihoods are affected, apart from the severity of illness, is the nature of work being undertaken by the person prior to diagnosis. The amount of manual effort involved, the number of hours, the ability to delegate or share the work and its flexibility all have a bearing on this issue.

Of the 43 still employed in Medawachchiya, the majority, 22 are into cultivation with 16 being Home Guards. In Padaviya too, 31 of the 48 are involved in cultivation.

Seeking treatment resulted in 44% in Medawachchiya and 40% in Padaviya losing their wages, thus affecting household income. Coping strategies to overcome such losses include changing shifts (possible for example for Home Guards), use of other family member labour and hiring labour.

Among the adverse livelihood consequences that are resulting from the patient's illness are loss of income, higher cost of production due to hiring labour and reduction in quality of output. Apart from the economic burden suffered by patients and their families, patients

are also undergoing psychic costs in terms of a feeling of guilt about the additional work created for the family in providing substitute labour and caring for them, and due to the feeling of dependence that results from not being able to work and earn as before.

Sickness has had impacts on the livelihoods of other household members as well, as reported by 51% and 38% of males in Medawachchiya and Padaviya and 40% and 41% of female patients at the two sites. The adverse impacts have occurred through loss of employment (14.4%) and decreased time for livelihoods (24%), while for other households it has resulted mainly in household members increasing their involvement in livelihood activities (32%) and finding jobs (9.3%).

Future Losses in Income

Using the scenario building technique lost earnings due to leaving the workforce can be calculated based on information from this sample.

In Medawachchiya, the modal income range is 7501 to 15,000 (mid-point 11,250). In Padaviya it is 2501-7500 (mid-point 5000).

Based on the unemployment information for the patient families, and considering the possible workforce omitting children, students, the elderly and disabled for these two sub-samples we find the unemployment rate to be 4.2% in Medawachchiya and 7.3% in Padaviya. Patient are generally in the age group 40 to 60.

This information is combined with the following assumptions:

- Life table values (W.I de Silva, IHP) are used to calculate probability of survival;

- Discount rate is 5%;

- Incomes grow at 3.5% per annum;

- Individuals could work, if not for their illness up to 60, but now leave the workforce at 50;

The lost earnings then for a decade, is Rs 1,034,909 in Medawachchiya and Rs 445,076 in Padaviya, the large difference stemming from differences in income and unemployment levels in the two locations. While accepting that the Scenario Building technique only provides a very rough estimate of future lost earnings, being constrained by the validity of the assumptions and data available, these figures are yet sufficient to suggest that the lost earnings will be a significant burden to the household and community.

Financing Cost of CKD

Considering the households afflicted by CKDu one notes that they are mainly involved in cultivation, followed by those in the Armed Forces and Home Guards (see table 2.4).

Around one third of these workers are involved in secondary occupations: again mainly involving cultivation in Medawachchiya and Padaviya and as minor employees in Padaviya. Such income is also uncertain, being strongly linked to weather conditions and crops. Thus the burden of lost income due to CKD further intensifies the hardships imposed by low agricultural income and uncertainty.

In response to the question “How did you cover the expenses of treatment?” the most common response was transfers from children, followed by using salary from previous month, using savings of patient, savings of other family members, pawning jewelry and in-kind help from friends and relatives.

CKD has had a major impact on consumption patterns of the household, with 94% and 98% of the male sub-samples in Medawachchiya and Padaviya reporting changes in consumption pattern, and 97% and 91% of female patient sub-samples doing the same.

Financially these households have to depend mainly on themselves: though 55% of households in Medawachchiya and 57% in Padaviya respond that they receive financial assistance due to CKD. Of those reporting receiving government aid due to CKD 63% in Medawachchiya mention the monthly CKD allowance but the percentage is low in Padaviya at just 19.3%. Whether this is a reflection of the disease still being in the early stages in the context of many in this area (tallying with our finding in comparing the two samples, that Padaviya had less stage 3 patients) or whether bureaucratic anomalies exist, needs to be further examined. A separate allowance is being given for dialysis, received by 9 patients in the sample, though only two reported receiving dialysis in the past month. A donation of Rs 500 is also mentioned by 51% of the Padaviya respondents. Samurdhi provides some assistance to households when patients are hospitalized but few have gained such assistance, and the amounts too are negligible.

NGOs have provided assistance in improving health care in the community but this assistance is mainly in kind, particularly targeted at improving drinking water quality in the area (filters, rain water tanks, water supply systems). Contribution by Community Based Organizations (CBOs) to the welfare of CKD afflicted households is negligible. Much of the CBO support seems to centre on the funeral: providing financial and in-kind assistance and services related to the funeral.

Relatives, friends and neighbors show their solidarity with patient households by providing financial and in-kind support as well as emotional support, particularly at two stages of the illness: firstly at the point of diagnosis and later when the illness is acute and the patient is hospitalized continuing to the point of the funeral. In-depth discussions with patient households however highlighted the fact that such support is sporadic and that during the course of the illness many households face tremendous financial and emotional pressures as well as a sense of isolation and despair that no systematic social security system exists to safeguard families in times of distress.

Long Term Economic Impacts

Impact of CKD has two major long term economic implications: the first through loss of physical assets and the second through potential loss of human capital. During the survey and in-depth interviews it was revealed that some households had sold land due to being unable to farm it now due to labour problems. Of the households 43% comment that household construction work is incomplete at present. In Padaviya it has resulted in many households selling livestock. Many households have also resorted to pawning jewelry in order to overcome financial difficulties.

More significant however is the potential loss of human capital arising from CKD. In Medawachchiya 20% of households report that the illness is affecting children's education while 18% do so in Padaviya. The impacts seem more severe when patients are male rather than female (comparing 25% and 11% male and female patient samples in Medawachchiya and 21% and 12% in Padaviya). This may be due to the greater economic impact imposed by illness in males that results in more lost employment and income, than in the case of female patients, many of whom would have been housewives/unemployed even prior to diagnosis. The educational impacts are varied: With regard to totally stopping school the numbers are 5 children in Madawachchiya and 1 in Padaviya, and 7 report students not attending school regularly in Medawachchiya compared to 2 in Padaviya. In the case of Padaviya 9 report being unable to spend sufficient time on their children compared to 5 in Medawachchiya, while 7 in Padaviya regret not sending their children regularly for tuition compared to 2 in Medawachchiya.

The impacts listed above suggest that CKD is affecting both the quantity and quality of education and are likely to have serious repercussions in terms of educational, employment and earning opportunities in the future. While the samples are too small to conclude definitely the results above hint at the

(d) Psycho-social impacts of Chronic Kidney Disease with unknown Etiology:

The empirical evidence of the community-based study clearly shows that there are many effects of CKDu on the everyday life of patient, his/her family and the entire community. As discussed in chapter three on community discourse of CKDu, the illness has been articulated within the local context as a tragedy, a struggle between the life and death that is associated with a fear and stigma. As explored in the previous chapter on economic impact of CKDu, it incurs out-of-pocket expenses for the patients and their families in accessing healthcare which includes transport, expenses during hospital stay, expenses during out-patient visits, special diets for patients, expenditure for medical care using complementary systems such as indigenous medicine, religious, ritual and other healing systems, and preventive measures such as obtaining or purchasing water from different sources etc. In addition to the above expenses, they also have to bear indirect costs such as lowering of productivity due to ill-health, absence from work due illness and all above resulted in pushing them into poverty.

Beside the above implications, the illness has brought many other social and psychological impacts on patients, their families and the entire community. The attempt of this chapter is to explore emotional/psychological and social impacts of CKDu on patient, his/her family and the community while examining the experience of everyday life of people who are in the crisis. In addition to analyzing illness narratives of 200 patients and the experiences of their families, the psycho-social impacts of CKDu throughout the process from diagnosis to termination of the life of patients are examined by analyzing the case histories of patients dead due to CKDu in the recent past in the same communities. It is important to take into consideration that, even though various dimensions of the illness-burdens (such as economic, emotional/psychological and socio-cultural) have been structured under

separate themes in this report, they are strongly interrelated with each other and are overlapping to a great extent.

Impact of CKDu on Psychological/emotional well being-

Illness is a phenomenon that is combined with many unfavorable psycho-social circumstances. Comparatively, the ill-health related to CKDu has further adverse effects on the mental wellbeing of the respective patients, their families and the entire community as the cause of illness is yet unknown/uncertain and therefore the prevention of it has become a greater challenge even though the problem has been identified in the locality more than two decades ago. Therefore, the mental wellbeing of patients, their family and the community needs to be thoroughly examined and evaluated in that particular context where human life has become more unsafe and uncertain.

It is important to take into account that there is no clear-cut distinction between mental wellbeing and physical wellbeing as these two concepts are always interconnected. The term 'mental wellbeing' refers to a capacity of an individual to deal with personal and social responsibility and emotions where the individual can make rational decisions, cope adequately with personal stresses and maintain satisfactory adjustments to society (Krist Ashman 2003: 361). Thus, the concept of mental wellbeing can be defined as a state of harmonic balance between the individual and the surrounding. This can be divided into two parallel and interrelated components as subjective wellbeing and objective wellbeing (Todur 1996).

The subjective wellbeing focuses on internal factors of an individual with positive emotions such as pleasure, happiness and life satisfaction etc. That can be further elaborated by reference to four domains explained by Bruni and Porta (2007). The four domains include contentment (pleasant, joy); unpleasant emotions (sadness, worry, anger, stress); global life judgments (life evaluation, fulfillment, meaning, success) and domain satisfaction (marriage, work, health, leisure etc.). Objective wellbeing focuses more on external factors such as the physical, material, social, political and aesthetic conditions in the surrounding, environment of an individual (Todur 1996). Therefore, the mental wellbeing of an individual or a community needs to be evaluated as an outcome of interaction between the subjective well being and the objective wellbeing. The following sections focus on understanding psychological/emotional impacts of CKDu on an individual, household and the community in the light of the above conceptual framework.

Psychological Wellbeing of the Individual /Patient -

The empirical evidence of this study clearly reveals that the mental wellbeing of all individual patients has deteriorated due to CKDu. The patients' narratives further reveal that fear; anxiety, anger, and sleeping disorders are some of the common symptoms among CKDu patients that would be an outcome of collusion between the social wellbeing and the objective wellbeing of respective patients who live in this locality. As mentioned in previous chapters, the illness is articulated as a struggle between life and death in the local context

where diagnosing as a CKDu patient itself has a major impact on the mental wellbeing of individuals.

Reactions of patients to similar situations differ. It is evident from this study that, some of the patients have been psychologically/emotionally affected very badly due to illness while there are some patients who have taken the risk of death due to illness as a challenge and are trying their level best to expedite fulfilling his/her responsibilities adopting various strategies. Accordingly, the mental wellbeing of each patient can be located at different levels that are influenced by interaction between subjective wellbeing and objective wellbeing of that particular individual. Nevertheless, as mentioned in chapter three many of the patients have resorted to various types of religious, ritual and supernatural healing practices up to its maximum level to restore and enhance their mental wellbeing for which they have expended out-of-pocket expenses, time and other resources.

Clinical limitations existing in both diagnosis of CKDu and its treatment have some negative impact on mental wellbeing of the respective patients. As mentioned earlier, the psychological dimension of CKDu has been extremely neglected in the clinical setting where the patients go for regular treatment. Some of the narratives of patients in this regard are as follows:

Box 5.1: Voice of Patients with regard to Clinical Limitations

“As doctors pointed out, I have a minor problem. However, I am also getting the same medicine that is prescribed to other patients who are in a critical condition. So, I can’t understand why all the patients get same medicine from the clinic. I think my health is ok but when I go to clinic I feel so bad and my mind goes mad while seeing patients with serious breathing difficulties”.

“The doctors come from Kandy see only some patients who are given with ‘R’ numbers. I have never got an opportunity to meet the doctors who come from Kandy”.

“Doctors never say anything about my problem. So I don’t know whether my problem is serious or not”.

“Some members of the staff are very cruel to us and they shout even at elderly people without paying any attention to their age. So I am fed up of going to the clinic”.

“While accompanying our mother to the clinic my husband had inquired from the doctor about the condition of her problem. The doctor got so annoyed and replied “why, are you going to treat her? So we are afraid to ask anything from them” (daughter-in law of a female patient).

While reviewing the illness narratives of CKDu patients, the empirical study has come across some of the limitations existing in clinical interventions with regard to the identification of CKDu patients and treating their illness. Communication gaps, internal arrangements/

organizational structure of the clinic, long waiting times and problems related to infrastructure facilities are some of the issues that have contributed in further deteriorating of the mental wellbeing of CKDu patients who visit the clinic for regular treatment.

Issues related to communication gaps between the patient and the healthcare providers is identified as one factor that should be given priority in this context. The patient is treated in the clinical setting as a passive object where he/she receives only instructions to follow but hardly gets any explanation with regard to his/her ill-health and relevant treatment which contributes in further deterioration of the mental wellbeing of patients concerned. The evidence further highlights the importance of integrating clinical social workers into the local healthcare delivery system urgently, in order to minimize and overcome the above limitations. Such clinical social workers can work in collaboration with health care providers to address the emotional wellbeing of patients.

Family as a Unit of Suffering -

It is important to locate the individual patients at the centre when evaluating his/her mental wellbeing. However, the empirical evidence of this study strongly suggests the importance of considering family as a unit when examining the psychological/emotional impact of ill-health related to CKDu. As Dwyer correctly pointed out, the Western conceptions of self and emotions stress that the human subject is held to be singular and unique. However in the Asian context, the individual is not an autonomous independent agent where it would be impossible to evaluate mental wellbeing of an individual by investigating them from the Western notion of authority (Dwyer 2003:111). As evident from this study, the family can be identified as a collective unit of suffering even though, the individual patients have responded quite differently to the similar situation based on his/her internal capacity.

All the illness narratives clearly show that the family functions as a unit of suffering with lots of burdens resulting from CKDu. The findings highlight the importance of family as a unit in dealing with the emotional dimension (along with all the other hassles) of ill-health that has been totally neglected by the professional sector of the healthcare delivery system. However, it is important to take into account that the whole family needs to be strengthened with necessary interventions throughout the process, regarding avoiding pain and seeking pleasure in the context of many burdens in order to enhance its capacity to face this long run disaster. The evidence strongly highlights the demand for family social workers in this context in order to address most of the adverse effects of CKDu on family. The following box provides some of the illness narratives in this regard.

Box 5.2: Family as a Unit of Suffering:- Voice of Patients and their Family Members

“When I heard that I am suffering from CKDu, the first question that came to my mind was that how I am going to tell this to my family members”.

“I discuss this problem only with my husband. I do not want to discuss it with my children because they are studying. My younger son is preparing for his A/L and I don’t want to see him suffering due to my illness”.

“My father is having a severe back pain and he is unable to move himself due to this problem. So, every month I go to clinic with his file (clinical records) to get medicine for him” (daughter of a CKDu patient).

“When I came and explained about my problem to my husband and children they cried and they were suffering a lot more than I suffer”.

“All the time my family members are trying their level best to ease my mind. They hardly ever allow me to be alone or allow me to be sad. They continuously keep an eye on me as I may suffer due to illness”.

“When I am getting frustrated and disappointed after attending the clinic my family members try their best to bring my mind back to normal and encourage me to go to the clinic”.

“I am sure we would not be this vulnerable if my husband was alive. I need to make arrangement to find suitable partners for my two young children. Sometimes I feel like I am mad and even lose my consciousness” (a widow from Padaviya who lost her husband due to CKDu).

“My wife has gone mad after we lost our only daughter and son due to CKDu. She was diagnosed as CKDu in 2001. We spent most of the money that we had on her illness. However, our daughter passed away on 8th August 2005 when she was 17 years old. It was a great difficulty for us to bear the loss of our daughter but somehow we were able to make up our mind as the son was with us at that time. However, he too got affected by the same illness and he passed away on 6th April 2011. My wife’s mentality went abysmally low immediately after our son’s death. By that time we lost not only both children but also most of the property that we had due to their illness and my wife became mad as she couldn’t tolerate the tragedy. My elder brother and his family took her to their place for a few months to look after her. I noticed that her illness was a bit ok when she was there with my bothers’ children. However, I went and accompanied her back as I was also unable to live alone in this house. My wife is at home now and the whole day she is continuously thinking and avoids any gathering. I have just started selling ice-cream to earn something for our survival. So we are now looking for a child for adoption if possible. If we were able to find a child, we will give him all the property that we have with us now (Father of two children who died due to CKDu in Padaviya)

Psychological Impact of CKDu on the Community -

Each person differs from the other depending on his/her internal factors as well as the influence of factors that are external to the individual. They may have unique experiences, different thoughts, or feelings. However, some common feelings and concerns are present since CKDu has become a social issue. The emotional wellbeing of not only the patient and his/her family, but the entire community has been gradually deteriorating due to illness where there is hardly any significant distinctions among different social categories based on their individual or social characteristics such as age, gender, social class, level of income, ethnicity etc.

The findings clearly suggest that the entire community needs to be considered as a vulnerable group when designing any intervention with regard to mitigating the adverse effect of CKDu. There are a number of occasions where the community has expressed their tension and dissatisfaction when interventions (such as distribution of water filters, clay pots, awareness raising programmes etc.) have been targeted only to CKDu patients but not the entire vulnerable community. The empirical evidence further suggests that there is a need for organizing and strengthening the community in order to mobilize its resources to face the challenge where the illness has already become a stigma and patients are discriminated due to illness (this factor will be elaborated further under the following section on social impact of CKDu). The empirical evidence strongly suggests that there is an urgent need for integrating community social workers to the local context who are capable of organizing such communities to mobilize their various resources at different levels to mitigate the disaster. The following section focuses on social impact of CKDu.

Social Impact of CKDu

Besides the emotional damage caused by CKDu, the same has many adverse effects on other domains of everyday life of a patient. The illness has direct impacts on patients' everyday life including livelihood activities, domestic tasks, consumption patterns and his/her participation in social activities at community level. The illness has brought about drastic changes within the unit of family in the domains of resource allocation, consumption patterns, setting priorities, maintaining social relationships and participation in community activities on behalf of the family etc. Finally the entire community has been affected due to CKDu deteriorating both valuable human resources and material resources in these communities. The above impacts will be elaborated in detail in the following sections.

The Impact of CKDu on Everyday Life of Patients

The empirical evidence of this study suggest that the everyday life of patient has been disturbed to a great extent not only due to physical discomfort and emotional damage caused by the illness but also due to issues related to the treatment process of ill-health and social/societal responses by labeling individuals as CKD patients (wakugadu karayo, wakugadu set eka etc). The impact of CKDu on patient's everyday life can be elaborated in relation to his/her participation in the domains of livelihood activities, domestic tasks including duties and responsibilities that are associated with various social roles (as head of the household, father, mother, spouse, son, daughter etc.), personal activities of the concerned patient (such as bathing and cleaning, food consumption, engage in religious/ritual activities, rest and leisure activities etc) and social activities at the community level.

The illness narratives reveal that there is a general pattern with regard to everyday life of CKDu patients. Accordingly, most of the patients struggle to continue with the same lifestyle with little adjustments even after their diagnosis as CKDu until physically they become inactive or incapable of movement. It is quite important to take into account that besides medical explanation, patients have their own criteria to evaluate his/her personal

health condition where physical fitness and the ability to work are crucial for the villagers in evaluating their health condition. The evidence suggests that most of the patients are compelled to continue with the same lifestyle if they feel physically comfortable in order to perform the particular task even though their productivity gradually deteriorates due to illness. Some of the patients in the sample have been diagnosed as CKDu when they were at a critical condition where the lifestyle of those patients had been changed within a short period of time after the diagnosis. It is of vital importance to note that there are some exceptional cases where patient's everyday life has become more active than in the past after diagnosis where patients have expedited certain tasks in order to fulfill his/her social responsibilities with regard to the family before ill-health becomes critical. It's a common feature that most of the patients have considerably increased the amount of time in their everyday life set aside to engage in religious and ritual activities due to illness, that can be seen as the main strategy adopted by them for restoring and enhancing mental wellbeing.

Impact of CKDu on Livelihood Activities and Domestic Tasks of the Patient

The empirical evidence of this study strongly suggests that impact of CKDu on livelihood activities of patients has an adverse effect on productivity. As mentioned earlier, most of the patients are farmers and they are compelled to continue with the same livelihood activities even after being diagnosed as CKDu patients until they become physically inactive. However, there are some changes with regard to the involvement of patients in their livelihood activities that are examined in detail under coping mechanisms in chapter six of this report. The illness has some adverse effects on the contribution of patients in his/her domestic tasks including duties and responsibilities that are associated with various social roles. As mentioned earlier, the patients try to continue with the same behavior as much as possible until he/she becomes physically inactive even though the productivity gradually deteriorates. Some of the voices of patients are as follows:

Box 5.3: Impact of CKDu on Livelihood from Patients' Voice

"I can work only half an hour per day now. But I used to work the whole day before this illness. Now I can't do even half of the work that I did previously due to this illness".

"I went to Pavankulum for Chena cultivation by my bicycle. I stopped it completely as I couldn't ride the bicycle for such a long distance due to my illness".

"The important decisions with regard to our family matters were taken by both of us together in the past. However, now I am not interfering in this regard and my wife takes all the decisions now".

"Earlier, we all took decisions as a group. But now the children take all the decisions and now I keep away and keep silent".

"My husband has reduced his interactions with fellow villagers because of this illness. Earlier he used to visit them quite often but now hardly visits them" (wife of a patient in Padaviya).

The narratives further suggest that most of the patients voluntarily become silent within the family by disengaging themselves from important activities while accepting the sick role when they started experiencing physical discomfort as a result of the progression of the illness. There is some evidence to prove that patients have taken immediate actions to fulfill some of the responsibilities with regard to children's matters before the sickness becomes critical (this issue will be discussed further under 'impact on family').

Impact of CKDu on Food Consumption Patterns

The empirical evidence suggests that most of the patients try to follow the food restrictions given by doctors to manage their ill-health related to CKDu. Accordingly most of them have limited taking certain food items such as tomato, fish, and meat while increasing certain food items as instructed by healthcare providers. Some patients have even started taking red rice, more vegetable etc not only to manage their ill-health but also for overall health promotion. In general, most of the patients have reduced the quantity of daily food intake due to the illness. However, as some of the patients pointed out they had initially followed food restrictions strictly but gradually neglected as the outcomes have been disappointing. Such a situation could naturally create frustration among patients and their families impacting on their wellbeing.

Impact of CKDu on Water Consumption Patterns

It should be highlighted that there are drastic changes with regard to water consumption by patients after diagnosing them as CKDu for which they have to bear extra expenses. In most of the cases it has been observed that the water consumption pattern of the whole family has been changed after diagnosing a patient as CKDu. Some of the behavioral patterns in this regard will be discussed under coping strategies.

The diagnosis of CKDu has not only resulted in a change in the consumption patterns but has created a certain amount of anxiety, uncertainty, insecurity and hopelessness in addition to the heavy burden on their daily expenses. The previous chapter explored the economic burden of these activities. The coping mechanisms of patients and their family members in this regard will be discussed in detail in the following chapter.

Impact of CKDu on Taking Alcohol, Smoking and Chewing Betel

As shown in patients' narratives, the majority of patients have totally stopped taking alcohol and smoking after their diagnosis as CKDu patients while some of them have reduced the usage and some still continue with the same behavior. However, there is hardly any change with regard to chewing betel, instead some of the patients have started chewing betel after being diagnosed as CKDu in order to avoid the unpleasant taste of medicine that they consume daily for the illness. It is important to note that the villagers use a plant called "talaa-kola" for this purpose instead of betel leaves that are commonly used in other areas of the country.

Impact of CKDu on Social Relationship of the Patient

Patients have gradually reduced their social activities when the illness became critical. Some patients have taken necessary action to replace themselves by another family member when they become quite inactive. The evidence of this study suggests that comparatively, social network of patients become active during the initial stage of diagnosis as CKDu where the neighbors as well as the relatives of patients who live in even distant places visit them to share the problem. However, the above social networks gradually deteriorate during the middle stage of the disease progression and once again they become active during the end stage of the process. In both early and end stages of the disease progression, the social network mobilizes its resources by visiting the patients with both emotional and material support. The long period of the middle stage of disease progression usually results in the neglect of the patient by the social network and limits the patient to his/her family and the immediate neighborhood.

However, the current trend in this regard is to keep the disease identity from the beginning as confidential even from relatives and neighbors due to stigma attached to the disease. As mentioned earlier, some of the patients try to hide the illness from relatives and neighbors in order to prevent adverse effects of stigma related to the illness. This behavior was observed as a general pattern in both Medawachchiya and Padaviya, where more interventions are required to address both issues related to stigma and also to strengthen the family as a unit to cope up with the crisis. At present there are no proper counseling services available to patients and his/her family in this regard.

Impact of CKDu on Patient's Family-

Family is one of the most important social institutions that help society in organizing most of the social roles for its smooth functioning. Thus, the family is responsible for activities related to both production and reproduction while mutually sharing its resources, fulfilling emotional needs of its members and providing care to needy members within it. The empirical evidence of this study shows that the family has been greatly affected by CKDu in various ways. As discussed earlier, the family is viewed as a unit of suffering that has been basically affected in three ways. Firstly, the family has been affected by low productivity of the ill- member due to his/her illness; secondly by allocating its resources, both human and material, to manage ill-health of that particular member and thirdly, the emotional and social cost of illness on family. These impacts are further elaborated under everyday life of family members, resource allocation and setting priorities within the family, consumption patterns, maintaining social relationships and participation in community activities.

Impact on Everyday Life of Family Members

The everyday lives of family members of CKDu patients have been affected by illness in various ways. On the one hand, the patient's family members have to replace the workload that was previously done by the patient concerned due to his/her illness. On the other hand, the family members have to accept an additional workload related to care giving for

the CKDu patient. In some families, the members had to find new income generating activities in order to cope up with additional expenses incurred due to illness. By contrast, there are some families where the members had to stop/reduce their livelihood activities in order to provide necessary care for the CKDu patient.

Box 5.4: Voice of Family Members with regard to the Impact of CKDu

“Son has to work as a laborer in road construction work even though he is an educated person. He wanted to continue with his education and he is very bright too. However everything has changed in our life after his father’s illness. I also struggle a lot to find something for our survival (Wife of a CKDu patient).

“I had to resign from my Garment job as mother alone is unable to look after our father. We have to take him to Anuradhapura for dialysis and we both have to go with him. So I had to stop going for work even though I earned Rs.10,000 to 15,000 per month” (daughter of a CKDu patient)

“Son was unable to sit for the A/L the second time due to my illness. Otherwise he could have got into the university. He had to find a job because of my illness”.

Daughter didn’t like to sit for AL second time because of my illness”.

It was observed that comparatively family-members have to suffer more when the patient functions as the head of the family. The spouse faces a lot of difficulties in order to deal with duties and responsibilities that are attached to the family unit. The children of the family were also affected badly when a parent became ill. As evident from this study most of the family members have adjusted to the situation by adopting different strategies where in most families the members have limited engaging themselves in leisure activities, scarified future endeavours etc. to cope up with the illness. The family members are further affected by illness as it gets critical time to time this in turn results in emotional harm. As mentioned by one of the family members “we also mentally go down when our son’s illness becomes serious and hardly do any work at that time”. The empirical evidence shows that the experience of patients and their family members differ from one to the other depending on available resources, the networks and specific characteristics of an individual which further suggest that each family needs to be considered as unique when designing interventions for mitigating the adverse effect of CKDu on the family. This could be done by using family social workers who could draw up care plans for patients and their families. The following section explores the impact of illness on resource allocation and setting priorities within the family.

The Impact of CKDu on Resource Allocation and Setting Priorities within the Family

The empirical evidence of this study clearly shows that the family has given its foremost priority to managing the health of CKDu patients while allocating most of both its material and human resources for this purpose. Thus, managing of ill-health related to CKDu has been receiving more attention within the family while neglecting, delaying or scarifying most of the needs of other members of the family. The case histories of patients who passed away due to CKDu provide a comprehensive representation in this regard which further verifies the fact that family needs to be considered as a unit of suffering.

Impact on Education

As revealed in the narratives of patients, the family has been affected by CKDu in many ways. The education of children has been affected as many of them have had to drop out of school due to sickness of one member in the family. In some cases the educational performance of children had decreased after a family member had been diagnosed as CKDu, while some children faced difficulties in attending extra classes for tuition due to financial problems within the family. The education of children is mostly affected when the patient is the head of the household where schooling becomes irregular as children have to get involved/ help in family income generating activities or for caring for the patient.

Impact on Marriage of family member/s

As revealed by empirical evidence, the impact of CKDu on marriage can be seen in two ways. In some cases, parents had arranged early marriages for their children due to illness of mother or father. In some cases marriages of children have been delayed due to sickness of either mother or father where the single parent has to take the whole responsibility in this regard. The empirical evidence suggests that finding suitable partners for the children of CKDu patients have become problematic due to many reasons. Some of the geographical locations in the area have been labeled as high risk areas for CKDu which also has a negative impact on people who live in those areas including in the context of marriage. It becomes further problematic as the illness is associated with stigma and also as genetic factors are considered as one of the causes of illness by lay people. There are some exceptional cases as well, for example where a young boy has decided never to marry as he has to look after his widowed mother since the father died due to CKDu.

Impact on development activities in the Family

The development activities related to family have been impacted by CKDu in many ways. As is evident, most of the construction work of family has been delayed due to illness but there are a few exceptional cases where the family has taken immediate action to complete construction of house and other arrangements quite rapidly before the patient's condition becomes critical. However most of the evidence suggests that people had sold some of their lands, livestock, vehicles and equipment related to agriculture due to CKDu of one of the members in the family while some people had to delay purchasing land, equipments etc. as they have given their main priority to managing the ill-health related to CKDu. The following box presents experiences that are reported by family members of a dead patient after kidney transplantation which further explores many dimensions of family suffering due to CKDu.

Box 5.5: Voice of Parents who Lost Their Elder Son due to CKDu

Our son was diagnosed as a CKDu patient in 2005 and he died on 15th September 2007. We spent more than a million for his illness. We took him to several places to confirm the diagnosis including Anuradhapura, Kandy and Colombo. He followed all the advice given by doctors. We took him several times to Anuradhapura for dialysis. Finally we went to Kandy hospital for kidney transplantation. It is not a game doing kidney transplantation: it required lot of money. We had to rent a house near the hospital in Kandy for which we paid Rs. 5000 per month for nearly two years. My wife stayed with our son and I went once a week from Padaviya to Kandy with rice, vegetables and all other goods that were required for their survival. We faced a lot of difficulties to find a kidney for him. I am still very sad to note that one day our daughter had gone to meet the doctor without even our consent to donate a kidney for her elder brother. However the doctor had explained the inability of taking her kidney as she was too young. Finally, mother decided to offer a kidney for which both mother and son had to undergo many tests including CT scan. I took both of them to Sri Jayawardenapura hospital for those tests for which I think we spent more than hundred thousand. The son had to go for dialysis until the transplantation took place.

So, earning money was like a war for us during that time. While mother and son were in Kandy we did so many things to earn the required money. Both younger son and daughter were studying at that time. So, both of them stopped their education and son joined the army and the daughter stopped her schooling and later joined the Nursing College as we were unable to spend for her education. She was a very bright student and was dreaming to go to Medical College. I am sure she would get that opportunity if she was able to sit for the A/L for second time. The only dream of the whole family at that time was to save the life of our son while sacrificing everything. However, he suffered a lot before his death not only due to his illness but also worried as he lost many of his friends due to his illness. People started discriminating and ignoring him. Most of the time he was treated differently even by his close friends whom he met during his school days. One day when he was travelling from Anuradhapura to Padaviya by bus nobody sat near him as he was wearing a mask. That day he felt very sad and told us that he has got a very bad illness. We had just started constructing a house when he was diagnosed as CKDu. We were able to finish only the foundation by that time. We had saved some money for this purpose. However, we spent all the money for his illness. We took loans from all the possible sources while selling animals that we had at that time. Even though we faced lot of financial difficulties during that time we constructed a comfortable room for him as he needed a good place to live after the transplantation for which our neighbors helped us a lot by providing their labor without getting a single cent. After the transplantation he gradually became disappointed as he was treated differently by the whole society. With this frustration he started not to take proper care of himself. He didn't even listen to us. Once again he became ill and then the doctors found that a germ had entered his kidneys. He died within a short time after that incident. When I see my wife, all the time my son comes to my mind. We all had done everything for him. However, finally we lost not only the son but also wife became a patient by giving her kidney for him. **(Father of a person dead due to CKDu in Padaviya).**

Impact on Family Consumption Patterns

The consumption patterns with regard to food and water have been changed within the family after diagnosing a member of the family as CKDu. Accordingly, some families have limited expenses on food due to economic difficulties. In most of the families, a separate meal is prepared for the patient while others eat whatever is available. Some people have started cultivating necessary vegetables in home gardens. However, a new trend is visible in Medawachciya where vehicles come to the village several times per week to sell vegetables that are brought from Dambulla market and villagers are compelled to buy them. It is very clear that most of the families spend out-of-pocket expenses to get potable water not only for the patient but also for the whole family from the sources that are believed not to be contaminated. Most of the families have bought water filters giving this purchase priority.

Impact on Family social relations and community activities

The empirical evidence suggests that social relationships of the family have been affected by CKDu both negatively and positively. The patient has attracted a lot of attention within the family where emotional bonds among the members have been further strengthened due to illness. The married children who live in distant places come to see the patient very often and even children who didn't have close relationship with family became closer due to mobilizing their resources to deal with the crisis situation. However, as mentioned earlier, the general pattern is that family ties with relatives and neighbors become strengthened at the initial stage of diagnosis of a family member as CKDu and they are weakened in the middle stage and re-strengthen at the end stage. In addition to the above pattern there are some occasions where the family networks become weakened throughout the process and as against some networks continuing while mobilizing their resources throughout the process to manage the patient's care.

The Social impact of CKDu on Community

CKDu has many adverse effects that concern communities as it devastates both human and material resources in the community having the sick population. The communities become more vulnerable when there are a large number of CKDu patients within the community as they are unable to help each other. The other issue is that there is a trend of labeling villages where there is a high prevalence of CKDu which is closely associated with stigma. The labeling itself has many negative impacts on the members who live in those communities while creating social problems. In Padaviya it was reported that one family had left the village in order to escape from labeling. Although this is just one case, in the time to come, if the problem is not addressed there can be more families moving out of these areas. The study locations are comparatively more vulnerable to many hazards such as drought, wild-elephant attacks etc. where CKD with unknown etiology has added further uncertainty to make the situation worse. The empirical evidence suggests that there are hardly any signs of addressing relevant issues at the community level even though there are some existing CBOs contributing in indirect ways to provide necessary resources only when the crisis becomes critical.

(e) Coping Behavior of Chronic Kidney Patients, Their Families and Community

The scientific community, both medical and other experts are still uncertain about the etiology of CKD. Nevertheless there are many speculations derived by experts that are available to the lay people. The importance given to these speculations differs from time to time where certain reasons/causes become dominant in the discourse. People too, based on their experiences, contribute to this discourse. As discussed in chapter three there is by now a well established community discourse on CKDu due to its high prevalence, resultant suffering and the fear generated in the area. There are many discussions, debates among villagers about the causes, symptoms, treatments received from healthcare practitioners and the facilities available at hospitals and clinics. Although the uncertainty is great, patients, their families and villagers in general are not passive in responding to the situation that has badly affected them. Therefore there are a number of coping mechanisms adopted both at individual and community levels which will be discussed in the present chapter. Firstly the coping behavior related to the preventive methods would be discussed. These behavioral patterns are adopted by patients, their families and non patients in both Medawachchiya and Padaviya DS divisions.

Definition of Coping

Coping strategies refer to the specific efforts, both behavioral and psychological, that people employ to master, tolerate, reduce, or minimize stressful events. Two general coping strategies have been distinguished: problem-solving strategies are efforts to do something active to alleviate stressful circumstances, whereas emotion-focused coping strategies involve efforts to regulate the emotional consequences of stressful or potentially stressful events. Research indicates that people use both types of strategies to combat stressful events (Folkman and Lazarus, 1980). The predominance of one type of strategy over another is determined, in part, by person's personality attributes (e.g., some people cope more actively than others) and also by the nature of the stressful event; for example, people typically employ problem-focused coping to deal with potentially controllable problems such as work-related problems and family-related problems, whereas events perceived as less controllable, such as certain kinds of physical health problems, prompt more emotion-focused coping (**Error! Hyperlink reference not valid.**).

An additional distinction that is often made in the coping literature is between active and avoidant coping strategies. Active coping strategies are either behavioral or psychological responses designed to change the nature of the stressor itself or how one thinks about it, whereas avoidant coping strategies push people to activities (such as alcohol use) or mental states (such as withdrawal) that keep them from directly addressing stressful events (<http://www.macses.ucsf.edu/research/psychosocial/coping.php>). Thus both types of coping, problem solving strategies and emotion-focused coping are evident among CKDu patients and their families. With regard to active and avoidant coping strategies, the present study reveals that instances of avoidant coping strategies are less and most have resorted to active coping strategies which are highlighted below under different issues.

Coping Strategies at the Individual and Family Level

This section explores both problem-solving and emotion-focused coping strategies adopted by the CKDu patients and their families in order to respond to the crisis situation.

Problem-Solution Coping Strategies-

Coping Behaviour Related to Preventive Aspects

As said before although there are a number of causes identified though not scientifically established, the poor quality of water in the area is one that has been discussed for many years. The villagers based on their experiences are also ready to accept the fact that the drinking water they use is not suitable. The villagers are made to believe that water is a decisive factor as some neighboring villages where water is consumed from spring wells have no reported cases of CKDu. However, there are some villagers, like experts who are skeptical of water being the sole reason for CKDu. In the midst of such uncertainty, the villagers, both patients and non patients in Medawachchiya as well as in Padaviya do not remain passive but have adopted a number coping strategies to overcome the situation. As discussed in chapter five, most of the patients and their family members have changed their sources of drinking water a CKDu patient/s were diagnosed. 71.5% of patients revealed that they used different strategies to consume safe water as discussed below.

Today, water is considered a precious good by everyone in the area. While people look for different ways to avoid the consumption of ground water they also use water sparingly. Both these strategies as explained in earlier chapters reflect negative impacts on the village population and make them more vulnerable. Until recently bottled water was associated with urban high and upper middle classes. However, today some villagers have resorted only to purchase bottled water from the market instead of ground water. Bottled water is readily available in the local market and it has become a lucrative business today. In fact there are some shops such as “water shops” that only sell bottled water. Nevertheless, the high cost factor has curtailed the access to this bottled water only to those who would afford to purchase it on a regular basis.

There are many villagers who go especially to Gonamariyava village in search of clean spring water. This factor was highlighted in a previous study carried out in 2009 by Liyange C. and Jayatilaka R. According to availability and affordability, the villagers use different modes of transport to bring water from the spring wells. It is a common sight to see three wheelers and vans parked near the spring wells. While some consumers use their own personal transport, others hire three wheelers or vans to go to the spring wells. Due to the overwhelming demand for spring water, there are some people who bring spring water to sell it in the village. In the village context traditionally water was seen as a commonly shared item but today it has become a commodity with a significant commercial value. This has increased daily expenses of families, and has become a great burden, especially to patients who have to meet considerable medical expenses as well.

Box: Voices of Villagers

“Today even a laborer with some money goes to Gonamariyawa to bring water. It doesn’t matter what happens to us. But we have to think about our children. Now the problem is not about eating but about drinking water”(FGD, Medawachchiya).

The use of water filters is another strategy adopted by the villagers to consume safe water. For most families a water filter is an essential household item. Different types of water filters are available in the market and they are purchased according to individual affordability. Once again the market forces have taken advantage as the State has not been able to provide safe water, a basic need for people who are suffering from a chronic illness in the area. Needless to say that these different coping strategies have become an extra burden to the families.

The use of rain water for drinking is another way of avoiding ground water for consumption. In Padaviya some years ago a project for rain water harvesting was introduced. The project was a failure as the villagers did not respond favorably showing their dislike to keep a huge tank in-front of the house which they called “musala tanki” (tanks of ill omen). However, today the critical situation has forced the villagers to ask for a rain water harvest project so that they could use it for drinking rather than water from their wells. This shows that villagers are flexible in changing their views and perceptions when there is a need which is a positive sign for health promoters in doing health awareness programmes which at present are lacking in other social contexts.

While different ways and means have been adopted to refrain from consuming ground water, water brought from outside is sparingly used as it is precious. Some villagers justified as to how they do not drink water from glasses and store water in bottles and drink from them so that what remains after drinking could be used again. Some villagers said that they drink less water as they cannot bear the expense on drinking water. This could have negative impacts as drinking less water in a dry environment could lead to dehydration and other complications. However, it is clearly evident that both patients and non patients have adopted different strategies to avoid the use of unsafe water rather than waiting for state intervention although the villagers very clearly see the need for such an intervention.

The heavy use of pesticides and fertilizers in cultivation is another factor identified as a cause for CKDu. In both Medawatchchiya and Padaviya cultivation is the main economic activity for most villagers. They cultivate both paddy and vegetables for which they use chemical fertilizers and pesticides to obtain a good crop to sell in the market. The villagers believe that the soil is infertile and the only way of getting a good harvest is to use chemical inputs. Chemical fertilizers are also widely used by the villagers for weeding due to labor shortage. Comparatively, mechanization is also less developed in this regard where villagers are compelled to use various types of chemical fertilizers from the local market for better output. There are some occasions where farmers mix different fertilizers to make it stronger for better impact. They also strongly believe that the food contaminated with chemicals is not good for health. Although many cultivators do not use precautionary methods such as using gloves, mask and other types of protection while applying chemicals, they cultivate separate crops in a small plot for their personal consumption where chemical

inputs are barely used. Therefore they differentiate between safe and unsafe food. While safe food is for personal consumption the unsafe food is to earn from the market.

There are some cultivators who cultivate entirely for the market without keeping anything for themselves. Such farmers purchase vegetables that are grown in the up country (brought into the village by the vendors) assuming that they are less contaminated by chemicals and are more suitable for consumption. While it is a coping strategy to avoid unsafe food for consumption, villagers are rather negative about using the vegetables that are freely available in the area which are more suitable for people living in the dry zone. The elderly villagers believe that in the past they consumed locally grown vegetables and fruits, that would act against dehydration and prevent renal and kidney diseases.

Thus, the issue of food security has emerged in the local context by not having safe food for consumption locally. The need for safe food has mostly arisen due to the prevalence of CKDu in the area. However, in the absence of a proper state level action to address this issue, the village population remains vulnerable to chronic diseases in many ways.

The use of aluminum pots for water storage and pans for cooking is considered as unhealthy and a cause for CKDu. The tendency to use aluminum utensils resulted with the availability of such items in the local market and the practical difficulties in using earthen or clay pots and pans. However, the discourse on the use of aluminum and CKDu has forced the villagers to revert to the use of clay pots and pans. In several instances, clay pots were distributed to families by different agencies. These factors clearly show the resilience of the people and their readiness to cope with the situation. However, the villagers are eager to know the definite causes of the sickness in order to mitigate the problem. Thus it is a challenge for the academic community to rapidly and successfully identify the causes for this deadly disease.

Coping Behavior during Sickness Process

As mentioned in the previous chapters when a person is diagnosed as a CKD patient it becomes a struggle between life and death to that person. Both patients and others identify the sickness with death. In such an emotionally devastating situation the responses and the coping strategies of patients and their families can be different from one another. However, there are certain patterns that could be identified through the narratives of patients, their families and villagers. At the very outset it is necessary to mention that except for a few patients who withdrew from engaging in activities due to a negative mindset, all others adopted different coping strategies to face the situation. As said before these coping strategies could be identified at different levels –individual, family and community. It is also important to explore whether or not the State and NGOs have used this positive attitude of the patients and their families to improve their wellbeing.

Livelihood Activities

According to the patients' profiles it is clear that a majority of the patients are the heads of households and most often the main income earner in the family. Many of them are cultivators and the illness has impacted on their livelihood activities to a greater extent as

explained in the previous chapters. While it is clear that the economic impact is severe on the patients and their families, they have resorted to different methods to continue with their activities. This is in order to cope with the situation. There are a few who have given up cultivation totally due to illness but most continue with adjustments. The following table reveals how the illness has affected them by gender and DS Divisions.

The Number and Percentage of Patients Whose Livelihoods were affected by sex and DS divisions

Gender	Affected or Not	Medawachchiya	%	Padaviya	%	Total	%
Male	Affected	53	85.5	56	91.8	109	88.6
	Not affected	9	14.5	5	8.2	14	11.4
	Total	62	100.0	61	100.0	123	100.0
Female	Affected	18	78.3	21	95.5	39	86.7
	Not affected	5	21.7	1	4.5	6	13.3
	Total	23	100.0	22	100.0	45	100.0
All	Affected	71	83.5	77	92.8	148	88.1
	Not affected	14	16.5	6	7.2	20	11.9
	Total	85	100.0	83	100.0	168	100.0

The above table shows that the livelihood of 83.5% in Medawachchiya and 92.8% in Padaviya has been affected. Except for a slight difference on a gender basis and by DS division, the illness has affected the livelihoods of the patients as a whole. However, it is important to note that other than a few (10.6%) who withdrew from their livelihoods, the others have continued to work reflecting their endurance to cope with the situation. The following table shows how the patients have responded to the issue.

The Coping Behavior related to Livelihood Activities

Coping Behavior	Medawachchiya	%	Padaviya	%	Total	%
Continuing activity despite the discomfort	12	12.2	32	29.1	44	21.2
Continuing activity with the help from family members	31	31.6	30	27.3	61	29.3
Using alternative measures	35	35.7	34	30.9	69	33.2
Withdrawing	13	13.3	09	8.2	22	10.6
Other	07	7.1	05	4.5	12	5.8
Total	98	100.0	110	100.0	208	100.0

The data clearly reveals that 21.2% patients do continue with their livelihood activities as before in spite of their sickness as the family income has to be sustained for survival. According to them, they have to bear the discomfort as continuing with their livelihood was essential for family survival. However, this is possible only at the early stages of the sickness as at subsequent stages the patient will be confined to the house.

Box : Voices of CKDu Patients

“I work as a casual laborer although I am sick. I have to earn for my family and do my duty”
“Even though I am sick I work. Isn’t that good? Some people cannot do anything. If I think so, surely I will go mad”
“I can at least do this much of work despite my sickness. Some others cannot work at all. I am happy that I can at least do this much of work”

There are 29.3% of patients who continue with their livelihood activities with the help of family members. This is possible only when family members are available to assist with the livelihood activity.

Box: Voices of Patients and Family Members

“Those days I used to do cultivation. Every day from morning till night I worked in the paddy fields without any respite. Now due to fatigue I cannot work like those days. It is my son who works in the paddy field. When I can, I go and watch him working” (CKDu patient).
“Previously my husband used to work all alone in the paddy field. But now it is done by my son. He is still schooling, but as we have no one else to help he gets absent from school during cultivation time to attend to the work. My husband stands by him and explains everything” (spouse of a CKDu patient).

When such an option is not available to the patient alternative measures are taken. According to the narratives a number of alternative measures are adopted, such as renting out the land for cultivation (Anda govitana), mortgaging land, use of hired labour, use of machinery. Some have given up cultivation and resorted to new livelihoods such as running a small shop/ boutique close to their home.

Box: Voices of Patients

“I used to work in the paddy fields. But now I am not working. I have given my land for rent (on Ande). But I can’t get the work done as I want”
“Ever since I fell ill I hire labour for cultivation. But I cannot get the work done the way I want. Once I settle the laborers and debts there is hardly anything at hand”
“Earlier I got an income by cultivation. But now we are running a boutique to earn. However, now we get a lower income”

There are also a few (10.6%) who have completely withdrawn from their livelihood activities and solely depend on others for their survival. This may be due to the acuteness of the illness. While all patients are economically vulnerable those who have completely withdrawn from the labour force are in dire straits as they have to depend entirely on others

Box : Voices of Patients

“Before I fell ill I did well in cultivation. But after falling sick I took Ayurvedic medicine and continued to work. But when I fell sick for the second time I took western medicine. After taking western medicine I do not do any work as I cannot tire myself”

“Before falling sick, I used to do everything, worked in the Chena, paddy fields, gave Attam (exchange labor) and had no problem. However, with this sickness everything came to a standstill. I cannot stay in the sun as I get faintish and sometimes I begin vomiting

The above voices show the resilience of patients facing the challenges of the illness. In such a situation, assistance from outside and social support systems are essential to improve the wellbeing of patients and their families.

Although the patients and their families have resorted to different measures to cope with the situation, their level of satisfaction is rather low as they are unable to generate an income as before. Therefore once again the need for a proper social support system is important in parallel to proper medical services. Patients’ level of satisfaction with the new practices adopted to cope with the situation is given in the following table.

The Coping Behavior related to Livelihood Activities

Gender	Answer	Medawachchiya	%	Padaviya	%	Total	%
Male	Satisfied	17	32.1	25	44.6	42	38.5
	Not satisfied	36	67.9	31	55.4	67	61.5
	Total	53	100.0	56	100.0	109	100.0
Female	Satisfied	5	27.8	7	33.3	12	30.8
	Not satisfied	13	72.2	14	66.7	27	69.2
	Total	18	100.0	21	100.0	39	100.0
All	Satisfied	22	31.0	32	41.6	54	36.5
	Not satisfied	49	69.0	45	58.4	94	63.5
	Total	71	100.0	77	100.0	148	100.0

The above table shows that a majority of patients both male and female from the two DS divisions are not satisfied with the new practices followed to cope with livelihood activities. A slight gender difference could be seen in both DS divisions where the number of unsatisfied females is higher than males.

Medical and Other Expenses

As discussed in chapter four, the medical expenses for a CKDu patient is quite high as she/he has to spend on drugs, testing, dialysis, transplantation etc. In addition to these direct expenses on the treatment, patients have to bear a huge cost for transport to

clinics/hospitals. However, it is clear that the patients have adopted a number of measures to cope with the situation while receiving medical treatment. Some of these measures are as follows:

- Using previous month's income
- Using patients' savings
- Support from family members
- Mortgaging jewelry
- Selling livestock
- Selling household items
- Borrowing money from relatives and friends
- Borrowing from money lenders
- Reducing consumption expenditure
- Receiving state support

The most common actions are depending on family support (33.5%) using patients' savings (18.5%) and borrowing from money lenders on credit (11%). It is important to note that only a few (3.5%) have benefited from state assistance as it is given only to the patients who are at the critical stage.

Box: Voices of Family Members of the CKDu Patients

"At the beginning the money that had been saved from cultivation was used for medical expenses. In due course more money was needed. We then mortgaged our land and we were unable to recover it. When we ran short of money we also pawned gold jewelry which we gradually recovered" (a Family member of CKDu patient).

We had to sell our cows and received Rs. 7000/=. We also had to pawn jewelry which we could not recover" (a Family member of a CKDu patient).

"When he was ill our children gave money for treatments. But when that money was not enough we pawned our jewelry and got money from the bank. At times my brothers also helped us" (a Family member of a CKDu patient).

These are clear active problem–solution coping strategies. However, it is important to note that although such coping strategies are needed for the patients to meet their medical expenses they could also push patients and their families into a vulnerable position. The risk of increasing vulnerability of the whole family is quite evident and it could have a disastrous outcome. Thus, the importance of institutional support systems is once again highlighted. In this respect the only assistance that the Government provides is an allowance Rs. 500/= per month (at the time of investigation) to the CKD patients who are diagnosed as stage three/four patients. While this could be of assistance to the patient and his/her families the lack of sensitivity on the issue has brought about some kind of unhappiness and depression to the patients and their families. Since the allowance of Rs .500 is given only to those who are critically ill, such patients get labeled as "wakugadu karayo" (Kidney people), "waku gadu set eka"(set of Kidney people), "waku gadu gansiya"

(a gang of Kidney patients) and also they are seen as critically ill and getting close to death. Some even call them as those who have received the 'ticket for death'. Since the patients themselves have to collect the allowance from the nearest post office, the issue of anonymity is lost and becomes a problem when a certain amount of stigma is attached to the sickness. Access to the above service is also an issue for the patients. As the patients are required personally to collect the allowance from the post office, for some patients it is a problem as they need to bear an extra cost for transport. The service providers are only concerned about the disbursement of the money that has been approved but they hardly regard the importance of the patient's perspective when deciding on matters that directly affect them. This becomes more problematic when there are no advocates to ensure that the voice of the patients is heard. The lack of professional social workers who could perform the task of advocates on behalf of the patients is a huge shortcoming in our medical and social systems.

Family Wellbeing

As discussed before most of the patients are adults, married and heads of households. While the patients are emotionally devastated and experiencing stress and pain some of them have taken a positive approach in fulfilling their responsibilities without submitting passively to death. Some patients felt the need to expedite important activities pertaining to family welfare such as construction of house, distributing land among children, giving children in marriage. This is because the patients have identified the sickness with death and they do not want the children to suffer.

Box: Voices of Patients and Their Families

"My engine will work only for five years. I need to expedite the activities in my life. But this will not be good for my health" (a CKDu patient).

"I distributed land among my children. The house was transferred to my youngest son. I advised my children not to fight over the land even though there could have been short comings" (a CKDu patient).

"Before my father died he told me that he wished to see me getting married. I was then only eighteen years and I had to get married. Later my sister was given in marriage" (a daughter of the patient who had died from CKDu).

"When my husband (a CKD patient who died) fell ill our youngest son was unmarried. My husband was very keen to get the son to marry as he would be alone after his death. Therefore, we expedited his marriage" (a spouse of a CKDu patient who had died).

The above actions of patients reflect the importance of the socio-cultural dimensions. In Sri Lanka, even though families are undergoing many changes, still the parent-children relationship is strong. Despite the children being grown the parents believe that it is their duty to take care of them until they get married and live independently. In Sri Lankan society the arranged marriage is still predominant and it is the duty of parents to look for a marriage partner for their child. This becomes a great burden to the patient as he/she has to bear a huge wedding cost in the midst of his/her medical expenses. However, when it comes to assistance no financial institution would give credit for such activities. At such a time the only option is to borrow from a money lender at a high interest rate. This shows

the importance of considering the different types of expenses that the CKDu patients have to bear in more ways than one.

Emotion Based Coping Strategies

As discussed in the previous chapter the emotional impact on the patient and his/her family is tremendous due to the fact that the disease is incurable and the feeling associated with imminent death. A desperate utterance of a patient “Children in our village will not see people with grey hair or walking with a stick” reveals the gravity of the problem. The villagers do not expect people to live long due to the illness. Thus an inevitable question would be “How do patients and their families cope with the situation?” This becomes more important as in Sri Lanka still the emphasis is only on the medical needs and not on the social and emotional needs of the patients. This gap is fulfilled by different informal ways to a certain extent but demands professional organized assistance to ease the pressure.

The Role of Religion

The study has clearly identified that the role of religion is important in reducing the anxiety and bringing hope to CKDu patients to live at least a few more years by delaying death. Buddhism is the main religion practiced by the patients in both Medawachchiya and Padaviya. However, while observing Buddhist religious practices many have followed other rituals as well. Thus, people do not restrict themselves to the practices of one religion in order to get mental satisfaction as emotional needs are not addressed in the services provided for patients.

The study did identify a number religious practices followed by the patients which will be discussed below. It is important to note that most of the patients believe that they need to be religious as it would help them in coping with the situation. Some patients said that after the sickness they became more religious and went regularly to temple, observed ‘Sil’ on all Poya days and listened to Dhamma sermons preached on the radio. Meditation is yet another popular event among patients. Some go to temples to meditate while many others meditate in their own homes. Some patients get a family member to read religious books. This phenomenon of religion being a resource for coping has been established by other researchers such as Harold G Koenig, David B Larson, and Susan S Larson who say, “Many studies, in fact, have documented a positive association between religious involvement and better adaptation to mental illness or to the burden of caring for those with mental illness. Some studies show that religious coping is even associated with improved attendance at scheduled medical appointments, and involvement in religious activity has also been associated with better compliance with antihypertensive therapy” (2001:354). The study has further elaborated by endorsing a positive relationship between religion and the wellbeing of the patient by highlighting how religious involvement gives better purpose and meaning to life, greater hope and optimism, less anxiety and depression for patients.

Other than the above mentioned religious practices an important and a popular practice followed by patients and their families is performing ‘Bodhi Puja’ (bathing the Bo tree and chanting Buddhist stanzas to bless the patient) for seven consecutive days. This is

performed by the priest and often is also done in private by the patient and his/her family. However, at times it is done for the patient by others such as relatives or neighbors. At present performing 'Bodhi Puja' has become almost a daily occurrence in the temple and has become an organized activity with one particular priest taking the responsibility.

Chanting Prith (Buddhist discourses) to bless is a popular religious practice among Buddhists. Generally the Buddhist priests chant 'Prith' at the temples or at times when the priests are invited to the house. However, in both Medawachchiya and Padaviya DS divisions in addition to Buddhist priest chanting 'Prith' lay devotees also perform the same task named as "Gihi Prith (Prith chanted by lay persons) .Although this was a traditional practice in rural areas, today it has become more regular and organized. It is performed by six to seven elderly men, considered as pious and religious. In Padaviya the group is led by a CKDu patient who is suffering from the sickness for nearly 15 years. He believes that he is blessed by his action while invoking blessings on others. Out of seven members in this group five are CKDu patients.

Patients and their families are not just limited to the above Buddhist practices but perform other religious and rituals practices. An important emotional coping strategy followed by many is getting the patient's horoscope read by an astrologer (horoscope reader). Generally when the horoscope is read the patient is instructed to perform certain rituals to get rid of the evil effects such as tying a talisman around the neck, taking a vow, offering items to the priests, releasing a cow that is about to be slaughtered etc. These actions rekindle the expectation of the patients that, at least that they could delay their death.

In the local context there are certain deities who are venerated by people in search good-will and protection. Thus this is another practice followed by the patients and their families to get relief and lessen their anxiety.

The previous sociological study on CKDu (Liyanage, C, and Jayathilaka, R. 2009) has pointed out the importance of healers to whom the patients went in search of relief. These healers were not from the same locality but from distant places. The patients were attracted to such healers and many of them participated in these healing sessions. However, it is significant to note that at present the attraction to such healers is less mainly because more assistance is available within the local context.

It is important to mention that these practices are not alternatives to medical treatment but they are performed in parallel to taking medical treatment, as complementary activities. Not that these patients perform one but a combination of these practices. Although such practices were in the traditional rural society today it is institutionalized and commercialized. Though performing these practices is important in providing emotional comfort it does add to the expenses of the patient and family as performing most rituals are costly. Religious and ritual practices have become more and more important in the absence of proper social support systems. The importance of such practices is highlighted in the patients' voices below.

Box: Voices of Patients and Their Family Members

“When we came to know of my husband’s illness we went to Pulyar Kovil (shrine of a local god) and made a vow. We also went to Anuradhapura and took a vow near the Bo tree. Then we got his horoscope read and since it was a bad time for him we performed certain rituals to ward off the evils. Moreover, we went to Dalada Maligawa (Temple of the Tooth relic) and took a vow to delay the death by at least five years” (the spouse of a CKDu patient).

“On hearing of my father’s illness we all at home got together and took him to a devale (shrine) in Kebithigollava and got him blessed. We also got Pirith chanted by the lay devotees” (Family member of a CKDu patient).

“We did not tie a talisman or took vows as they couldn’t do anything for this illness. But my father observed sil performed Bodhi Puja and offered requisites to the priest” (Family member of a CKDu patient).

“I did seven days of Bodhi Puja at the temple. I also participate when there are Bodhi Pujas for others. I try to make up my mind by performing these religious activities. They are useful to make me forget about the suffering but it is not always possible” (a CKDu patient).

“I participate in meditation classes. I also meditate at home. It brings relief to my mind. It is also good for my next birth” (a CKDu patient).

“I think what is important is to comfort the patient” (a family member of a CKDu patient).

The Importance of Social Capital for Individuals

Social capital is also another resource that is used by patients and their families for both types of coping strategies. Social capital is about the value of social networks, bonding similar people and bridging between diverse people, with norms of reciprocity (Dekker and Uslaner 2001). In rural society people identify themselves as “Äpi eka game minnissu” (we are of the same village) which helps people to bond together and network for reciprocal gains. In both Medawachchiya and Padaviya DS divisions the patients and their families have benefited by informal social networks, especially due to the assistance received from relatives and neighbors.

Although the patients restrict their visits to relatives and neighbors, in fact, social relationships and networks have strengthened due to illness. This is because of the solidarity shown by relatives, neighbors and friends. However, according to the patients’ narratives there are instances where such social networks had broken down after the death due to family conflicts.

The patients highly appreciated the assistance received from relatives as they came as financial assistance and psychological support. The financial assistance is of great value as it helps to reduce the economic burden on the patients and their families. Similarly the psychological support such as visiting and spending time and discussing about the illness with the patient and family has helped to reduce anxiety and stress. Such social relationships help the patient to strengthen the bonds with other persons and develop solidarity among them.

The neighbors have also shown their solidarity by visiting and spending long hours with the patients and their families. Often the neighbors and friends take cooked food to the patients showing their concern. They also at times help the patient by accompanying

him/her to the clinic. Such actions have motivated the patients and their families to cope with the situation as per the following voices of patients.

Box: Voices of Patients

“My relatives paid me a visit and brought some gifts for me. No one showed sadness in front of me. Neighbors too came to see me. At times they spent long hours with me till it becomes dark. They try to comfort me”

“Neighbors brought cooked items. My brother also came and he stayed a few days with us”

“My neighbors bring me cooked food. Eating their food and talking to them extends my life span it gives me life”

Coping Strategies at the Community Level

Community Based Organizations (CBOs) are resources for community life as they provide different types of assistance (financial, material, knowledge etc.), develop solidarity among people and empower them. These CBOs can be of two categories- i) CBOs that have emerged from the people due to a common need such as funeral Aid ii) CBOs that are formed from outside for specific purposes such as Samurdhi Society, Women’s Society etc. In both Medawachchiya and Padaviya there are a number of such CBOs operating. However, still there is no society that has emerged directly to address the issue of CKD. In time to come such a society may come up as the need is overwhelming in both DS divisions.

Among the CBOs, the Funeral Aid Society is the most popular and the second popular society is the Temple Devotees’ Society as shown in the following table.

Membership of Either Patient or Family Member at Community Based Organizations at Medawachchiya

Medawachchiya	Name of Society	Male Patients		Female Patients		Total Patients	
		No.	%	No.	%	No.	%
	Funeral Aid Society	65	100.0	34	97.1	99	99.0
	Temple Devotees Society	35	53.8	23	65.7	58	58.0
	Women’s Society	20	30.8	17	48.6	37	37.0
	Farmers’ Society	28	43.1	13	37.1	41	41.0
	Samurdhi Society	11	16.9	09	25.7	20	20.0
	Elders' Society	02	3.1	04	11.4	06	06.0
	Other	07	10.8	03	08.6	10	10.0

Membership of Either Patient or Family Member at Community Based Organizations at Padaviya

Padaviya	Name of Society Society	Male Patients		Female Patients		Total Patients	
		No.	%	No.	%	No.	%
	Funeral Aid Society	64	97.0	31	91.2	95	95.0
	Temple Devotees Society	34	51.5	15	44.1	49	49.0
	Women's Society	14	21.2	10	29.4	34	34.0
	Farmers' Society	29	43.9	06	17.6	35	35.0
	Samurdhi Society	04	06.1	06	17.6	10	10.0
	Elders' Society	05	07.6	06	17.6	11	11.0
	Other	03	04.5	03	08.8	06	06.0

As said before although the above CBOs were formed not to address the issue of the CKDu directly they have been of some assistance to the CKDu patients, their families and communities. In both Medawachchiya and Padaviya DS divisions the Funeral Aid Societies function well, however in Medawachchiya the society is much more organized. The Funeral Aid Societies in Medawachchiya has different committees established to perform specific tasks such as providing meals during the days the body is kept at home, attending to activities at the cemetery, putting up decorations for the funeral, welcoming people who come to the funeral etc. Thus in both DS divisions assistance is provided in the way of finance, material and labor. Such assistance is particularly important for family members of the CKDu patients as they would have exhausted their financial assets, physical and emotional strength by the time of the patient's demise. Therefore the assistance received from the Funeral Aid Societies is much valued by the patients' families in coping with the situation. Other than at the time of death, the society also gives financial assistance in the way of loans on a low interest rates.

The Women's Society is another CBO which provides assistance at the time of death. The society gives financial assistance and also provides food during the funeral days. The Temple Devotees Society which is popular among villagers functions mainly for the temple development activities. However, the members assist the CKDu patients and their families in fulfilling their emotional needs by spending time with them, organizing Bodhi Pujas and Gihi Prith. The Samurdhi Society also helps at the time of death by giving a financial donation of Rs. 10,000 to its members. Once in Medawachchiya lunch packets were distributed at a mobile clinic. The members of the Elders Committee also provide emotional strength to the CKDu patients and their families by spending time with them.

Box: Voices of Family Members of the CKDu Patients

“When our father died the Funeral Aid Societies gave us Rs. 15,000. They gave food and treated the people who came for the funeral. They made all the decorations”.

“When my father was ill no one helped us. But when he died different societies helped us. The Funeral Aid Society gave us Rs. 10,000. They also helped us with the activities at the cemetery. The Women’s Society gave food during the funeral”.

Suwa Sahana Kamituwa (Health Aid Committee) is yet another society which has been recently established in villages. The leadership is taken by the Public Health Midwife (PHM) attached to the Medical Officer of Health (MOH) Office. Each PHM area has a Suwa Sahana Kamituwa that includes the GN, PHI, Samurdhi Officer, Ayurvedic Community

Development Officer, Agricultural Officer and village leaders representing different CBOs. The main task of the society is to address the wellbeing of the people and focus on prevalent health issues in the area. However, in Padaviya the society has been established recently and most of the villagers were unaware of it. In Medawachchiya the society did function, but the main concern was on the prevention of Dengue and some of the reproductive health related issues so sufficient attention has not yet been given to address the issues related to CKDu. The society also has addressed certain social problems in the area but the issue of CKDu was not directly addressed. The society had the problem of enrolling volunteers as they do not receive any recognition. However, many of the CKDu patients and their families were unaware of such a society. However, this organization can be strengthened and mobilized in order to address the burning issues related to CKDu at village levels and can be utilized as the coordinating body when implementing interventions to mitigate the disaster.

Patients and their families believe that CBOs should offer better assistance to CKDu patients and their families. However, there are a few who feel that CBOs do not have the capacity to assist the patients and their families. This is revealed by the following table.

Patients' Requirements through Community Based Organizations

Assistance Seek	Medawachchiya	%	Padaviya	%	Total	%
Assist in livelihood activities	28	19.6	4	3.8	32	12.9
Form a separate society for CKDu	6	4.2	6	5.7	12	4.8
Financial support	36	25.2	10	9.5	46	18.5
Donating materials	24	16.8	6	5.7	30	12.1
Spending time with patients to forget loneliness	15	10.5	2	1.9	17	6.9
Helping patients to go to the clinic	6	4.2	0	0.0	6	2.4
Establishing a drinking water scheme	2	1.4	8	7.6	10	4.0
Conducting religious activities	11	7.7	1	1.0	12	4.8
Constructing houses for needy	3	2.1	1	1.0	4	1.6
Other	3	2.1	6	5.7	9	3.6
No idea	0	0.0	21	20.0	21	8.5
Can't help	9	6.3	40	38.1	49	19.8
Total	143	100.0	105	100.0	248	100.0

Providing financial assistance and helping in livelihood activities has figured as the most essential assistance. It is important to note that some patients have requested emotional support. Although the numbers are small the earlier discussion clearly shows the need for such assistance to cope with the situation.

Other than the CBOs, villagers at times get together as ad hoc committees or groups to help CKDu patients and their families. In Medawachchiya once a family member of a CKDu patient was given Rs. 40,000 to go to India on a pilgrimage. The money was collected from among the villagers.

Discussions and Conclusions

The main purpose of the community-based study on CKDu was to understand the illness burden at individual, household and community levels to identify the methods of mitigating the adverse effects. Thus, the study was focused on evaluating the economic and psycho-social impacts of CKDu on individual, households and affected communities, modes of coping adopted by them to minimize those effects and in turn the impact of those coping mechanisms on the family and the community with the intention of recommending the best options for implementing interventions on a wider scale. This chapter summarizes the main findings with conclusions and recommends interventions to support the affected individuals, households and communities.

Main Findings of the Study with Conclusions:

The community-based study has gained comprehensive understanding of the impact of CKDu at individual, family and community levels from a phenomenological perspective. There is hardly any difference between the two communities in Medawachchiya and Padaviya DS Divisions in relation to the impact of CKDu even though there are some structural distinctions between the two locations where the greater majority of the population in Padaviya are migrants under the government resettlement programme initiated since late 1950s. Comparatively, the Medawachchiya DS Division is constituted with traditional villagers where the social integration is little higher than that of Padaviya. The main findings of the study with conclusions are summarized as follows:

1. Community Discourse Developed on CKDu

A community discourse has been developed with regard to CKDu which explores the lay perception of the prevalence of this particular health hazard in their locality, cause/s of illness and the preventive measures that they have adopted in this regard. The lay discourse has been developed through decades of illness experience, shaped by the whole process of identification of the CKDu patients and discovering the etiology of illness by different experts. Within the community discourse, CKDu has become the most sensitive issue of everyday life for the villagers. Thus, the illness is articulated in the context as a struggle between 'life and death'. Therefore, the impact of CKDu needs to be understood within the particular socio-cultural context where it is equally important to take into account that the whole community as a vulnerable group while paying specific attention to each individual and the families concerned in designing interventions to mitigate the adverse effects of CKDu.

2. Increasing Economic Burden on Families of CKDu Patients

The economic burden of CKDu is due to four factors: firstly the households being considered are often poor even prior to diagnosis; secondly livelihoods are agricultural, with uncertain and low incomes; thirdly the patients are mainly in the age group 41 to 60 (majority of patients are the chief householder) the peak point of household economic activity; and fourthly there is a large dependent population, so that the loss of income and labour has major adverse impacts on the household budget and time allocation. Lost earnings are a major economic burden, and this cost together with the medical care cost of treating CKD in the latter stages clearly argue for the cost effectiveness of screening programs. The withdrawal of children from schools due to income generating and patient care needs will have major economic repercussions in the future, and will contribute to intergenerational poverty.

3. The Farming Community Lacks a Proper Social Security Scheme

A vast majority of the study population in both Medawachchiya and Padaviya are farmers, 69 percent of them are head of households and the majority belongs to the age groups between 51 to 60 years and 61 years and above highlighting two important implications;

one is the implication on the labor force and the loss of the main income to the family. Second is the burden on the family in the absence of any social security schemes for old age. Agriculture in Sri Lanka comes under the informal sector where there is no systematic social security system developed even though small percentage of farming community is covered by the farmers' pension scheme which is also not functioning properly. Thus, the labor laws and regulations too are not substantial enough in this context where farmers have no way to claim for losses or hazards in the course of their employment.

4. Importance of Regular Screening Programmes

The patients' profiles suggest that there is a need for regular screening programmes for CKDu with proper counselling and other necessary interventions. The evidence shows that the vast majority (81 percent) of the study sample were diagnosed as CKDu only during the time they visited a doctor/ hospital seeking treatment for some ailments and only 19 percent of them were diagnosed through screening programmes conducted at the grass root levels and no patients were diagnosed through self-screening for CKDu by the patients themselves.

5. Marginalization of Villagers in the Process of Discovering Etiology

The empirical evidence suggests that the villagers were marginalized throughout the process of discovering etiology of CKDu by limiting their participation to get necessary objects and some of the body-parts for scientific investigations rather neglecting the illness experience and risk behavioral practices of concerned patients.

6. Drinking Water as a Commercial Good in the Locality

The villagers strongly believe that the unsafe drinking water is one of the main causes for CKD and therefore, the majority spends out of their pocket to get potable water from the sources that they believe are not contaminated. The villagers have already recognized spring wells as one of the better sources of potable water so some of them walk several miles for spring water while some others buy the same from venders in the village. It is also visible that new shops are emerging in the locality for selling water. There are different types of water filters available in the local market for high prices due to the great demand from the villagers.

7. Misuse of Fertilizers and Pesticides as a Risk Factor for CKDu.

The villagers have identified unhealthy practices with regard to the application of chemical fertilizers and pesticides as one of the main risk factors for CKDu. However, they are compelled to continue with the same risky behavior as they hardly have any alternative due to the labor shortage for weeding, unfertile land, and the seeds that they buy from the market strongly demand such chemical fertilizers and pesticides for good harvests. Thus, the villagers are compelled to mix different fertilizers seeking better outcomes and to use chemicals for destroying weeds which is one of the less merchandisable activities in agriculture. They do continue with unsafe practices in using fertilizers that require better

awareness and sensitization programmes with behavior changing communication strategies.

8. High Demand for Government Hospital for Regular Treatment

The nearest government hospital is the main source of regular treatment for CKDu. People visit the private sector only for certain services such as for testing, to get a second opinion etc. The evidence suggests that there is no demand for indigenous medical systems as a treatment for CKDu. However, Ayurveda plays a significant role in overall health promotion at grass root level with a lot of interventions. There is an increasing demand for religious and ritual healing systems as complementary to Western medical system.

9. Limitations in the Healthcare Delivery System

It is significant to note that the Public healthcare delivery system plays a dominant role in both identifying the CKDu patients and treating them for their ill-health. The patients and their families were highly appreciative of the contribution made by the healthcare delivery systems as well as the role of the local healthcare providers in this regard. However, the healthcare delivery system has some limitation in implementing different interventions with regard to CKDu. They are as follows:

Limitations Located within the Clinical Setting

Communication gaps between the healthcare providers and the patient, internal arrangements/ organizational structure of the clinic, long waiting times and problems related to infrastructure facilities are some of the issues that further deteriorate the mental well-being of the CKDu patients who visit the regular clinic. Even people at the very early stage are labeled as CKD creating a problem at the community level. The patients at different levels of sickness should be handled differently with more explanations and counseling being provided. Health providers see all patients as similar without understanding the gravity and the different levels of the sickness and the different capacities of the patients as interventions should follow accordingly.

- **Communication gaps** - Addressing the issues related to communication gaps between the patient and the healthcare providers is identified as one of the main priorities in this context. The gaps are mainly due to representation of different perspectives by the practitioner and the patient which actually demands a collaborative approach instead. The collaborative approach can be strengthened by integrating clinical social workers with the local healthcare delivery system so that most of the limitations can be minimized/overcome.
- **Shortage of medications** - Very often the patients receive the prescribed medication from the clinic. However, there are some occasions where the patients have to buy certain prescribed medicine from outside due to dearth of medicine at the clinic. The shortage occurs only during certain times of the year. The patients also have to go to private sector to do certain tests so affordability becomes a problem for many patients.

- **Lack of basic facilities-** Basic facilities such as toilets and number of counters for the distribution of medicine need to be expanded as the demand for such services is on the rise.

Emerging Fears of Dialysis

The public healthcare delivery system has very limited facilities for dialysis as against the ever increasing number of patients. The service providers face some barriers in prioritizing the patients to provide the limited facilities in the local context where they are compelled to ration the patients based on some apparently unusual criteria such as a young rather than old, married vs. unmarried, with more children than less children etc apart from the severity of the illness. As a result, most of the time the patients get an opportunity to receive this service when they are at a critical stage only so the process ends up with a negative outcome. There is a misconception among the villagers that the patient would end up his/her life on or before three times of dialysis. The drawback can be identified as a limitation that coincides with the local healthcare delivery system for which most of the patients are referred for dialysis. They are referred only at a very critical stage due to shortage of financial and other resources. However, the patients are not aware of the above drawbacks of the delivery system and there is a negative perception regarding dialysis. Therefore, at present even if the doctor recommends a patient for dialysis there is a trend to avoid dialysis by the villagers leading to worsening health and a further collapse of their mental well-being.

Kidney Transplantation not an Alternative Solution for CKD for Villagers

As evident from this empirical study, not only are patients unable to afford kidney transplantation as an alternative method of treatment but also the socio-cultural environment is not yet ready to accept such a service. As a result, most of the villagers have negative attitudes towards kidney transplantation as there are number of failures in their locality after spending a lot of resources. The evidence suggests that more social interventions are required in parallel to the expanding of facilities for kidney transplantation.

Emotional Dimension of CKDu Neglected by the Professional Healthcare Delivery System

The mental well-being of not only the patients and their family members but also the entire community has been deteriorating gradually due to CKDu since it is articulated as a struggle between life and death in the local context that requires proper counseling systems at both clinical and social settings. However the emotional dimension has been seriously neglected by the professional healthcare delivery system. Patients and their families have resorted to various types of religious and ritual healing practices in order to restore and enhance their mental well-being at the cost of their money, time and other resources. However the evidence strongly suggests the need for a professional counseling system to address the emotional impact of CKDu at individual, family and the community levels.

10. Gradual Development of Stigma with Regard to CKDu

The empirical evidence clearly reflects that stigma is gradually developing with negative impacts on the individual and his/her family. As a result, at present there is an emerging trend of hiding the illness even from their close relatives and the neighborhood in order to avoid such a social cost while bearing the loss of social capital for the sake of maintaining the patient's confidentiality throughout the process of diagnosing a person as CKDu, providing treatment for ill-health and assisting them with psychosocial support. Some geographical locations in the area have been labeled as high risk areas for CKDu with negative impacts on both the patients and the other residents in those villages that require social intervention to enable the entire community to cope with the situations. The situation has further aggravated as the villagers are compelled to believe that genetic factors are one of the causes of CKDu based on their observation as there are sometimes more than one member in the same family suffering from CKDu.

11. Family as a Unit of Cohesive Suffering

The empirical evidence of this study strongly elucidates the importance of considering family as a unit of suffering when designing any intervention to reduce the economic and psychosocial impact of ill-health related to CKDu. The family has given its foremost priority to manage the ill-health of CKDu patient while neglecting or delaying most of the needs of the other members within the unit including education, nutrition, marriage and other development activities of the family. Basically, the family has been adversely affected in two ways due to CKDu. Firstly, its productivity has been deteriorating due to ill-health of the patients and its emotional cost for the whole family. Secondly, most of the existing resources of the family have been allocated to manage the CKDu patients. As a result not only the quality of life of the patient but also the whole family has been gradually declining within a short period of time. However, the experience of the patient and his/her family members may differ from one to another depending upon the available resources, the social networks and specific characteristics of an individual patient which suggest that each case should be considered as unique rather than universal when designing interventions to mitigate adverse effects of CKDu on a family. The findings strongly highlighted the importance of strengthening the capacity of family as a unit to move forwards as against long term distress caused by illness that demands professional family social workers into the local context.

12. Difficulties in Continuing Gender Based Division of Labor

In the village context most of the economic and social activities have been organized on the basis of gender dimension. As is evident from this study, women face lot of difficulties in order to continue with some of the activities related to cultivation and animal husbandry without getting assistance from their male counterparts. Therefore, most of the women are willing to move away from those activities and are interested to find alternative income generating activities from their locality while attending to domestic tasks including taking care of the CKDu patient. The women in Padaviya particularly made this demand as they experience lot of difficulties in order to continue with animal husbandry and cultivation where the social capital is rather weak compared to Medawachchiya. At present there are

no such alternatives in the concerned localities and hence both government and Non-Governmental Organizations that are working on income generating activities for women should give their priority to such vulnerable groups.

13. Destructive Nature of Existing Coping Mechanisms and Emerging of a New Type of Poverty

The evidence shows that the vulnerability is on the rise due to coping with the sickness. As mentioned earlier even in the context of deteriorating productivity, the family has given the foremost priority to manage the ill-health of CKDu patient by allocating most of its resources for this objective. As per this study, the family started coping with ill-health by using family savings and then they get loans, sell productive goods, reduce most of the expenditure on consumption of goods and services etc. The above situation makes way for a new type of poverty in the local context that needs urgent attention to strengthen the social protection and social support mechanisms to address the relevant issues. However, interestingly the patients and their families are not passive and they are flexible and ready to adjust. Their main concern is for the future generation.

14. The Community as a Whole A Vulnerable Group in Designing Interventions

The entire community has been affected by CKDu which has led to the deterioration of both its invaluable human resources and the material base in these communities. The findings clearly suggest that the whole community should be considered as a vulnerable group while designing any intervention to mitigate the adverse effects of CKDu. In a number of occasions the community has expressed their tension and dissatisfaction that the interventions are focused only on the CKDu patients and not on the vulnerable community as a whole. According to the empirical evidence there is a need for organizing and strengthening the community in order to mobilize its resources to encounter the challenge as the illness has already become a stigma related issue and the patients are discriminated due to illness which emphasizes an urgent need for integrating community social workers into the local context who are capable of organizing such communities to mobilize their various resources at different levels to mitigate the disaster.

15. Social Capital at Family and Community Levels

Social Networks that Operates at Personal Level

The evidence suggests that comparatively, the social network of the patients and the family become very active only during the initial stage of diagnosis as CKDu patient and at the latter stage of the disease where family receives more attention from their social networks which mobilize their resources by visiting the patients with both emotional and material support. However the networks gradually become less active in the long run during the middle stage of the disease where the family has to bear the entire burden by themselves.

Social networks that operates at community level

There is a number of Community Based Organizations (CBOs) even though only a few of them are very active in the village context. However, at present, there are no CBOs that operate at village levels to address the issues related to CKDu directly except some CBOs that contribute indirectly by providing loans with low interest rate and assistance at funerals. However, there is a possibility of strengthening some of the active organizations such as the Funeral Aid Society, Women's Association etc. in order to mobilize its capacity to deal with the issues related to CKDu which required mediation from outside the village.

Suwa Sahana Kamituwa (Health Aid Committee)

The villagers are aware of the development of a committee called "Suwa Sahana Kamituwa" in their villages for health promotion. The "Suwa Sahana Kamituwa" plays a major role in addressing some of the current health issues at village level. However, it is not well organized in order to address the issues related to CKDu that can be strengthened by integrating other CBOs to implement most of the interventions at grass root level.

16. The Significant Role of CKDu Prevention Unit at NCP

Establishment of CKDu Prevention Unit at NCP is a timely need that was implemented by the Ministry of Health in 2009. At present the Unit is headed by a medical officer that includes two research assistants, a health education officer and few other assistants. The unit has already started preparing and maintaining a patient registry which is updated every month. The Unit conducts various types of awareness programmes at grass root level while having regular field visits to monitor the activities implemented under the health care delivery system.

The empirical evidence suggest that there are number of extension officers at grass root level to deliver various types of services in the area of health, education, agriculture and other social services. However there are no proper mechanisms to coordinate, monitor and evaluate their activities. The CKDu Prevention Unit can be further mobilized as the coordinating body in implementing all the intervention with regard to CKDu Prevention in the region.

Interventions to Mitigate the Disease Burden

The community-based empirical study has identified a number of gaps in addressing the issues related to CKDu in the area. As highlighted by the above analysis, the medical perspective plays a dominant role whereas equal attention is required in order to address the economic, social and psychological dimensions of CKDu. Therefore, the following recommended interventions focus more on social support mechanisms which are essential to be implemented at an individual, family, community and institutional levels to mitigate the adverse effects of CKDu. The empirical evidence strongly verifies that patients, their family and the entire community are not passive and are ready to adjust which is a positive factor for bringing interventions to the local context.

Interventions at Institutional Levels:

1. Multidisciplinary Research to Discover the Etiology of CKD

The evidence suggests that patients are marginalized when conducting scientific research on etiology of CKDu. No attempt is there to mobilize the community as a valuable resource. Multidisciplinary research needs to be continued in order to find the cause/s of illness with the participation of all concerned stakeholders where risky behavioral patterns of villagers need to be taken into account

2. Need for a Scientific Investigation to Confirm the Correlation between Potable Water (from Spring Well) and the Probability of Disease Prevalence.

Community relates the disease to water and therefore demands that water testing be carried out systematically and scientifically and that the results be shared promptly with them. Currently the idea that the disease is waterborne is leading to major economic and day to day problems for the people: they are spending on bottled water, filters, travelling long distances at a high cost to collect spring water, reducing water consumption etc. It's important to conduct a screening programme in one of the villages so that people have an access to spring water for drinking for a long time while continuing behavioral patterns similar to disease prone areas in order to observe the correlation between potable water and the prevalence of CKDu. We recommend the village "Gonamariyawa" in Medawachciya for this investigation as it was confirmed by a sociological study on CKDu where the behavioral patterns were almost similar to that of the villages where the illness is prevailing except the source of water i.e. the spring well (Liyanage,C., Jayathilaka, R. 2009).

If the outcome is positive, proper mechanisms should be developed in order to distribute spring water among the villagers. All the spring wells in this locality need to be identified and mapped out before starting community based water projects.

3. The Need for Early Detection of CKDu.

Even now people associate the illness with symptoms to be observed in the acute stage and this suggests a need for better health education regarding the need for screening and knowledge on early symptoms of the disease. Community is keen on regular screening and they request such a service, through mobile clinics if possible. However, the importance of confidentiality of diagnosis needs to be considered when screening patients at grass root level.

4. Collaborative Approach in the Clinical Setting

Human resource development at the clinical setting is essential in order to bridge the gap between the user and the provider for which a collaborative approach needs to be implemented through which clinical social workers can be incorporated into the local healthcare delivery system. At least one social worker should attach to each clinic for

CKDu. The social worker can address the emotional dimension of CKDu and prepare care plans for each individual by collaborating with all the relevant stakeholders.

5. Enhancing Social and Cultural Competency of Service Providers

When dealing with patients, the health providers should be more sensitive about their emotional needs. The lack of such sensitivity may be due to the practical problem in handling many patients at a given time or/and the lack of understanding of the social issues related to the sickness as their training has been on the bio-medical model. This gap could be minimized by employing clinical social workers to collaborate with healthcare providers. At the same time social and cultural competency of service providers should be enhanced by implementing sensitization and communication skill development programmes for better performance and to respond to the needs of special patient groups. Universities can design and conduct such short term programmes for various types of service providers in the locality.

6. Integration of Counseling Services along with Dialysis and Kidney Transplantation Services

A proper counseling service should be incorporated along with the services such as dialysis and kidney transplantation where the patient and family should be empowered to face social barriers associated with these treatment methods. Clinical Social Workers can be appointed to these institutions for this purpose.

7. Strengthened the Capacity of CKDu Prevention Unit as the Coordinating Body

The special unit of CKD Prevention established at RDHS Office in Anuradhapura is a positive action taken by the Ministry of Health to deal with the issues related to CKDu. This unit could be utilized better by giving authority to coordinate and monitor the activities to prevent and mitigate the adverse effects of CKDu. This unit could be strengthened by providing better facilities, employing staff and recognizing the work they render. At present the unit is staffed with one medical officer, two research assistants, one health education officer and a few other assistants. In addition to the present staff, a cadre for a social worker should be created.

As of now the community participation is lack in addressing the issues related to CKDu. All the interventions are conceptualized and implemented from top to bottom rather than listening to community voices. This has created a number of negative impacts on the patients and their families. As against the CKDu Prevention Unit can develop proper mechanisms to strengthen the relationship with the community through “Suwa Sahana kammitu” that are operated at village level. Thus the CKDu Prevention Unit should take up a community base approach in designing and implementing interventions to prevent CKDu and mitigate adverse effects of illness. The CKDu Prevention Unit is the most suitable body of coordinating all the activities at national, regional and community levels with a holistic approach.

8. Increasing the Financial Assistance

There are limitations in providing financial assistance provided to the CKDu patients. The amount of this financial assistance should be increased and it should be provided to patients at the early stages of illness. A better mechanism to disburse the allowance to the patients should be adopted instead of the patient having to present at the Post Office to collect the allowance. Due to the critical stage of illness and distance in travelling to the Post Office the patients encounter many difficulties.

There should be transport concession system for the CKDu patients to visit clinics and hospitals. Different mechanisms can be adopted in this regard such as providing a bus pass or financial assistance to utilize the transport facilities or particular transport service on clinic days.

9. Strengthening “Suwa Sahana Kammitu” with Capacity Building

Establishment of Suwa Sahana Kammitu” at village level is very vital in order to bridge the gaps from the top to bottom in the healthcare delivery system. However this organization should be further strengthened with integrating community leaders, various types of service providers at community level, representing Community Based Organizations and volunteers including patients and their family members. The community should be at the centre not only designing and implementing interventions but also monitoring and evaluating of those activities. The human resources should be developed by providing time to time capacity building programmes. The social workers can involve with necessary activities to enhance the capacity of Suwa Sahana Kammitu to perform well in both prevention and mitigation of CKDu.

The committee can be strengthened with capacity building not only to implement various types of interventions but also to coordinate most of those interventions from both top to bottom and vice versa in order to mitigate the adverse effects of CKDu at individual and community levels. The committee would be one of the best options to incorporate all the local level service providers deliver services related to health, education, agriculture etc. and the community/village leaders enabling a holistic perspective in order to address the issues related to CKDu.

10. Development of Infra-structure Facilities at the Clinic

The number of Toilets, seating arrangements and counters for distribution of medicine at CKDu clinics should be increased at the earliest.

11. Behavior Changing Communication Strategies to Reduce the Misuse of Fertilizer by Farmers

There is a firm belief that soil is infertile in this area and therefore intensive use of fertilizer is essential in farming. However, the farmers are not taking even basic precautions to safeguard their health in the course of using fertilizers. Therefore, it is essential to conduct

awareness programmes for farmers with effective behavior change communication strategies couples with a methodology to monitor and evaluate the outcome of such programmes.

12. Necessity of Alternative Income Generating Activities

Both government and non-governmental organizations can promote alternative income generating activities in these localities particularly women targeted opportunities as they are able to continue with economic activities apart from taking care of the patient.

13. Patient Centered Psychosocial Interventions by Social Workers

The findings highlighted the economic and psycho-social impact of CKDu on individual patients. However, the patients are not homogeneous as they have different needs, opinions, expectations, skills, resources, social capital and so on that require an individual centered intervention to mitigate the impact of CKDu on each patient rather than generalizing and simply putting them into a single category as 'CKDu patients'. Interventions that come from top to bottom may not be feasible for this purpose. Therefore, it is important to integrate the Social Workers into the local context so that they can play a greater role in mediating with necessary interventions that are required for each individual which may be instrumental, informational or emotionally oriented. Mapping, individual planning, empowerment and recovery plan are some of the methods and techniques that the social worker can use in order to provide necessary assistance for the patients to mitigate the adverse effects of CKDu.

Family Centered Psycho-social Interventions by (Family) Social Workers

The family should be considered as a cohesive unit of suffering that requires more psychosocial assistance to cope up with the situation. As highlighted by the above analysis the family copes up with the situation by neglecting, scarifying or delaying most of the family needs. However, common interventions are not feasible to address the above issues as the expectations, resources, socio-capital and capacity of the members of each family to face the challenge is different from one another. Integration of family social workers into the local context can be very vital as they can play a major role in improving the quality of life of the whole family while adopting relevant strategies and methods from the discipline. The role of a Social Worker as the mediator is very crucial as she/he helps the family constantly to achieve its goal rather than neglecting, scarifying or delaying most of the needs of the family due to the illness of the family member. The type of interventions and the timeframe of implementing those interventions may differ from one family to the other based on its needs.

Community Centered Interventions

The empirical evidence strongly suggests that the entire community should be taken into consideration as a vulnerable group when designing interventions to address the issues related to CKDu. On the one hand the community demands some interventions to face the vulnerable circumstances that have emerged due to illness in their locality while on the

other, the community support is extremely helpful to the CKDu patients as well as their families to cope up with the crisis. The support groups provide information gained from their own experience and social networks. It is important for the patients as well as the family members and friends to learn as much as possible about CKDu which is greatly instrumental in coping. Family support is crucial, yet family members often do not know what to do or how to help. Support groups, as well as health care providers, can offer suggestions and guidance. Social support is referred to as a social network's provision of psychological and material resources for the benefit of an individual's ability to cope with crisis. The support can be expanded mainly in three areas such as instrumental, informational, and emotional support. Instrumental support involves the provision of material aid (*e.g.*, financial assistance), while informational support refers to the provision of helpful information (*e.g.*, guidance) and the emotional support deals with the expression of empathy and provides opportunities for emotional expression etc.

Organizing relevant communities by strengthening their social integration in order to face the crisis situation is one of the main challenges in the local context due to which the productivity and most valuable human resources have already been affected. Strengthening social capital is a greater challenge in the context where a large number of people are affected by the disaster. Addressing social stigma related issues yet is another issue. The social workers' role is very significant as they are professionally competent for capacity building of the concerned communities while adopting necessary methods and techniques. Common interventions as well as context-specific interventions are necessary in organizing the community to face the challenge. Some of the common interventions can be listed as follows:

- Emergence of different types of awareness and sensitization programmes for various social groups in the community with regard to the illness such as the risk factors, preventive measures, early detection etc.
- Emergence of different types of awareness and sensitization programmes for various social groups in the community to avoid stigma and discrimination due to illness.
- Providing information and awareness to the community members on the needs of patients and their families
- Sensitization of the community to help the patients and families who need instrumental, informational or emotional assistance.
- Coordination- linking patients, their families and communities with resources such as specific human resources, organizations, institutions which provide specific programmes or activities to help people.
- Formation of self-help groups- identifying needs and strategies as a group and achieving them as a collective effort.
- Emergence of the awareness and empowerment programmes for patients and their families to encounter the stigma and discrimination related issues.
- Encouraging and strengthening community participation in various activities related to not only prevention of CKDu but also the overall health promotion such as good practices in agriculture, organic farming, campaign for alcohol and drug prevention, healthy lifestyle etc. Integration of indigenous medical practitioners is significant in this regard.

- Strengthening community based organizations is very important as it enhance the social capital for the patients and their families.

There is no clear-cut distinction with the above proposed social interventions listed under different levels as most of those interventions are interrelated and overlapped to a greater extent. A collaborative approach with holistic perspective to address the interrelated issues that are inherited with CKDu is a key factor in this regard. It is important to note that most of the required human resources are already available for resilience except social workers into the local social context. The social workers can be incorporated into the local healthcare delivery systems as well as other sectors that provide social welfare at the grass root level. The clinical social workers can be integrated urgently into local clinics that conduct CKDu clinics. This particular category already exists in certain areas of healthcare delivery system in Sri Lanka such as mental health that and can be expanded to clinics and hospitals which provide services for the CKDu patients in the region. At present the Ministry of Social Welfare produces a number of social work graduates annually who can be absorbed into the Social Welfare Delivery System in order to work with families and communities where CKDu has become a problem. However a proper coordination is required among various service providers who come from different organizations. The CKDu Prevention Unit can coordinate all relevant activities at community level with the assistance of Suwa Sahana Kamitu. The CKDu prevention Unit also can coordinate the interventions at regional and national levels.

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Data collection formats used for community based study

Socio-economic Impact of Chronic Kidney Disease in the North Central Province and Interventions to Support the Affected Households

Serial No.	
Name of the Investigator	
Date	

(Circle the relevant answer/s)

I). D.S.Division :

II). G.N.Division :

III) Name of Village :

IV). Name of Respondent :

V). Address :

VI). Gender : 1) Male 2) Female

VII). Ethnicity:

1) Sinhala 2) Tamil 3) Muslim/Malay 4) Other

VIII) Religion:

1) Buddhist 2) Hindu 3) Christian/ Catholic 4) Islam
5) Other

IX). Number of Household Members:

X). Household composition/ family type:

1) Nuclear family 2) Extended family 3) Other

XI). Samurdhi Subsidy:

1) Yes 2) No

XII). Nature of Household:

1) Permanent 2) Semi- permanent 3) Temporary

XIII). Ownership of Land

1) Owned 2) Shared 3) Rent/Lease 4) Unpermitted 5) Other

Section 1: Household Information

1) Basic information of Household members

Member Ser/ No.	1.1) HH member's name	1.2) Relationship to House hold Head	1.3) Sex 1 Male 2 Female	1.4) Age (Year)	1.5) Marital status	1.6) Education level	1.7) Activity	1.8) Main Occupation	1.9) Secondary Occupation	1.10) Monthly income Rs.	1.11) CKD
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											

Codes

1.2. Relationship	1.5. Marital Status	1.6 Education	1.7. Activity	1.8/1.9.Occupation
1 Spouse	1 Never Married	1 No formal Schooling	1 Child (below 5 years)	1 Administrative
2 Son / daughter	2 Married	2 Primary (1-5 yrs.)	2 Student	2 Clerical
3 Parents	3 Separate	3 Secondary (6-11 yrs).	3 House work	3 Teaching
4 Brother/Sister	4 Divorced	4 Passed GCE O/L	4 Employed	4 Salesman
5 Grand- Son/daughter	5 Widow	5 Followed G.C.E. A/L	5 Unemployed	5 Cultivation
6 Uncle/ Aunt	6 Passed GCE A/L	6 Retired 6 Fishing		
7 Other Relatives		7 Post-AL Vocational training	7 Elderly	7 Casual
8. Other	8 Degree or Professional training		8 Disabled	8 Minor Employers
		9 Postgraduate Degree	9 Sick	9 Forces
10 Other			10 helping for the family busnes	10 Home Guard
11 Other			11 Technical work/Skilled worker	
12 Transport worker				
13 Employed in Factories				
14 Conducting Private tuition Class				
15 Other				

depth-In (b)l: interviews

As mentioned earlier households where death reported was due to CKDu were selected for 22 , the study as it would social impact -sive picture on economic and psychopprovide a chomphrehen depth interviews were conducted with the caregiver-In .of CKDu on family and the community and other family members of the person who died due to CKDu if they were willing to contribute depth-In .veral issues related to illness burden were discussed in detailSe .in this regard interviews were also conducted within the sample of patients when they voluntered to share their .expearence in detail

The questionnaire used for in depth interviews:

Instructions for the field Investigators:

Fill a separate questionnaire for each patient in the household. Social identity of the patient (age, gender, civil status) should be taken into consideration while collecting information. Circle the relevant answer/s

Serial No. of the questionnaire	
Serial No. of the patient	

2). Migration

- 2.1) How long are you a resident of this village?
1. From Birth 2. Migrant (Number of Years:.....)

If migrated

- 2.2) When did you migrate?
2.3) From Where?
(1). With in the D.S.Division
(2). With in the District
(3). Out of the Distric (specify)
2.4) Why did you migrate?

3). History of the Disease :

- 3.1) When did you come to know about your illness (diagnosed as CKD patient)? :
3.2) How did you come to know about your illness:
3.3) Were you suffering from any other illness before diagnosed as CKD patient, ?
1). Yes 2). No
3.4) If yes explain
3.5) What did you do first, immediately after identification of CKD ?
3.6) Have you taken any treatment for that ? 1).Yes 2). No
3.7) If yes, Describe in detail the treatment options that you have been using from the identification of CKD up to now? (Multiple options simultaneously may be possible)

A) .The Order	B). The Place where the treatment get	C). Treatment Option/s	D). What factor/s led you to choose the particular option/s
01			
02			
03			
04			
05			
06			
07			
08			
09			
10			

4). Health Seeking Behavior related to CKD

4.1) Stage of the renal failure (Don't ask this question directly from the patient and see the available records to get this information)

4.2) Do you receive any treatment at present for CKD? 1. Yes 2. No

4.3) If yes, what?

4.4) If not, explain why you are not receiving any treatment at present?

4.5) As you think, What are the reasons for CKD?

4.6) Are you suffering from any other illness in addition to CKD?: 1. Yes 2. No

4.7) If yes explain

4.8) Access to Health Care Facilities

4.8.1) Give information about the treatment options and utilization of that treatment (from the point of identification of CKD up to now)

a) The Health Care Facility/s	b) Have you ever used these facilities 1. Yes 2. No	c) Distance (Km)	d) utilization*	e) Number of hours generally spent on getting treatment (including travel time)
1).Central Dispensary				
2.) Medawachchiya Hospital				
3).Padaviyal Hospital				
4).Anuradapura Hospital				
5).Kandy Hospital				
6).Ayurveda Hospital (Mention the place)				
7).Traditional Practitioner				
8). Private Western. Practitioner				
9). Pharmacy				
10). Mobil Clinic (specify)				
11). Other (specify)				

codes: d) 1. Daily 2. Weekly 3.Once in two week 4. Once a month 5.Once in three month 6 other(specify)

4.8.2 Indicate the experience of the patient and the family members when they received the above treatment (Multiple options simultaneously may be possible)

a) Treatment obtained (indicate the number according to the above table)	b) Experience of the patient and the family*

codes:

- 1). Lack of transport facilities (specify)
- 2). Difficulty to get drugs (specify)
- 3). Travel is too costly
- 4). No one to take over family duties
- 5). Affects livelihood activities/studies
- 6). Distance to hospital/clinic
- 7). Affects other family members' daily activities
- 8). Difficult to afford the Time cost
- 9). Difficult to find accommodation facilities when go to Anuradhapura/ Kandy hospitals
- 10). No one is to go with the patient for care
- 11). Able to get necessary drugs
- 12). The kindness of Health care provider/s
- 13). Other (specify)

4.9) Social Access to Treatment

4.9.1) Do you engage with any activity at your household at present? 1. Yes 2. No

4.9.2) If yes, what are the alternative arrangements that you use to fulfill the tasks when you go for treatment/s? Explain

.....

4.9.3 Normally when you go for treatment

1. Go along 2. Go with someone

4.9.4 If you go with someone, kindly provide the following information

A) Location	B) Person/s who generally accompany you	C) Number of hours generally spent on getting treatment (including travel time)	4) How does going for treatment affect his/her work (leave, self-employed or family work)
1). Central Dispensary			
2). Medawachchiya Hospital			
3). Padaviyal Hospital			
4). Anuradapura Hospital			
5). Kandy Hospital			
6). Ayurveda Hospital (Mention the place)			
7). Traditional Practitioner			
8). Private Western. Practitioner			
9). Pharmacy			
10). Mobil Clinic (specify)			
11). Other (specify)			

5. The Financial cost of treatment/s

5.1) How much did you spent to get treatment for CKD and related problems

a) Facility	b) Cost for travel*	c) Cost for Medicine**	d) Cost for Testing	e) Cost for food*	f) Other (specify)	g) Total
1).Central Dispensary						
2.) Medawachchiya Hospital						
3).Padaviyal Hospital						
4).Anuradapura Hospital						
5).Kandy Hospital						
6).Ayurveda Hospital (Mention the place)						
7).Traditional Practitioner						
8). Private Western. Practitioner						
9). Pharmacy						
10). Mobil Clinic (specify)						
11). Other (specify)						
Total						

Codes: b) * should include the cost of both the patient and who ever accompany

c) ** For one month

e) *** food take at the time when go to the take treatment

5.2) Due to seeking treatment did you face any other cost and wage loss during last month?

1. Yes

2.No

5.3) If yes provide the following information

A) Location	B) Wage loss for patient	C) How did you find money to meet this cost	D) Wage loss for accompanying persons	E) How did you find money to meet this cost	F) Did you get any assistance from institution or person in meeting this cost
1).Central Dispensary					
2.) Medawachchiya Hospital					
3).Padaviyal Hospital					
4).Anuradapura Hospital					
5).Kandy Hospital					
6).Ayurveda Hospital (Mention the place)					
7).Traditional Practitioner					
8). Private Western. Practitioner					
9). Pharmacy					
10). Mobil Clinic (specify)					
11). Other (specify)					
Total					

5.4) Did you do urine, blood or any other testing within last three months?

1. Yes 2.No

5.5) If yes, give following detail

A) Name of the test	B) Number of times	C) Cost for the test (per test)	D) Cost for travel and other expenses (per test)*s	E) Total Cost for last three month
Urine				
Blood				
Other (specify)				
Total				

Codes: D* should include the cost of both the patient and who ever accompany

5.6) Cost for dialysis (ask only from the relevant patient after checking the clinical report/s)

5.6.1) How many times did go for dialysis within the last month?

.....

5.6.2) Cost per dialysis-event Rs:

5.6.3) Other expenses per dialysis event (Food & transport cost for both the patient and who ever accompany) Rs:

5.6.4) cost for last month dialysis Rs.....

5.7) In addition to the above cost, do you have any other cost more than Rs. 1000 after identification of CKD, 1. Yes 3 No

5.7.1) If yes, for what (Multiple answers possible)

- 1.For specialist medical service
- 2.For scan
- 3.Blood test
4. Religious healing systems
5. Ritula treatment (Thovil etc)
6. Other (specify)

5.7.2) How did you cover the above expenses that spent for treatment? (Multiple answers would be possible)

1. From the salary/earnings of the previous month
2. Using cash and savings of the patient
3. Using the savings of family member/s
4. Mortgage jewelries
5. Selling livestock
6. Selling durable and productive assets
7. Borrowing money from relatives
8. Borrowing money from friends
9. Borrowing money from money lenders
10. Receiving support from children
11. Receiving in-kind help from friends and relatives
12. Reducing consumption expenditure(explain)

.....Receiving state
 support (specify)
 13. Other (specify)

6) Type of Coping Behavior

6.1.) How did you cover the above expenses for treatment during last month? (Multiple answers would be possible)

1. From the salary/earnings of the previous month
2. Using cash and savings of the patient
3. Using the savings of family member/s
4. Mortgage jewelries
5. Selling livestock
6. Selling durable and productive assets
7. Borrowing money from relatives
8. Borrowing money from friends
9. Borrowing money from money lenders
10. Receiving support from children
11. Receiving in-kind help from friends and relatives
12. Reducing consumption expenditure(explain)

.....Receivin
g state support (specify)
13. Other (specify).....

6.2) Do you receive any financial assistance from the government to manage your ill-health?
1. Yes 2.No

6.3) If yes what?

- 1). Monthly allowance given for CKD patients(Rs.)
- 2). Other (specify)

6.4) . Do you receive any support from NGOs in order to obtain health facilities?
1. Yes 2. No

6.5) If yes describe:
.....

6.6) Do you receive any support from CBOs in order to receive health facilities? 1. Yes 2. No

6.7) If yes describe?
.....

6.8) In addition to the above sources, do you receive any assistance from an organization or an individual to manage your ill health?
1. Yes 2. No

6.9) If yes describe the support that you receive
.....

7) Emotion Focused coping behavior

7.1) when you realized about symptoms/ identified at screening of CKD, did you confide to any one? 1. Yes 2. No

7.2.) If yes whom ? (Multiple answers would be possible)

- 1) Family members
- 2) Relatives
- 3) Neighbors
- 4) Friends
- 5) Public Health Midwife
- 6) Religious leader
- 7) Leaders of CBO
- 8) Members of Suwa Sahana
- 9) Others (specify)

7.3) Describe the support you receive

.....

7.4) Did you seek any religious and ritual support to manage your ill health? (probe to get the information) 1. Yes 2. No

7.5) If yes describe

8) The impact of ill-health on the social and everyday life of the patient

Time Management

8.1) On an average working day, what percentage of your time was spent on the following before you diagnose as CKD patient and after diagnosed

A) Activity	B) Percentage of time prior to diagnose CKD (No of hours)	C) Percentage of time after diagnose
8.1.1) Working		
8.1.2) On family/ household care activities		
8.1.3) Social activities		
8.1.4) Religious activities		
8.1.5) Personal activities (eating, bathing)		
8.1.6) Sleeping/resting		
8.1.7) Other (specify)		

Contribution to the household activity

8.2) Does your health problem have an impact on your everyday life (Probe to get relevant information in detail)

No.	A) The activity	B) The impact(explain)
8.2.1	Contribution to the household income	
8.2.2	Household decision making	
8.2.3	Household chores	
8.2.4	Religious activities	
8.2.5	Social relationships with the villagers	
8.2.6	Social activities	
8.2.7	Other (specify)	

Change of consumption patterns

8.3) Did your sickness make any change of your consumption patterns (Food and water consumption, use of alcohol, smoking, chewing betel etc..) 1. yes 2. No

8.4) If yes describe

A) Consumption patterns	B) Changers
Food consumption	
Water consumption	
use of alcohol	
smoking	
chewing betel	
Other (specify)	

9) The impact of ill-health on Household income generation and consumption patterns

9.1) Did you engage with livelihood activity before diagnose as CKD patient (focus on primary and secondary occupations)? 1. Yes 2. No

9.2) If yes what?

9.3) Did your sickness affect your livelihood? 1. Yes 2. No

9.4) If yes, describe the impact of disease on livelihood activity

9.5) Explain how did you/ your family cope up with the situation?

1. Continue with the same by ignoring the discomfort
2. Continue with the same activity with the help of other members of the family
3. Continue with the same with the support received from the neighbors
4. Took alternative measures (hiring labour, hiring machines, given the land to a tenant etc. , specify)

5. Stopped completely

6. Other (specify)

9.6) Are you satisfied with the above arrangements? 1. Yes 2. No

9.7) If yes give reasons

9.8) If no give reasons

10. Impact on Houshold

10.1) Did your sickness affect the livelihood/s of your family member/s? 1. Yes 2. No

10.2) If yes describe

10.3) Did your sickness make any change with regard to the consumption of goods and service of your family member/s

10.4) If yes describe

10.5) Does your illness affect your children's education (ask only if it is relevant)

1. Yes 2. No

10.6) If yes describe

10.7) How does the illness impact on your household resource allocation?

No.	A) The item	B) Describe the impact
1	Food consumption patterns	
2	Getting drinking water	
3	Construction work House, agro well etc.	
4	Purchasing land	
5	Purchasing livestock	
6	Purchasing vehicle	
7	Purchasing agricultural equipment	
8	Furniture and other household equipments	
89	Other investments or development activities(specify)	
10	Other (specify)	

10.8) How does your illness affect on the everyday life of your family members (Leisure activities, social relationship, mental wellbeing etc..)

10.9) Who is the person in your household who take care of you ? (ask only the patients dependent on others)

10.10) What impact has made on that person? Describe

10.11) How does your illness affect on your family relationships (Strengthening family bonds, New conflicts etc..)

10.12) How does your illness affect on the relationships with neighbors, relatives (Strengthening or weakening etc..)

11) Social Capital

9.1)CBO and their functions

A) Community Based Organization	Membership Yes/No	A) The functions of the CBO and the help receive
1.Funeral Aid society		
2.Religious society		
3.Women's Association		
4.Agriculture society		
5.Youth society		
6.Patients' associations		
7. Other (specify)		

11.2) Do you receive any kind of assistance from your community to manage your ill-health and other difficulties caused by the disease (probe to get relevant information. There may be self-help groups and other kind of gatherings).....

12) Suggestions for future interventions

12.1) Overall, what are the main difficulties you face while managing your ill health?

12.2) In your opinion what kind of immediate assistance that you need to manage your ill-health related to CKD?

12.3) In your opinion, how can the community help CKD patients and their families

12.4) In your opinion how can the health care providers help CKD patients and the families

12.5) In your opinion how can the government help CKD patients and their families

12.6) In your opinion how can the nongovernmental organizations help CKD patients and the families.....

12.7) In your opinion what are the measures that can be taken to prevent CKD from your locality.

13) Do you have any questions to ask from us?

1. Yes 2. No

13.1) If yes, What is it ?

Thank you for your co-operation and participation in this survey!

#



Hospital Based Study

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Scientific Scope of the project

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The main objective of the overall study was to estimate the socio-economic impacts of CKDu in the study area, and to identify methods of easing these burdens.

The specific objectives of this particular component of the study were to estimate the costs of CKDu hospital care to the households and to the health system.

The community costs are also determined in order to understand the magnitude of the CKDu problem at provincial and national level.

Materials & Methods

The Setting and the Sample of the Study -

Hospital-based Costing Studies

The studies were done in a range of facilities to estimate costs of care in the health system: Padaviya, Medawachchiya, (to represent Divisional Hospitals) and Anuradhapura Teaching Hospital and Renal Care and Renal Research Centre in Anuradhapura to provide information regarding care at the tertiary level.

Cost of hospitalization (including dialysis visits) to the household were estimated by interviewing patients or accompanying persons or carers regarding the cost of hospitalization in Anuradhapura hospital, Padaviya and Medawachchiya.

Provincial and National impact of CKDu

Estimation of the economic impact on income and output were determined through the community study [5] and these values were combined with the direct and indirect costs of CKDu on households and the healthcare system.

Study Design

The design of the study took into account logistics and efficiency of data gathering, resulting in a two stage process being adopted.

- i. Hospital-based studies to determine systemic and household costs of care
- ii. Economic analysis and estimation of income and output loss

Hospital Based Studies

Data was gathered from hospitals on services provided: out-patient and in-patient. The selected hospitals included Padaviya, Medawachchiya, and Anuradhapura. Questionnaires were used to obtain the following information:

- a. The average duration of hospital stay
- b. Medical costs during each visit (e.g. laboratory tests, drugs, interventions such as dialysis, blood transfusions, transplantation, personnel costs).
- c. Average cost per outpatient visit (e.g. drugs, diagnostic tests, personnel etc)

Economic Analysis

The economic impact was analyzed according to the following situations:

- (a) Costs to households of treatment and care based on the community survey
- (b) Costs to households of hospital stay including dialysis visits based on data collected from patient surveys in Anuradhapura, Padaviya, and Medawachchiya.
- (c) Hospital costs for clinic and inpatient care
- (d) Indirect costs from low productivity, absence from work and premature death

Prior to the commencement of the study detailed consent was obtained from all participants using the format which can be found at the end of this section which included an information sheet and a consent sheet.

The Data Collection Methodology

All questionnaires (see end of this section) were pre-tested prior to the study. Interview guidelines were prepared to collect information. Newly qualified sociology graduates were used as research assistants to conduct the survey under the supervision of the study team. They were trained intensively prior to the commencement of the field work.

Data Analysis

Descriptive data on the household cost of hospitalization and clinic care are presented as medians and inter-quartile ranges.

Cost of hospitalization in the renal unit, Teaching Hospital, Anuradhapura was estimated based on the following assumptions:

1. Workload of the personnel is distributed between in-patient and out-patients services in a ratio of 3:2
2. Overhead and utility costs are distributed between in-patient and out-patient services in a ratio of 3:1
3. Overhead and utility costs can be distributed between cost centres of the hospital according to the utilization pattern

Based on a sample of patients who underwent haemodialysis in the high dependency unit of the Anuradhapura Teaching Hospital, cost of an episode of hospitalization for haemodialysis was estimated. Cost of hospitalization was estimated as 50% of the cost per patient day as this was a day procedure where patients did not stay overnight in the hospital. Cost of one session of haemodialysis in the private sector was considered for this estimation after deducting 30% for hospital costs and the profit margin.

hical Considerations

The overall project was approved by the Ethics Review Committee of the Faculty of Medicine, University of Colombo. Permission was also obtained from the Provincial Health administration to conduct the study. Patients gave their informed written consent for the study.

#

(a) Clinic Patients

Demographic Characteristics

In this component the results relate to 305 clinic patients who were sampled from the three hospitals. Table below shows the distribution of the sample by hospital.

Distribution of the study sample by hospital

Hospital	Number	Percentage
TH- Anuradhapura	100	32.8
BH-Medawachchiya	104	34.1
DH- Padaviya	101	33.1
Total	305	100.0

There were 227 (74.4%) males. Mean age was 56 (SD = 11.1) years. Table below shows the distribution of participants by sex and age group

Distribution of the sample by sex and age group

Age group	Male	Female	Total
< 30 years	4 (1.3)	2 (0.7)	6 (2.0)
30-39 years	8 (2.6)	3 (1.0)	11 (3.6)
40-49 years	51 (16.7)	15 (4.9)	66 (21.6)
50-59 years	82 (26.9)	27 (8.9)	109 (35.7)
60-69 years	60 (19.7)	23 (7.5)	83 (27.2)
70-79 years	17 (5.6)	6 (2.0)	23 (7.5)
80-89 years	5 (1.6)	2 (0.7)	7 (2.3)
Total	227 (74.4)	78 (25.6)	305 (100.0)

A large majority of the participants were Sinhalese. Ethnic distribution of the sample is given in table overleaf.

Distribution of the study sample by ethnicity

Ethnicity	Number	Percentage
Sinhalese	299	98.0
Tamil	2	0.7
Muslim	4	1.3
Total	305	100.0

Majority of the sample were Buddhists. Distribution of the sample by religion is given in table below.

Distribution of the study sample by religion

Religion	Number	Percentage
Buddhist	300	98.4
Hindu	1	0.3
Islam	4	1.3
Total	305	100.0

Distribution of the study sample by occupation

Occupational category	Number	Percentage
Managers	1	0.3
Professionals	2	0.7
Technicians and associate professionals	1	0.3
Clerical support workers	0	0.0
Service and sales workers	0	0.0
Skilled agricultural and fishery workers	151	49.5
Craft and related trade workers	5	1.6
Plant and machine operators and assemblers	0	0.0
Elementary occupations	7	2.3
Armed forces	19	6.2
Unemployed	119	39.0
Total	305	100.0

Distribution of the sample by occupation is given in table 5. A large percentage (39%) of the participants was unemployed. There was only one participant holding a managerial post and two in professional categories. Percentage involved in agriculture was 49.5%.

Distribution of the sample by reported monthly family income

Income (LKR)	Number	Percentage
< 5000	47	15.4
5000-9999	76	24.9
10000-19999	89	29.2
20000-34999	57	18.7
35000-49999	26	8.5
≥ 50000	7	2.3
No data	3	1.0
Total	305	100.0

Majority of the sample reported a moderate monthly income between LKR 10,000-35,000. Distribution of the sample by reported monthly family income is shown in table above

Direct Costs in seeking treatment

Type of transport used to reach the clinic was diverse. Majority (74.1%) used the bus. Bicycle and motorcycle was used by about 10% each. Use of hired vehicles was very low. Distribution of the sample by the mode of transport is shown in table 7.

Mode of transport used to reach the clinic

Mode of transport	Number	Percentage
Walking	4	1.3
Bicycle	29	9.5
Motorcycle	30	9.8
Three wheeler –own	14	4.6
Automobile – own	0	0.0
Other vehicles-own	0	0.0
Three wheeler-hired	2	0.7
Automobile-hired	0	0.0
Other vehicles-hired	0	0.0
Bus	226	74.1
Train	0	0.0
Total	305	100.0

Costs incurred by the participants for the last clinic visit is shown in table 8. A direct cost was incurred by 300 (98.4%) participants. Median total direct cost of the clinic visit was LKR 280.50 (inter-quartile range 150.00-520.00). 102 (33.4%) participants had incurred a cost for purchasing drugs while 37 (12.1%) participants had incurred a cost for laboratory investigations conducted in the private sector.

Direct cost of the last clinic visit of the participants

Cost item (n)	Median (LKR)	Inter-quartile range
Travel (n=274)	100.00	58.75-140.70
Accompanying person (n=64)	131.00	61.00-261.00
Food (n=279)	80.00	50.00-100.00
Drugs (n=102)	200.00	90.00-316.25
Laboratory investigations (n=37)	300.00	105.00-450.00
Other (n=53)	50.00	40.00-70.00
Total (n=300)	280.50	150.00-520.00

Indirect cost of seeking clinic care

Median time spent on the clinic visit by a participant was 8 (inter-quartile range 7-10) hours.

Indirect cost of the last clinic visit of the participants

Cost item (n)	Median(LKR)	Inter-quartile range(LKR)
Lost income by patient (n=11)	495.00	350.00-550.00
Payment for covering work (n=43)	1000.00	800.00-1000.00
Lost income by family members (n=35)	900.00	625.00-1000.00
Total (n=84)	900.00	625.00-1000.00

Long duration spent in seeking clinic care is attributable mainly to waiting time, as the numbers seeking care were large, while the number of doctors available to attend to clinic patients was too few, given that they also attended to other patients in the hospital

(b) Inpatients (including those on dialysis)

In this component 132 hospitalized patients were sampled from three sub-units in the Renal Unit of Teaching Hospital, Anuradhapura. Table 10 shows the distribution of the sample by the sub-unit.

Distribution of the study sample by sub-unit

Ward	Number	Percentage
Peritoneal dialysis unit	17	12.9
High Dependency unit	58	43.9
Renal ward	57	43.2
Total	132	100.0

There were 94 (71.2%) males. Mean age was 49.3 (SD=11.7) years. Table shows the distribution of the participants by sex and age group.

Distribution of the sample by sex and age group

Age group	Male	Female	Total
< 30 years	3 (2.3)	2 (1.5)	5 (3.8)
30-39 years	17 (12.9)	7 (5.3)	24 (18.2)
40-49 years	27 (20.5)	9 (6.8)	36 (27.3)
50-59 years	31 (23.5)	9 (6.8)	40 (30.3)
60-69 years	12 (9.1)	10 (7.6)	22 (16.7)
70-79 years	4 (3.0)	1 (0.8)	5 (3.8)
Total	94 (71.2)	38 (28.8)	132 (100.0)

The younger age group noted here is due to dialysis being limited due to systemic constraints to those below the age of 40.

Median duration of hospitalization for the total sample was 1 day (inter-quartile range 0-3 days). Median duration of stay in both peritoneal dialysis unit and high dependency unit was less than a day. Median duration of stay in renal ward was 4 (inter-quartile range 2-5) days.

A large majority of the patients (93.2%) were Sinhalese. Ethnic distribution of the sample is given in table below.

Distribution of the study sample by ethnicity

Ethnicity	Number	Percentage
Sinhalese	123	93.2
Tamil	7	5.3
Muslim	2	1.5
Total	132	100.0

Majority of the sample were Buddhists (91.7%). Distribution of the sample by religion is given in table below.

Distribution of the study sample by religion

Religion	Number	Percentage
Buddhist	121	91.7
Hindu	4	3.0
Christian/ Catholic	5	3.8
Islam	2	1.5
Total	132	100.0

Distribution of the study sample by occupation

Occupational category	Number	Percentage
Managers	0	0.0
Professionals	0	0.0
Technicians and associate professionals	6	4.6
Clerical support workers	0	0.0
Service and sales workers	6	4.6
Skilled agricultural and fishery workers	51	38.6
Craft and related trade workers	0	0.0
Plant and machine operators and assemblers	2	1.6
Elementary occupations	2	1.6
Armed forces	2	1.6
Unemployed	63	47.7
Total	132	100.0

A large percentage (47.7) of the participants was unemployed. Percentage involved in agriculture was 38.6%. Distribution of the sample by occupation is given in table below.

Majority of the sample (24.2) reported a moderate income between LKR 20000-35000. Distribution of the sample by reported monthly family income is shown in table below.

Distribution of the sample by reported monthly family income

Income (LKR)	Number	Percentage
< 5000	27	20.5
5000-9999	27	20.5
10000-19999	26	19.7
20000-34999	32	24.2
35000-49999	12	9.1
≥ 50000	6	4.5
No data	2	1.5
Total	132	100.0

Distance between home and the hospital was reported by 125 patients. Median was 40 (inter-quartile range 25-58) km. Commonest type of transport used to reach the hospital was the hired three wheeler (56.1%) followed by bus (19.7%). None of the patients walked to hospital. Use of their own vehicles to reach hospital was very low. Distribution of the sample by the mode of transport used to reach the hospital is shown in table .

Mode of transport used to reach the hospital

Mode of transport	Number	Percentage
Walking	0	0.0
Bicycle	2	1.5
Motorcycle	6	4.5
Three wheeler -own	4	3.0
Automobile - own	5	3.8
Other vehicles-own	0	0.0
Three wheeler-hired	74	56.1
Automobile-hired	1	0.8
Other vehicles-hired	1	0.8
Bus	26	19.7
Train	0	0.0
Other	13	9.8
Total	132	100.0

Direct costs incurred by the patients for this episode of hospitalization are shown in table 17. A direct cost was incurred by the entire sample. Median total direct cost of this hospitalization was LKR 1225.000 (inter-quartile range 755.00-2960.00). All patients incurred a travel cost. Median travel cost amounted to LKR 365.00 (inter-quartile range 240.00-830.00). Only 11 (8.3%) patients had incurred a cost for purchasing drugs. A majority had incurred substantial costs on accompanying persons (n=99) and for purchasing food (n=117) during the hospitalization.

Direct cost of the hospitalization

Cost item (n)	Median (LKR)	Inter-quartile range (LKR)
Travel (n=132)	365.00	240.00-830.00
Accompanying person (n=99)	310.00	200.00-480.00
By-stander (n=21)	100.00	55.00-755.00
Food (n=117)	220.00	155.00-440.00
Visiting (n=67)	750.00	240.00-2000.00
Drugs (n=11)	200.00	90.00-250.00
Medical consumables (n=3)	150.00	100.00-235.00
Laboratory investigations (n=2)	915.00	70.00-1760.00
Non-medical consumables (n=49)	180.00	70.00-300.00
Payments to staff (n=3)	20.00	(20.00-30.00)
Total (n=132)	1225.00	755.00-2960.00

Fifteen patients (11.4%) reported that their family members have conducted religious rituals to invoke blessings on him/ her during this hospitalization. Median cost of these practices was LKR 250.00 (inter-quartile range 150.00-700.00).

Three patients (2.3%) reported a loss of income from his/ her occupation due to the hospitalization and seven patients (5.3%) reported having incurred an expense for covering up his/ her absence from self-employment. 29 patients (22%) reported a loss of income by family members due to this hospitalization. An indirect cost of hospitalization was incurred by 36 patients (27.3%). Median indirect cost of the hospitalization was LKR 800.00 (inter-quartile range 525.00-1000.00). Indirect costs incurred by the patients due to this hospitalization are shown in table below.

Indirect cost of the hospitalization

Cost item (n)	Median (LKR)	Inter-quartile range (LKR)
Lost income by patient (n=3)	500.00	500.00-600.00
Payment for covering work (n=7)	800.00	800.00-800.00
Lost income by family members (n=29)	1000.00	600.00-1000.00
Total (n=36)	800.00	525.00-1000.00

Indirect costs are low in this case because majority of patients are either unemployed or involved in agricultural work. The burden is greatest due to loss of income to family members. The need for family members to be bystanders is greater in this stage, as the patients are at more severe stage of the illness and needing more intensive care.

(c) Costs to Health System

Cost of Clinic Care

Information was obtained regarding the main inputs for the provision of clinic services to patients at the Anurdahpura Renal Unit.

Cost of clinic care in the renal unit

Item	Detailed cost per month (LKR)	Total cost per month (LKR)
Personnel		1,347,543.23
Medical	260,177.83	
Nursing	897,913.40	
Paramedical	58,746.60	
Support	130,705.40	
Overheads		81,781.71
Cleaning services	32,049.86	
Laundry services	11,809.01	
Security services	13,843.74	
Meals	24,079.09	
Utilities		98,745.52
Fuel	13,607.49	
Water	15,152.06	
Electricity	68,940.27	
Telecommunication	1,045.70	
Total		1,528,070.46

Average number of patients attending the renal clinic per month is 1763. Based on this, the unit cost of clinic care is LKR 866.74 per patient visit.

Inpatient and Dialysis care

Renal Unit, Teaching Hospital, Anuradhapura has full time staff. Cost of overheads and utilities, and laboratory reagents are available as aggregated costs for the entire hospital. Hotel cost of hospitalization in the renal unit, Teaching Hospital, Anuradhapura was estimated based on the following assumptions

- Workload of the personnel is distributed between in-patient and out-patients services in a ratio of 3:2
- Overhead and utility costs are distributed between in-patient and out-patient services in a ratio of 3:1
- Overhead and utility costs can be distributed between cost centres of the hospital according to the utilization pattern

Cost of hospitalization in the renal unit

Item	Detailed cost per month (LKR)	Total cost per month (LKR)
Personnel		2,231,781.22
Medical	390,266.75	
Nursing	1,346,870.09	
Paramedical	88,119.90	
Support	406,524.48	
Overheads		783,988.99
Cleaning services	307,241.55	
Laundry services	113,205.47	
Security services	132,711.12	
Meals	230,830.84	
Utilities		946,610.19
Fuel	130,446.34	
Water	145,253.08	
Electricity	660,886.30	
Telecommunication	10,024.47	
Total		3,962,380.40

Patient data over three months in the Teaching Hospital, Anuradhapura and the renal unit are presented in table below.

Patient data in Teaching Hospital, Anuradhapura including the renal Unit

Month	In-patients				Out-patients		
	TH	Renal Unit			TH		Renal Unit
		DU	Ward 34	Ward 36	OPD	Clinic	Clinic
Month 1	10000	855	106	134	16779	29571	1710
Month2	10001	864	128	231	17117	30289	1456
Month3	9775	873	136	218	16970	30986	2124
Average	9925	864	123	194	16955	30282	1763

Average number of patients hospitalized per month in this unit is 1182. Based on this unit cost of hospitalization is LKR 3351.32 is per patient per day (median duration of stay is one day).

Cost of Dialysis

Cost of haemodialysis was estimated in a sample of 58 patients who underwent haemodialysis in the high dependency unit of Teaching Hospital, Anuradhapura. Results are presented in table below.

Cost of haemodialysis

Cost item	Cost (LKR)
Hospitalization	1675.66
Haemodialysis	4900.00
Drugs	607.47
Total	7183.13

(d) Economic analysis of the burden of CKDu

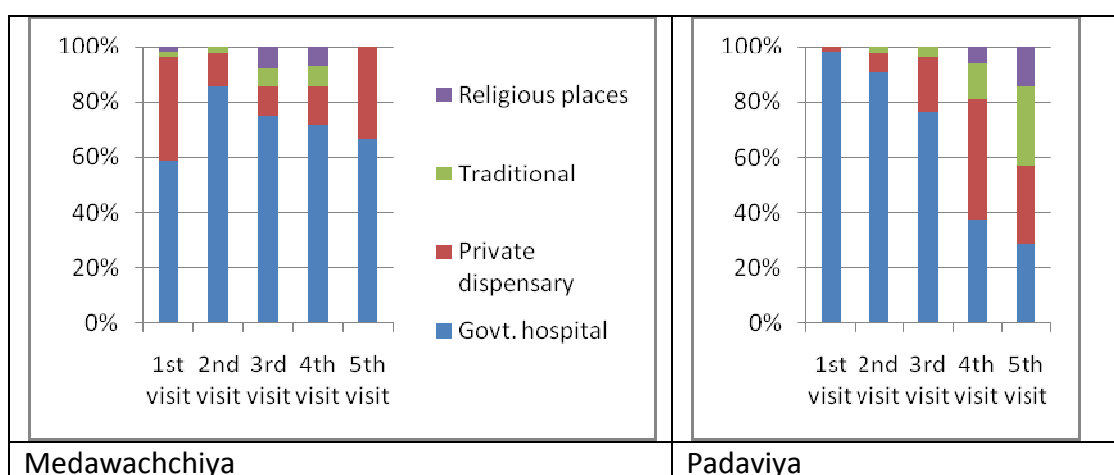
Cost of illness to the community

Sample of 200 patients, was chosen from different GN divisions in the Medawachchiya and Padaviya DS Divisions, taking 100 from each location. Choice of these two areas was based on the large number of patients reported to be suffering from CKD, as recorded in previous work in this field. Both the selected locations are inherently rural, and have farming as their main livelihood.

Poverty is clearly seen in these areas. Given that the poverty line (minimum expenditure per person per month to fulfill basic needs) in the Anuradhapura district for December 2011 was Rs 3241 and assuming a four member household, then the household poverty line would be 12964. In Medawachchiya 29.1% and in Padaviya 48.7% of households earn less than Rs 7500 with another 25.1% and 25.0% earning between 7501 and 15000. Considering total household income 29% in Madawahchiya and 49% in Padaviya gain less than 15,000 rupees per month. Poverty clearly is a major issue among these households. Of the patient's families 52% in Medawachchiya were Samurdhi recipients, while only 20% were so in Padaviya. Medawachchiya has better social infrastructure than Padaviya, but both are adversely affected by transport problems and shortages of health manpower.

The majority of patients in this sample were not yet in the severe stage of illness. Therefore the economic repercussions may still not be as significant for these households, as they have not had to bear the burden of hospitalization and still remain for the most part able to contribute to their households in terms of earning and labour sharing.

Patients, in general are predominantly seeking care at present as OPD patients from government hospitals (94.2% considering both samples). The patterns of treatment, as reflected by choice of location per visit, seem to differ by location: for every visit clearly the government hospital is the major option in Medawachchiya but in Padaviya the importance of this source diminishes systematically over the visits.



Source: CKDu S-E Survey

From a cost of care perspective, three issues emerged:

- the issue of travel costs are important since many in the sample are accessing regular clinic care, sometimes at more than one location.
- The need for multiple clinic visits should be examined, as it may be resulting in a wastage of resources, both to the health system and the household
- What type of care is classified 'as care when needed' that results in patients accessing further off hospitals/private sector should be examined, to see if the closest hospital could not be equipped to cope with such contingencies, as this would reduce the burden to households of travel, consultation and treatment costs.

Cost on drugs borne by households

Hospital	No penditure	<100	101-500	501-1000	>1000	Total
Medawachchiya	17	5	24	2		48
	35.4	10.4	50.0	4.2	0.0	100.0
Padaviya	26	1	14	4	1	46
	56.5	2.2	30.4	8.7	2.2	100.0
Anuradhapura	1	2	3			6
	16.7	33.3	50.0	0.0	0.0	100.0
Private Sector	1	7	4	2	2	16
	6.3	43.8	25.0	12.5	12.5	100.0

Source: CKDu S-E Survey

Putting systems in place for forecasting the increased demand for CKD drugs and rationalizing drug provision to state hospitals to avoid shortages, is of immense importance, particularly given that the cost of these drugs is high in relation to household incomes in this area.

Cost on Medical Investigations

Hospital	No expenditure	<100	101-500	501-1000	>1000	Total
Medawachchiya	28	1	5	2		36
	77.8	2.8	13.9	5.6		100.0
Padaviya	15	8	15	4		42
	35.7	19.0	35.7	9.5		100.0
Anuradhapura	2	2	1	1		6
	33.3	33.3	16.7	16.7		100.0
Private Sector		1	4	2	4	11
	0.0	9.1	36.4	18.2	36.4	100.0

Source: CKDu S-E Survey

The majority is undergoing diagnostic testing at no expenditure to households accessing Medawachchiya Hospital, though for those accessing Padaviya Hospital and Anuradhapura Hospital some costs are borne by households suggesting that they are accessing private sector diagnostic facilities. It should be noted that travel and other costs have to be borne even in accessing state diagnostic services, and this burden is greater when testing and giving of reports occurs in some instances on days other than the clinic visit days.

The modal category with regard to transport for both sample sites is less than Rs 100; for drugs it is between Rs 101 and 500; for medical investigations it is no cost in Medawachchiya but between Rs 101 and 500 in Padaviya; cost on food during the time of seeking outpatient medical care is less than Rs 100 and the majority bear no other costs in accessing care.

The number undergoing dialysis is very small at present: only one male and one female in the Medawachchiya sample. This is due to the number of patients in stage 3 being small in these samples as yet, and possibly the age of the patients in general that precludes dialysis.

Inability of the patient to attend to household activities either increases the workload of other household members, necessitates hiring out activities that were previously done at home such as replacing home cooked food with that bought in boutiques or sending washing to the laundry or hiring labour for housework. In addition to changes in the patient's provision of labour, reduction in family labour could also result from the responsibilities of patient care.

Relatives, friends and neighbours show their solidarity with patient households by providing financial and in-kind support as well as emotional support, particularly at two stages of the illness: firstly at the point of diagnosis and later when the illness is acute and the patient is hospitalized continuing up to the funeral. In-depth discussions with patient households however highlighted the fact that during the course of the illness many households face tremendous financial and emotional pressures as well as a sense of isolation and despair that no systematic social security system exists to safeguard families in such times of distress.

Early diagnosis of CKD, through screening is important. The majority of these patients have been diagnosed more than four years ago, most when they were being treated in the context of another disease. These patients seem to be afflicted by a large number of co-morbidities, in many cases that predate the diagnosis of CKD. These findings suggest that NCD screening including CKD screening is of paramount importance in coping with the challenges of health transition in Sri Lanka. Likewise it is important to provide comprehensive and close to client NCD care in these areas as this could have major repercussions on prognosis of CKD. Poor health contributes to the economic burden through creating unemployment, as well as adversely affecting the psycho-social welfare of patient and family.

Impacts on the labour market and household income

The problem of CKDu while affecting both males and females, seems to take a more severe form in the case of males [1]. This could be what is causing the strong gender imbalance evident in the case of this hospitalized and treatment seeking sample. Gender differences can have two main dimensions: they could affect expenditure on treatment and source of funding; they also affect the cost of caring for the patient and the burden on the household. Average age of patients was around 57 years. The majority of patients: 67% in Medawachchiya and 71% in Padaviya were household heads. This is likely to have a major bearing on the economic status of the family. The survey found that even in the early stages of the disease, there was an effect on the number of hours persons could work and an effect on the productivity of workers, while progression of the illness led to workers (and sometimes carers) withdrawing from the work force, and in some cases to premature death.

Patients income as percentage of family income on average

	Male	Female
Madawachchiya		
Number of patients	44	56
Number reporting income	31	24
Average % patient income to household income	56.9	52.3
Padaviya		
Number of patients	61	39
Number reporting income	44	13
Average % patient income to household income	59.2	46.9

Source: Calculations based on CKDu S-E Survey

In the case of patients only 43% were employed in Medawachchiya and 27% in Padaviya as 41% and 54% respectively reported that they were too sick to work. The severity of the CKDu burden is reflected in these statistics. Of those employed the majority were into cultivation. As this involves hard physical labour it makes it challenging for those even in the early stages of CKDu to remain productive.

The table above shows that while many patients do not report current earnings, particularly among the females, that where earnings are reported they are a significant share of household income. This suggests that the loss of such an income as the disease progresses will be a heavy blow to the household economy.

The financial implications of the illness are striking, even though many are still in the early stages of the disease, since only 23% in Medawachchiya and 20% in Padaviya report no impact. The majority: 45% and 48% respectively note a decrease in income, while another 32% in each location report having totally lost their income due to this illness. Such outcomes are inevitable given that the 90.5% in Medawachchiya and 42.9% in Padaviya are into cultivation, with many others are involved in manual work as casual labourers.

Sickness has had impacts on the livelihoods of other household members as well, as reported by 51% and 38% of males in Medawachchiya and Padaviya and 40% and 41% of female patients at the two sites. The adverse impacts have occurred through loss of employment (14.4%) and decreased time for livelihoods (24%), while for other households it has resulted mainly in household members increasing their involvement in livelihood activities (32%) and finding jobs (9.3%).

The spread of CKDu has had a significant impact on the use of hired labour in these areas, and has resulted in the cost of hiring labour rising. Previous cooperative activities in agriculture have changed, possibly due to changing social structures in general, but such changes are being attributed by the community to the illness affecting some families, making them unable to contribute, and by others to their disinclination to seek assistance when they are unable to reciprocate as well.

Premature death or withdrawal from the labour force

The main responses to the diagnosis of CKD with regard to livelihood were stopping work (Medawachchiya male 38% and female 50% and Padaviya 34% and 81% respectively) and reducing working time (49% male Medawachchiya, 48% among males in Padaviya and 39% and 19% for females in Medawachchiya and Padaviya respectively).

The magnitude of monthly income lost per worker who is laid off due to illness can be approximated based on the earnings of the others in the sample: in Medawachchiya the modal monthly earning category of patients is between 7501-15000, while for Padaviya it is 2501-7500. The major factor that influences if livelihoods are affected, apart from the severity of illness, is the nature of work being undertaken by the person prior to diagnosis. The amount of manual effort involved, the number of hours, the ability to delegate or share the work and its flexibility all have a bearing on this issue.

Considering future loss of income, using the scenario building technique to estimate lost earnings and the following assumptions

- Model income range in Medawachchiya Rs 7501-15,000 (mid-point 11,250) and Padaviya 2501-7500 (mid-point 5000);

- Unemployment rate is 4.2% in Medawachchiya and 7.3% Padaviya (based on survey data);
- Patients are generally in the age group 40 to 60;
- Individual could work, if not for their illness up to 60, but now leaves workforce at 50;
- Life table values (W.I. de Silva, IHP) used to calculate probability of survival;
- Individual's income grows at 3.5% per annum;
- Discount rate is 5%;

The lost earnings then for a decade (loss to labour force at 50 with potential to have worked till 60) is Rs 1,034,909 in Medawachchiya and Rs 445,076 in Padaviya. The large difference in these values stems from differences in modal income level and unemployment rates.

The scenario building technique provides only a rough estimate of future lost earnings, with its validity being largely dependent on the appropriateness of the assumptions and the data available.

The lost earnings however are likely to be even greater in reality, since the majority of workers are agricultural workers, who are not bound by a retirement age and would generally continue in production up to around 70 if in good health. Likewise modal incomes could increase even faster than 3.5% given the current demographic transition in the country that is pushing up wages as well as inflation rates. Unemployment rates could likewise fall in the face of demographic transition since female labor force participation continues to remain low, even in the agricultural sector.

Provincial and national losses due to workers moving out of the labour market or facing premature death can be estimated by multiplying these values by the number of patients. These estimates have taken into account males, so similar estimation for females is needed as is gender, age and geographically disaggregated data regarding the epidemiological burden, in order to calculate provincial and national burden of CKDu.

The economic burden of CKD is major due to four factors: firstly the households being considered are often poor; secondly livelihoods are agricultural, with uncertain and low incomes; thirdly the patients are mainly in the age group 41 to 60 (majority of patients are the chief householder) the peak point of household economic activity; and fourthly there is a large dependent population, so that the loss of income and labour has major adverse impacts on the household budget and time allocation, including affecting education. Added to this are the costs of care imposed by scarcity of drugs and diagnostic facilities

The results show considerable costs incurred by households to care for these patients with CKDu. Indirect costs to the household appear to outweigh direct costs. This demonstrates the relative effectiveness of the health sector in mitigating household expenditures in contrast to the social service sector, as reflected in the community study [5]. One major factor for the loss of earnings (i.e. indirect costs) however is the time spent for a single clinic visit (i.e. almost a full working day).

Large numbers of patients are seeking care, during clinic sessions at Padaviya and Medawachchiya and are being referred to Anuradhapura for treatment, including dialysis. In addition patients are often self-selecting to by-pass the smaller institutions, to access services and obtain drugs from Anuradhapura, while in some cases patients are utilizing multiple services.

The long delays at clinics and overcrowding at the Renal Unit in Anuradhapura clearly indicate the need to expand CKDu care services, particularly through increasing the number of Medical Officers allocated to such healthcare institutions. Much of the early treatment is sought from Anuradhapura, with the hospitals in Padaviya and Medawachchiya having mainly terminally ill patients as inpatients. In the smaller hospitals, more specialized training and the designating of separate doctors for CKD care is important.

The special unit on CKDu Prevention established at Anuradhapura is a positive action taken by the Ministry of Health. This unit could be utilized better by giving authority to coordinate and monitor activities related to prevention and mitigating the adverse effects related to CKDu. This unit could be strengthened by providing better facilities, staff and recognition for work rendered. At present the unit is staffed with one medical officer, two research assistants, one health education officer and a few other assistants. In addition to the present staff, a cadre for a social worker should be created to ensure and enhance patient welfare.

An appreciable proportion of direct costs are for investigations and drugs, a situation that should not arise in public sector institutions, because the state sector is dedicated to provide such services at zero costs to the user. Non-medical direct costs included expenditures for travel and food. This is compatible with other studies showing a large financial impact of chronic kidney disease on households, the health system and the country's productivity.

Measures must be taken to ensure regular drug supply to these institutions. The allowance given to such patients needs to be adjusted in line with treatment costs, taking into account the direct and indirect costs involved in accessing continual care.

Rationing of dialysis currently occurs based on age. While this seems inevitable given the high cost associated with what is an on-going process up to transplantation, adopting alternative funding sources to meet such expenditure seems important.

A recent review found an appreciable burden from chronic renal failure in developing countries. The figures were for well known diseases such as diabetes, glomerulonephritis, and hypertension. Since Sri Lanka is facing an epidemic of diabetes and hypertension, the rates of chronic kidney disease requiring care is likely to increase in the future. To this significant burden, we would now have to add the cases of CKDu, an added burden to the national health expenditures. Since CKDu affects a productive and younger age group, its impact on the national economy is likely to be very significant.

The heavy losses incurred at household level, in terms of medical costs, ritual costs and livelihood related costs and mainly in the form of lost earnings due to premature death and disability makes implementing measures to prevent CKDu imperative.

Discussion & Conclusion

The economic burden of CKD is major due to four factors: firstly the households being considered are often poor; secondly livelihoods are agricultural, with uncertain and low incomes; thirdly the patients are mainly in the age group 41 to 60 (majority of patients are the chief householder) the peak point of household economic activity; and fourthly there is a large dependent population, so that the loss of income and labour has major adverse impacts on the household budget and time allocation, including affecting education. Added to this are the costs of care imposed by scarcity of drugs and diagnostic facilities

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An appreciable proportion of direct costs are for investigations and drugs, a situation that should not arise in public sector institutions, because the state sector is dedicated to provide such services at zero costs to the user. Non-medical direct costs included expenditures for travel and food. This is compatible with other studies showing a large financial impact of chronic kidney disease on households, the health system and the country's productivity [6, 7, 8].

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The heavy losses incurred at household level, in terms of medical costs, ritual costs and livelihood related costs and mainly in the form of lost earnings due to premature death and disability makes implementing measures to prevent CKDu imperative.

CKDu results in considerable costs to households, the health system and to the economy. Therefore there should be a concerted effort to mitigate these effects. The following are the recommendations that emanate from this study

- At a household level support should be provided by a comprehensive social welfare system. The current provisions should be considerably increased, and linked to inflation to ensure that patient welfare is safeguarded.
- Other areas of support too should be available (e.g. better modes of transport to hospitals and clinics)
- The health system allocations should be increased to face with the epidemic. It is quite costly to care for persons affected with chronic kidney disease. Therefore, an appreciable increase in health allocations is required, at least to the regions affected by the epidemic. This will reduce the indirect costs faced by long waiting times at clinics and for OPD care, reduce the need for households to purchase drugs and undergo investigations in the private sector and also enable more persons to undergo essential life-saving renal replacement therapy.

- The health system needs to respond to the continuing direct costs incurred by patients, by ensuring an efficient and effective service for these areas. This involves systematic forecasting of needs, planning for the expansion and coordination of services and ensuring that secondary and tertiary prevention strategies are adopted to contain the adverse effects of the illness.
- Providing the patient allowance at an earlier stage of the illness to encourage regular care seeking could be crucial in terms of tertiary prevention that apart from limiting the adverse impacts on the patient also significantly lowers systemic costs on the care of terminal patients.
- The country should invest in urgent measures to prevent the epidemic because we estimate a significant economic impact as a result of CKDu. These effects are predominantly transmitted through the labour market effects of lost productivity, withdrawal from the labour force of patients and carers or premature death, while the costs of seeking care are also significant for households, given their income levels. The economic impact on households has the capacity to further impoverish the affected rural areas.

In addition the following recommendations are proposed as means of improving patient and household welfare:

- Ensuring close to client care: currently the hospitals in Padaviya and Medawachchiya are addressing this need to an extent, but ensuring regular drug supplies, improving investigation facilities, improving inpatient care facilities, increasing the number of Medical Officers designated for CKDu care would improve the quantity and quality of CKD services
- Increasing patient empowerment through awareness creation among patients both about their illness and their rights as care seekers is important. Currently households are making sub-optimal treatment and lifetime decisions due to lack of information.
- Better training of health care providers in psycho-social impacts related to long term and terminal illness, so that they can understand the need for greater patient empowerment and actively contribute to such an objective.

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Formats Used

Participant Information sheet & Consent form

**Patient survey on the household cost of hospitalisation and the health system
cost for chronic kidney disease
Participant Information Sheet**

Sir/ Madam,

You are invited to participate in a survey on the household cost of hospitalisation for treatment of kidney disease. Aim of this survey is to determine the cost and the economic loss incurred by you and your family due to this hospitalisation and the cost incurred by the hospital and the health system for your treatment and medical care.

If you decide to participate in this survey, a doctor will ask a few simple questions from you or an informant nominated by you or your family, once in every two days during your hospital stay. It will take about 5-10 minutes to answer these questions. The confidentiality of the information provided will be maintained and the information will be used only for the purpose of this survey.

In addition, details of the treatment and medical care provided to you in the hospital will be obtained from your Bed Head Ticket. Any additional information that is relevant will be obtained from the ward staff.

If you decide not to participate in this survey, you will receive the routine medical care. Your decision not to participate in the survey will not affect your treatment and medical care in any way.

If you need any more information before you decide to participate in this survey, please ask from the doctor who gave you this information sheet. If not, contact the principal investigator of the survey on the given telephone number (Tel: 077xxxxxxx).

(signature)

Prof.....

Principal Investigator

**Survey on the household cost of hospitalisation and the health system cost
for chronic kidney disease
Consent form**

Code-----

- 1 I have read the above information \$ Above information was read to me
- 2 I had the opportunity to ask questions about the survey
- 3 Questions asked by me were answered satisfactorily
- 4 My participation in this survey is entirely voluntary
- 5 I know that I have the right to withdraw from this survey at any time
- 6 I had sufficient time to make the decision to participate
- 7 I agree to participate in this survey

Participant's Name-----

Participant's signature-----

Date-----

To be completed by the investigator:

I have clearly explained the survey to the participant giving him/ her the opportunity to ask questions and if any, answered them. He/ she has indicated willingness to participate in the survey.

Name of investigator (**BLOCK CAPITALS**).....

Signature of the investigator

Date:

Questionnaire for Survey on the household cost of hospitalisation for chronic kidney disease:

Questionnaire 1

Code		Hospital Code		DOA			
Ward No.		BHT No.		DOD			
1	Basic information						
1-1	What is your name?						
1-2	What is your address?						
1-3	What is the Medical Officer of Health (MOH) division/ Divisional Secretary (DS) Division you live in?						
1-4	What is your date of birth			YY	MM	DD	
1-5	What is your occupation?						
1-6	What is the highest educational level you attained?						
	No formal schooling						
	Below Grade 5						
	Passed Grade 5						
	Passed Grade 8						
	Passed G.C.E. Ordinary Level						
	Passed G.C.E. Advanced Level						
	Higher education						
1-7	How much is your monthly family income?						
	Less than Rs.5000						
	Rs 5000-Rs 9999						
	Rs 10000- Rs 19999						
	Rs 20000- Rs 34999						
	Rs 35000- Rs 49999						
	Rs 50000 or more						
1-8	What is your relationship to the head of your household?						

1-9	Describe all your household members (excluding you) below:					
No	Relationship to the head of the	Age (years)	Sex	Highest educational	Occupation	

	household			level attained	
1					
2					
3					
4					
5					
6					
2	Transport				
2-1	What is the distance to this hospital from your home in km?				
2-2	What was mode of transport you used to come to this hospital for this hospital stay? ^You can mark more than one response&				
	Walking				
Your own vehicle	Bicycle				
	Motorcycle				
	Three-wheeler				
	Automobile (car/ van)				
	Any other vehicle (tractor, lorry etc)				
Hired vehicle	Hired three-wheeler				
	Hired automobile (car/ van)				
	Any other hired vehicle (tractor, lorry etc)				
Public transport	Bus				
	Train				
	Any other mode of transport (specify)				
2-3	What was the total cost of transport incurred to come to the hospital?				Rs.
2-4	What is mode of transport you will use to go home after discharge from hospital? ^You can mark more than one response&				
	Walking				
Your own vehicle	Bicycle				
	Motorcycle				
	Three-wheeler				
	Automobile (car/ van)				
	Any other vehicle (tractor, lorry etc)				
Hired vehicle	Hired three-wheeler				
	Hired automobile (car/ van)				
	Any other hired vehicle (tractor, lorry etc)				
Public transport	Bus				
	Train				
	Any other mode of transport (specify)				
2-5	What is the estimated total cost of transport that you will incur to go home after discharge from hospital?				Rs.
3	Persons accompanying the patient (family members and others)				
3-1	Did anybody accompany you when you came to hospital for this stay?				
	Yes		No		If No; go to question 3-4
3-2	Did you incur any cost for the people who accompanied you to hospital?				
	Yes		No		If No; go to question 3-4
3-3	Indicate the items for which the cost was incurred and the amount				
Cost	Rs	Cts			
Transport					
Food and beverages					

Other			
Total			
3-4	Will anybody accompany you when you go home from hospital after discharge?		
	Yes		No
3-5	Will you incur any cost for the people who would accompany you home from hospital?		
	Yes		No
3-6	Indicate the items for which the cost will be incurred and the amount		
Cost item	Rs	Cts	
Transport			
Food and beverages			
Other			
Total			
4	Persons accompanying the patient (family members)		
4-1	Did any of your household member/s accompany you when you came to hospital for this stay?		
	Yes		No
			If No; go to question 4-4
4-2	Did that person/ those persons take leave from work to accompany you to hospital?		
	Yes		No
			If No; go to question 4-4
4-3	How much money did that person/ those persons lose from their wages due to taking leave from work to accompany you to hospital?		
	Rs		
4-4	Will any of your household member/s accompany you home from hospital when you are discharged?		
	Yes		No
			If No; go to question 5
4-5	Will that person/ those persons take leave from work to accompany you home from hospital?		
	Yes		No
			If No; go to question 5
4-6	How much money will that person/ those persons lose from their wages due to taking leave from work to accompany you home from hospital?		
	Rs		
5	Costs incurred in hospital		
5-1	Did you have a bystander/ bystanders during this hospital stay?		
	Yes		No
			If No; go to question 6
5-2	Did you pay your bystander/s?		
	Yes		No
			If No; go to question 6
5-3	What was the total amount paid to bystanders during your entire hospital stay?		
Day	Amount (Rs)	Day	Amount (Rs)
1		8	
2		9	
3		10	
4		11	
5		12	
6		13	

7				14		
Total (Rs)						
5-4	In additions to the payment, did you incur any other cost for the bystander/s?					
	Yes		No	If No; go to question 6		
5-5	Indicate the items for which the costs were incurred and the amount					
Cost item		Rs	Cts			
Transport						
Food and beverages						
Other						
Total						
6	Cost of meals					
6-1	During this hospital stay, did you or your household members buy meals (food and beverages) for your consumption?					
	Yes		No	If No; go to question 7		
6-2	Indicate the total cost incurred for meals that were bought for you during this hospital stay					
Day	Amount (Rs)			Day	Amount (Rs)	
1				8		
2				9		
3				10		
4				11		
5				12		
6				13		
7				14		
7	Cost of visiting the patient					
7-1	Did any of your household members visit you during this hospital stay?					
	Yes		No	If No; go to question 8		
7-2	Indicate the number of household members visited and the cost incurred by them on each day					
Day	No. of household members	Cost	Day	No. of household members	Day	
1			8			
2			9			
3			10			
4			11			
5			12			
6			13			
7			14			
8	Other types of costs in hospital					
8-1	During your hospital stay, did you or your family incur any other cost in hospital?					
	Yes		No	If No; go to question 9		
8-2	Indicate the items for which the cost was incurred and the amount					
Cost item		Rs	Cts			
Medications (drugs)						
Surgical consumables						

Laboratory investigations			
Other consumable items			
Any other costs			
Total			
9		Cost of religious and cultural practices focussing on the patient	
9-1		During your hospital stay, did your family engage in any religious or cultural practice/s to evoke blessings on you?	
	Yes		No
If No; go to question 10			
9-2		Indicate the total cost incurred to conduct the above religious and cultural practices	
Rs.			
9		Loss of income by the patient	
9-1		Did you take leave from work due to this hospital stay?	
	Yes		No
If No; go to question 10			
9-2		What is the total number of days-off taken from work due to this hospital stay?	
	Days		
9-3		What is the total income lost by you due to this hospital stay?	
	Rs		
10		Loss of income by the household members	
10-1		Did any of your household members take leave from work due to this hospital stay?	
	Yes		No
If No; go to the end of the questionnaire			
10-2		Indicate the total number of days-off taken from work by each household member and the total income lost by them	
Household member		Total no. of days	Total income lost (Rs)

Thank you for your co-operation and participation in this survey!

Questionnaire 2

Code		Hospital Code				
Clinic No.		Date of visit	YY	MM	DD	Arrival time at hospital am/ pm
1	Basic information					
1-1	What is your name?					
1-2	What is your address?					
1-3	What is the Medical Officer of Health (MOH) division/ Divisional Secretary (DS) Division you live in?					
1-4	What is your date of birth		YY	MM	DD	
1-5	What is your occupation?					
1-6	What is the highest educational level you attained?					
	No formal schooling					
	Below Grade 5					
	Passed Grade 5					
	Passed Grade 8					
	Passed G.C.E. Ordinary Level					
	Passed G.C.E. Advanced Level					
	Higher education					
1-7	How much is your monthly family income?					
	Less than Rs.5000					
	Rs 5000-Rs 9999					
	Rs 10000- Rs 19999					
	Rs 20000- Rs 34999					
	Rs 35000- Rs 49999					
	Rs 50000 or more					
1-8	What is your relationship to the head of your household?					
1-9	Describe all your household members (excluding you) below:					
No	Relationship to the head of the household	Age (years)	Sex	Highest educational level attained	Occupation	
1						
2						
3						
4						
5						

2	Transport	
2-1	What is the distance to this hospital from your home in km?	
2-2	What was mode of transport you used to come to this hospital today? ^You can mark more than one response&	
Your own vehicle	Walking	
	Bicycle	

	Motorcycle	
	Three-wheeler	
	Automobile (car/ van)	
	Any other vehicle (tractor, lorry etc)	
Hired vehicle	Hired three-wheeler	
	Hired automobile (car/ van)	
	Any other hired vehicle (tractor, lorry etc)	
Public transport	Bus	
	Train	
	Any other mode of transport (specify)	
2-3	What was the total cost of transport incurred to come to the hospital?	Rs.
2-4	What is mode of transport you will use to go home today? ^You can mark more than one response&	
Your own vehicle	Walking	
	Bicycle	
	Motorcycle	
	Three-wheeler	
	Automobile (car/ van)	
	Any other vehicle (tractor, lorry etc)	
Hired vehicle	Hired three-wheeler	
	Hired automobile (car/ van)	
	Any other hired vehicle (tractor, lorry etc)	
Public transport	Bus	
	Train	
	Any other mode of transport (specify)	
2-5	What is the estimated total cost of transport that you will incur to go home from hospital?	Rs.

3	Persons accompanying the patient (family members and others)			
3-1	Did anybody accompany you when you came to hospital today?			
	Yes		No	If No; go to question 4
3-2	Did you incur any cost for the people who accompanied you to hospital?			
	Yes		No	If No; go to question 4
3-3	Indicate the items for which the cost was incurred and the amount			
Cost		Rs	Cts	
Transport				
Food and beverages				
Other				
Total				

4	Cost of meals for the patient			
4-1	Did you or your household members buy meals (food and beverages) for your consumption during this visit to the hospital?			
	Yes		No	If No; go to question 5
4-2	Indicate the total cost incurred for your meals during this hospital visit			
Rs				

5	Other types of costs due to the hospital visit			
5-1	Did you or your household incur any other cost due to this hospital visit?			
	Yes		No	If No; go to question 6
5-2	Indicate the items for which the cost was incurred and the amount			
Cost item		Rs	Cts	
Medications (drugs)				
Surgical consumables				
Laboratory investigations				
Other consumable items				
Any other costs				
Total				

6	Loss of income by the patient			
6-1	Did you take leave from work due to this hospital visit?			
	Yes		No	If No; go to question 7
6-2	Did you lose any wages due to this hospital visit?			
	Yes		No	If No; go to question 7
6-3	What is the total income lost by you due to this hospital visit?			
	Rs			

7	Loss of income by the household members			
7-1	Did any of your household members take leave from work due to this hospital visit?			
	Yes		No	If No; go to the end of the questionnaire
7-2	Did he/she/they lose any wages due to this hospital visit?			
	Yes		No	If No; go to the end of the questionnaire
7-3	What is the total income lost by your household members due to this hospital visit?			
	Rs			

Departure time from hospital	am/ pm
---------------------------------	--------

Thank you for your co-operation and participation in this survey!

Data Extraction forms

Socio-economic impact of chronic kidney disease in North Central Province and interventions to support affected household Patient survey on the household cost of hospitalisation and the health system cost for chronic kidney disease Data Extraction Form

Part 1. Please complete this check-list before proceeding to Part 2

Cross (X) the relevant cage

1.1 Diagnosis documented as chronic kidney disease of unknown origin (CKDu)?	Y	N
1.2 Has the patient left against medical advice or reported missing?	Y	N
1.3 Was the patient transferred for further management?	Y	N

Part 2. Write the relevant information in the space provided or mark the relevant cage with a ✓

2.1 Code		2.2 Hospital Code			
2.3 Ward		2.4 BHT No.			
2.5 Date and time of Admission	DD	MM	YY	Admission Time	a.m./ p.m.
2.6 Name					
2.7 Age (years)			2.8 Sex	M	F
2.9 Stage of CKDu					

2.10	Did this patient have any blood transfusions during this admission?	Yes		No	
2.11	Did this patient have any haemo-dialysis during this admission?	Yes		No	

2.12 Procedures performed:

	Date	Procedure	No		Date	Procedure	No
1				7			
2				8			
3				9			
4				10			
5				11			
6				12			

2.13 Other investigations:

	Date	Investigation	Number		Date	Investigation	Number
1				8			
2				9			
3				10			
4				11			
5				12			
6				13			
7				14			

2.14 IV fluids given (throughout the stay):

	IV Fluid	Volume	Total units
1			
2			
3			
4			
5			
6			

2.15 Blood transfusions given

	Blood product	Volume	Total units
1			
2			
3			
4			
5			
6			

2.16 Medications given (throughout the stay):

	Drug	Dose	Route	Frequency	Total No. of doses	Total units
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						

2.17 Date and time of discharge:

DD	MM	YY	Discharge time
			a.m./ p.m.

2.18 Comments:

Please indicate whether this patient was referred for kidney transplantation at the end of this stay

**Socio-economic impact of chronic kidney disease in North Central Province
and interventions to support affected household
Patient survey on the household cost of hospitalisation and the health
system cost for chronic kidney disease
Out Patient-Data Extraction Form**

Cross (X) the relevant cage

Diagnosis documented as chronic kidney disease of unknown origin (CKDu)?

Y	N
----------	----------

Write the relevant information in the space provided or mark the relevant cage with a ✓

2.1 Code		2.2 Hospital Code			
2.3 Clinic		2.4 Clinic No.			
2.5 Date and time of data collection	DD	MM	YY	Time	a.m./ p.m.
2.6 Name					
2.7 Age (years)			2.8 Sex	M	F
2.9 Stage of CKDu					

2.10 Any procedures performed during the clinic visit:

	Procedure	No	Procedure	No
1			3	
2			4	

2.11 Investigations conducted by the hospital during the clinic visit:

	Investigation		Investigation
1		5	
2		6	
3		7	
4		8	

2.12 Medications given from the clinic:

	Drug	Dose	Route	Frequency	Total No. of doses	Total units
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						

2.13 Comments:

IV. Nephrotoxic herbal remedies used in Sri Lanka

Introduction/ Background

Herbal / Ayurvedhic medicines, containing Aristolochic acid is implicated as a causative factor of renal disease. As the people in the North Central province have been using herbal medicines made of *Asristolochia indica* (Sapsanda) which contain Aristolochic acid for treatment of various conditions this might be a contributory factor in the causation of CKDu. The reason behind this is that the Aristolochic acid is a major nephrotoxic compound causing renal failure in addition to acting as a cause for many cancer situations and mutations. There have been many reports about incidences of nephrotoxicity resulting from ingestion of different herbal products from several countries. Hence the identification of plants used in herbal remedies that have nephrotoxicity effects in Sri Lanka is important.

Scientific Scope of the Project

The major objectives of this study were:

- To examine the species of *Aristolochia* that grow in Sri Lanka particularly in the CKDu high prevalence areas
- To list the species, if any, is/ are ingredients of traditional/ herbal remedies used in Sri Lanka particularly in the CKDu high prevalence area

Materials and Methods

Literature survey was done by referring statistical reports of Ministry of Health, Sri Lanka, books on medicinal plants, hand books and manuals of Ayurveda prescriptions, journals and many other related articles published by WHO and other institutions. Field and Ethno botanical Surveys were conducted by visiting the medicinal plant gardens located in Bandaranayke Memorial Ayurveda Research Institute, Maharagama and many places where *Aristolochia* species are found. The preserved samples were observed referring to herbariums available in the same institute. Direct and indirect observations were recorded at focus group discussions organized with the participation of experienced full-time Ayurveda doctors, botanists and many other related resource persons.

Results/outputs

Distribution of *Aristolochia* species:

More than 500 species of *Aristolochia* have been identified. Collectively they are known as birthworts, pipevines or Dutchman's pipe. They are widespread and occurred in diverse climates. Jaffna, Matale and Hantana are common natural habitats and they are also found in many conserved herbal gardens located in Bandaranayake Memorial Ayurvedha Research Institute, Girandurukotte, Bathgoda, Pallekelle, Faculty of Agriculture/ University of Ruhuna and Peradeniya Botanical gardens.

Table below shows the listed *Aristolochia* species that are found worldwide figures 1 to 16 shows some identified *Aristolochia* species. Among these, *Aristolochia indica* (in Sinhala, Sapsanda or Sassanda) (Fig. 1.) is the commonly seen species in most of the areas of Sri Lanka including North Central Province and it is the commonest species used in Ayurvedic Medicine. Also *Aristolochia labiosa*, *Aristolochia littoralis*, *Aristolochia bracteolata* and some other species are considered to occur as well, but further investigations should be done to identify the correct species and to obtain information on the usage as Ayurvedic medicines.

Botanical description of *Aristolochia indica*

Scientific classification:

Kingdom	:	Plantae
(Unranked)	:	Magnoliophyta
(Unranked)	:	Magnoliids
Order	:	Piperales
Family	:	Aristolochiaceae
Genus	:	<i>Aristolochia</i>
Species	:	<i>indica</i>
Binomial Name	:	<i>Aristolochia indica</i>

Aristolochia is a genus of evergreen and deciduous woody vines and herbaceous perennials belonging to Aritolochiacea family of which the smooth stem is erect or somewhat twining. The simple leaves are alternate and cordate, membranous, growing on leaf stalks. There are no stipules. The flowers grow in the leaf axils. They are inflated and globose at the base, continuing as a long perianth tube, ending in a tongue-shaped, brightly colored lobe. There is no corolla. The calyx is one to three whorled, and three to six toothed. The sepals are united (gamosepalous). There are 6 to 40 stamens in one whorl. They are united with the style, forming a gynostemium. The ovary is inferior and is 4 to 6 locular. These flowers have a specialized pollination mechanism. The plants are aromatic and their strong scent attracts insects. The inner part of the perianth tube is covered with hairs, acting as a fly-trap. These hairs then wither to release the fly, covered with pollen. The flowering season is September to January and found in humid environments where the elevation is up to 3,000 ft.

Identified Aristolochia species worldwide

<i>Aristolochia acuminata</i>	<i>Aristolochia gigantea</i>	<i>Aristolochia pentandra</i>
<i>Aristolochia acutifolia</i>	<i>Aristolochia gorgona</i>	<i>Aristolochia pfeiferi</i>
<i>Aristolochia allemanii</i>	<i>Aristolochia grandiflora</i>	<i>Aristolochia pilosa</i>
<i>Aristolochia anguicida</i>	<i>Aristolochia griffithi</i>	<i>Aristolochia pistolochia</i>
<i>Aristolochia arborea</i>	<i>Aristolochia guentheri</i>	<i>Aristolochia poecilantha</i>
<i>Aristolochia arcuata</i>	<i>Aristolochia hainanensis</i>	<i>Aristolochia pontica</i>
<i>Aristolochia auricularia</i>	<i>Aristolochia hians</i>	<i>Aristolochia prostrata</i>
<i>Aristolochia baetica</i>	<i>Aristolochia hirta</i>	<i>Aristolochia pubera</i>
<i>Aristolochia bilabiata</i>	<i>Aristolochia holtzei</i>	<i>Aristolochia raja</i>
<i>Aristolochia billardieri</i>	<i>Aristolochia inflata</i>	<i>Aristolochia reticulata</i>
<i>Aristolochia bilobata</i>	<i>Aristolochia iquitensis</i>	<i>Aristolochia ridicula</i>
<i>Aristolochia bodamae</i>	<i>Aristolochia kaempferi</i>	<i>Aristolochia ringens</i>
<i>Aristolochia bottae</i>	<i>Aristolochia kewensis</i>	<i>Aristolochia rotunda</i>
<i>Aristolochia bracteolata</i>	<i>Aristolochia klugii</i>	<i>Aristolochia rugosa</i>
<i>Aristolochia bridgesii</i>	<i>Aristolochia indica</i>	<i>Aristolochia schippii</i>
<i>Aristolochia burelae</i>	<i>Aristolochia leuconeura</i>	<i>Aristolochia scytophylla</i>
<i>Aristolochia californica</i>	<i>Aristolochia islandica</i>	<i>Aristolochia sempervirens</i>
<i>Aristolochia cauliflora</i>	<i>Aristolochia labiata</i>	<i>Aristolochia serpentaria</i>
<i>Aristolochia caudate</i>	<i>Aristolochia leuconeura</i>	<i>Aristolochia silvatica</i>
<i>Aristolochia clematitis</i>	<i>Aristolochia lindneri</i>	<i>Aristolochia siphon</i>
<i>Aristolochia chachapoyensis</i>	<i>Aristolochia lingulata</i>	<i>Aristolochia socorroensis</i>
<i>Aristolochia chapmaniana</i>	<i>Aristolochia littoralis</i>	<i>Aristolochia sprucei</i>
<i>Aristolochia chilensis</i>	<i>Aristolochia longa</i>	<i>Aristolochia stomachoides</i>
<i>Aristolochia colossifolia</i>	<i>Aristolochia macrophylla</i>	<i>Aristolochia surinamensis</i>
<i>Aristolochia constricta</i>	<i>Aristolochia macroura</i>	<i>Aristolochia tagala</i>
<i>Aristolochia cordiflora</i>	<i>Aristolochia manchuriensis</i>	<i>Aristolochia taliscana</i>
<i>Aristolochia cordigera</i>	<i>Aristolochia mathewsii</i>	<i>Aristolochia thozetii</i>
<i>Aristolochia cucurbitoides</i>	<i>Aristolochia maurorum</i>	<i>Aristolochia thwaitesii</i>
<i>Aristolochia cornuta</i>	<i>Aristolochia maxima</i>	<i>Aristolochia tomentosa</i>
<i>Aristolochia coryi</i>	<i>Aristolochia moupinensis</i>	<i>Aristolochia tricaudata</i>
<i>Aristolochia cymbifera</i>	<i>Aristolochia nana</i>	<i>Aristolochia trilobata</i>
<i>Aristolochia daemonioxia</i>	<i>Aristolochia oblique</i>	<i>Aristolochia tuberosa</i>
<i>Aristolochia dalyi</i>	<i>Aristolochia odoratissima</i>	<i>Aristolochia urupaensis</i>
<i>Aristolochia delavayi</i>	<i>Aristolochia orbicularis</i>	<i>Aristolochia utrififormis</i>
<i>Aristolochia deltantha</i>	<i>Aristolochia ornithocephala</i>	<i>Aristolochia watsonii</i>
<i>Aristolochia deltoidea</i>	<i>Aristolochia pallid</i>	<i>Aristolochia westlandii</i>
<i>Aristolochia durior</i>	<i>Aristolochia parviflora</i>	<i>Aristolochia wrightii</i>
<i>Aristolochia erecta</i>	<i>Aristolochia paulistana</i>	<i>Aristolochia yunnanensis</i>
<i>Aristolochia eriantha</i>	<i>Aristolochia peltata</i>	<i>Aristolochia socorroensis</i>
<i>Aristolochia esperanzae</i>	<i>Aristolochia foveolata</i>	<i>Aristolochia sprucei</i>
<i>Aristolochia fangchi</i>	<i>Aristolochia galeata</i>	<i>Aristolochia stomachoides</i>
<i>Aristolochia filipendulina</i>	<i>Aristolochia glandulosa</i>	<i>Aristolochia foetida</i>
<i>Aristolochia fimbriata</i>	<i>Aristolochia gibertii</i>	



Fig. 1: Aristalochia indica (Sapsanda/ Sassanda)



Fig. 2: Aristalochia littoralis



Fig. 3.: A. littoralis flower



Fig. 4: Aristolochia lindneri



Fig. 5: Aristolochia macrophylla on a tree



Fig. 6: Aristolochia pistolochia



Fig. 7: Aristolochia maxima



Fig. 8: *Aristolochia pontica*

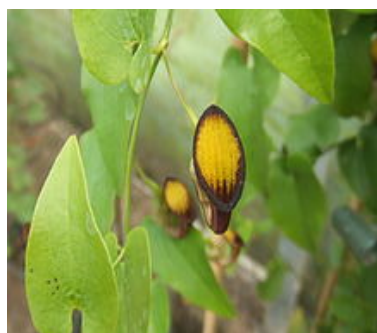


Fig. 9: *Aristolochia sempervirens*



Fig. 10: *Aristolochia arborea*



Fig. 11: *Aristolochia eriantha*



Fig. 12: *Aristolochia gibertii*

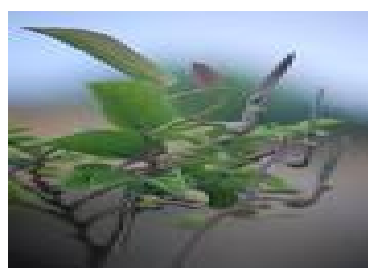


Fig. 13: *Aristolochia bracteolata*

Usage of *Aristolochia* species

Aristolochia clematitis is highly regarded as a medical plant since the ancient Egyptians, Greeks and Romans, and on to until the early modern era. It also plays a minor role in traditional Chinese medicine. Virginia Snakeroot (*Aristolopchia serpentaria*) is thus named because the root is used to treat snakebite with a rather uncertain degree of success. *Aristolochia pfeiferi*, *Aristolochia rugosa* and *Aristolochia trilobata* are used in folk medicine to cure snakebites. Aristolochic acid does indeed appear to bind and deactivate the Phospholipase A₂ of certain snake venoms.

Others claim that a decoction of birthwort stimulates the production and increases the activity of leukocytes (white blood cells), or that pipevines contain a disinfectant which assists in wound healing. *Aristolochia bracteolata* is colloquially known as "worm killer" due

to supposed anti-helminthic activity. *Aristolochia indica* is reported as a widely used plant in many Ayurveda medical remedies in Sri Lanka.

Aristolochia species are being frequently used as an ingredient in Ayurvedic treatments in Sri Lanka. Most preferable plant parts used in herbal remedies are whole plant, seeds, vines, roots and leaves. Though many other species are also used, the commonly using species is *Aristolochia indica* which is known as Sapsanda or Sasanda in Sinhala. According to tables .2, 3 and .4, in Sri Lankan Ayurvedic medicine, there are more than 66 recipes which contains *Aristolochia indica* (Sapsanda/ Sasanda) as an ingredient used in the treatment of more than 20 disorders.

Table below gives the list of pre-prepared commonly used Ayurvedic remedies found in Ayurvedic Pharmacopeia, which is considered as the Bible of Ayurveda. Table 3. gives the list of miscellaneous pre-prepared remedies found in Traditional Manuscript of Olases obtained from ancient Ayurvedic practitioners (Vaidyacharya). Table .4 shows the miscellaneous mixed recipes containing *Aristolochia* (Sapsanda/ Sasanda) as an ingredient, obtained from the same traditional Olases. Most of the time *Aristolochia* sp. is included in recipes to cure snake and other poison bites, diarrhoea, fever, body pains , pain in eyes, teeth, throat and ears, post-partum depression, labour pain, indigestion, stomachache, and headache like common diseases.

Aristolochia ringens (in Sinhala, Guruluraja) (Fig.14) is another *Aristolochia* species found in a few Sri Lankan Ayurvedic prescriptions. There is a ready to drink (pre-prepared) syrup called 'Guruluraja Thailaya' referred in some handbooks proving the usage of Guruluraja in Ayurvedic Medicine. But in most of the Sri Lankan literature, the plant species known as Guruluraja is not considered as a medicinal plant, but considered as the flower of Uva Province. The synonyms for that plant are 'Foxtail Orchid' and 'Batticaloa Orchid', and in Uva province website it has been identified as *Rhynchostylis retusa* which is belonging to Orchidaceae family and not to Aristolochiaceae family. Therefore the study team concluded that the Guruluraja which is included in Ayurvedic prescriptions should be another plant, which is still to be correctly identified.

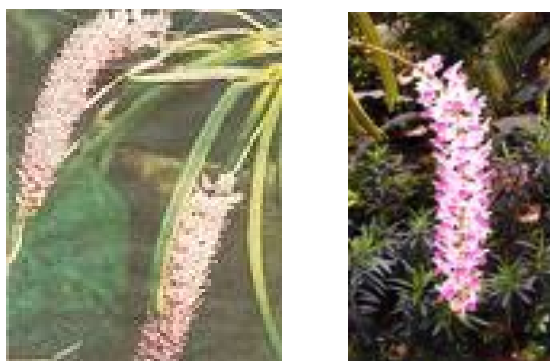


Fig. .14: Guruluraja (*Rhynchosyilis retusa*) flower found in Badulla area(Uva Province)



Fig. 15: *Aristolochia ringens* (Sinhalese name should be identified for this species)

Other than this *Aristolochia* species, *Asarum* species (Wild Ginger) are considered to be contained Aristolochic acid and no evidences were found to prove that they are in usage in Sri Lanka.



Fig. 16: *Asarum* (wild ginger)

Pre-prepared (ready-made) commonly used remedies

No.	Source	Name of the remedy	Disorder/ Disease	Method of Application	Plant part
1	A. P. 1 page 152	Waalu Kasaya I	Delivery and Post Delivery Depression, Delivery stress, Fever, Headache, Neuritis, Thriving,	Internal (Drinking)	Root
2	A. P. 1 page 152	Waalu Kasaya II	Delivery and Post Delivery Depression, Delivery stress, Fever, Headache, Neuritis, Thriving,	Internal (Drinking)	Root
3	A. P. 1 page 152	Waasa Musthakadee Kwathaya I	Fever, Diarrhea, wheezing	Internal (Drinking)	Leaves
4	A. P. 1 page 181	Abin Guliya	Vomiting, Diarrhea, Indigestion, Warm infections	Internal (Eating)	Leaves and Roots
5	A. P. 1 page 274	Dasa waga Prameha Thailaya	Urinary Disorders, Wheezing, Constipation, Heart Diseases, Eczema, Filarial fever	Internal (Eating)	Roots
6	A. P. 1 page 276-277	Nawapatala Thailaya (Kesarasingha Nawapatala Thailaya)	Headache, Catarrh, Eye Diseases,	Internal and External	Leaves and Roots
7	A. P. 1 page 279	Neelaraja Thailaya	Rabies, Snake Bites, Scorpion Bites, Earth worm Bites, Rat Bites and other poison bites	Internal (Drinking)	Vine with Leaves
8	A. P. 1 page 289	Maha Waayuraksha Thailaya	Post Delivery Depression, Fit, Muscle pains	Internal (Drinking)	Roots
9	A. P. 1 page 290-291	Yama devaraja Thailaya	Fit, Thyroid Disorders, Tonsils, Respiratory track infection and swelling , Tumors	Internal (Drinking and Inhalation)	Roots
10	A. P. 1 page 296	Vishagarrbha Thailaya	Muscle pains	Internal (Drinking)	Vine with Leaves
11	A. P. 1 page 300	Saththawaade e Thailaya	Mental disorders, Delivery Depression, Hiccup	Internal (Drinking and Inhalation)	Roots

Source: Ayurvedha Pharmacopoeia, Volume 1, Part 1, Department of Ayurveda, Colombo, Sri Lanka

Miscellaneous pre-prepared remedies containing Aristolochia indica as an ingredient

No	Source	Name of the remedy	Disorder/ Disease	Method of Application	Plant part
1	Book No. 05, 29ii	Gandhakadee Rasaya	Indigestion, Diarrhea	External and Internal	Leaves and Roots
2	Book No.05, 43ii	Kolaraja Kalkaya	Fever, Chest pains, Cold and cough, Wheezing	Internal (Drinking and eating)	Roots
3	Book No. 616, page 4	Maha Jeevaanada Thailaya (Sannipatha Thailaya)	Fever and other acute situations	Internal (Drinking)	Leaves
4	Book No. 616, page 2	Sarwalokeshwar a chinthaamani Thailama/ Yamadevaraja Thailaya	Stomachache, Pains in ear, Vomiting, Diarrhea, Stomach discomfort.	Internal (Drinking and inhalation) and External	Leaves
5	Book No. 7, 32 nd poem	Kudaamaalu Kasaya	Post delivery pains, Thirsty, Headache, Fever, Rabies	Internal (Drinking)	Roots
6	Book No. 09, 43 rd poem	Udaranda Guliya	Tonsils, Body pains, Fever	Internal (Drinking and Eating)	Roots
7	Book No.04, 31 st section	Kaalaraaja Guliya	Headache, Catarrh, Cold	Internal (Drinking and inhalation)	Roots
8	Book No.04, 33 rd section	Grahanaaraayan a Thailaya	Tonsils, Cold	Internal and External	Roots
9	Book No.04, 45 th section	Grahana Maandam Guliya	Constipation, Fever, Milk vomiting,	Internal (Drinking and Eating)	Seeds
10	Book No.11, paragraph 01	Vishnu Thailaya	Headache, Toothache, Lesions in tongue.	Internal (inhalation)	Roots
11	Book No.59	Mahayoga Churnaya	Wheezing, Indigestion, Various body pains,	Internal (Drinking and Eating)	Roots
12	Book	Yamadevaraaja	Throat pains	Internal (Drinking)	Leaves

	No.134,	Thailaya			
13	Book No.140, Page 15	Chinthamanikya Thailaya	Fever, Swelling, Pains	Internal (Drinking)	Leaves
14	Book No.196,	Anada Bahirawa Kayama	Fever, Cough, Stomachache, Stomach cancers, Malnutrition, Delivery pains	Internal (Drinking)	Roots and Leaves
15	Book No.89	Sarwalokeshwar a Chinthamanikya Thailaya	Diarrhea	Internal (Drinking)	Leaves
16	Book No.86	Siyalu wishwanelee Thailaya	Snake bites, Poison bites, Plant toxicities, Scorpion bites	Internal (Drinking)	Leaves

Source: Traditional manuscript of Olas coming from ancient Ayurveda Vaidyacharya (practitioners) - available at the Library, BMARI. Navinna, Maharagama, Sri Lanka

Miscellaneous mixed recipes containing Aristolochia indica as an ingredient

No.	Source	Name of the remedy	Disorder/ Disease	Method of Application	Plant part
1	Book No. 05, 8ii	Mixed recipe	Diarrhea	Internal (Drinking)	Leaves
2	Book No. 05, 18ii	Mixed recipe	All Fevers	Internal (Drinking)	Root
3	Book No. 05, 20ii	Mixed recipe	All Fevers	Internal (Drinking)	Leaves
4	Book No. 05, 31la	Mixed recipe	Severe Fever	Internal (Drinking)	Vine with Leaves
5	Book No. 05, 31ib	Mixed recipe	Severe Fever	Internal (Drinking)	Vine with Leaves
6	Book No. 05, 33ii	Mixed recipe	Severe Fever	Internal (Drinking) and External	Vine with Leaves
7	Book No. 05, 36i	Mixed recipe	Pains in Throat and Ear	Internal (Drinking)	Fruit Juice
8	Book No. 05, 37i	Mixed recipe	Snake Bites	Internal (Drinking) and External	Leaves
9	Book No. 05, 38i	Mixed recipe	Toothache, pains in Eye and Ear, problems in vision and at their increased symptoms, Delivery	Internal (Drinking)	Leaf Juice

			Pains, Wheezing, Cold		
10	Book No. 05, 41i	Mixed recipe	Urinary problems	Internal (Drinking)	Roots
11	Book No. 616, page 23(ii)	Mixed recipe	Pains in throat, ear and eye	Internal (Drinking and Eating) and External	Roots and Leaf Juice
12	Book No. 605, 14 th poem	Mixed recipe	Severe Fever	Internal (Drinking)	Leaf Juice
13	Book No. 09, 173 rd poem	Mixed recipe	Body pains, Stomachache and stomach discomfort	Internal (Drinking)	Roots
14	Book No. 04, 19 th section	Mixed recipe	Tonsils, Cold, Catarrh	Internal (Drinking)	Roots
15	Book No.614, page 05	Mixed recipe	Snake Bites	Internal (inhalation) and External	Roots and Leaves
16	Book No.614, page 03	Mixed recipe	Snake Bites and other poison bites.	Internal (inhalation)	Roots
17	Book No.614, page 02	Mixed recipe	Snake Bites and other poison bites.	Internal (inhalation)	Roots
18	Book No.46, page 05	Mixed recipe	Fever, Sleepy, Vomiting, Headache	Internal and External	Vine with Leaves
19	Book No.87, Paragrap h 01	Mixed recipe	Fever, Sleepy, Vomiting,	Internal (Drinking)	Roots
20	Book No.85, Paragrap h 01	Mixed recipe	Post delivery pains	Internal (Drinking)	Vine with Leaves
21	Book No.126, Paragrap h 01	Mixed recipe	Fever	Internal (Drinking)	Vine with Leaves
22	Book No.130, Page 7	Mixed recipe	Post delivery depression	Internal (Drinking)	Leaves
23	Book No.130, Page 7	Mixed recipe	Fever	Internal (Drinking)	Leaves

24	Book No.212,	Mixed recipe	Body pains	Internal (Drinking)	Vines
25	Book No.227,	Mixed recipe	Headache, Ear pains	Internal (Drinking) and External	Leaves
26	Book No.228,	Mixed recipe	Lunatic situations, Fever, Cough, Child diseases	Internal (Drinking) and External	Leaves
27	Book No.106	Mixed recipe	Fit, Eye pains,	Internal (Drinking)	Leaves
28	Book No.614, Page 11	Mixed recipe(Paste)	To facilitate Delivery of blue babies(Dead baby)	External Applying	Vine with Leaves
29	Book No.614, Page 16	Mixed recipe	All body pains	Internal (Drinking)	Leaves
30	Book No.95, Page 95(3)	Mixed recipe	Post delivery pains, Fever, Headache, Sleeplessness, Rabies	Internal (Drinking)	Roots
31	Book No.85	Mixed recipe	Poison bites	Internal (Inhalation/Drinking) and External	Roots
32	Book No.03, page 14	Mixed recipe	Diarrhea, Fever	Internal (Drinking)	Leaves
33	Book No.03, page 13	Mixed recipe	indigestion, Diarrhea	Internal (Drinking)	Leaves
34	Book No.03, page 27	Mixed recipe	Diarrhea	Internal (Drinking)	Vine with Leaves
35	Book No.03, page 21	Mixed recipe	Indigestion	Internal (Drinking)	Leaves
36	Book No.03, page 19	Mixed recipe	Any Diarrhea conditions	Internal (Drinking)	Leaves
37	Book No.03, page 550	Mixed recipe	Diarrhea	Internal (Drinking)	Roots
38	Book No.03, page 675	Mixed recipe	Diarrhea	Internal (Drinking)	Leaves
39	Book No.03, page 110	Mixed recipe	Diarrhea, Fever	Internal (Drinking)	Leaves

Source: Traditional manuscript of Olas coming from ancient Ayurveda Vaidyacharya (practitioners) - available at the Library, BMARI, Navinna, Maharagama, Sri Lanka

A work-shop was also conducted at the Aurvedic General Hospital Anuradhapura to collect information on usage of nephrotoxic herbal medicines by Ayurvedhic practitioners in North Central province. Only 10% of participants said that they still use *Aristolochia* species in their remedies. That is also mostly for external uses as a formula (mixture) rather than as a single ingredient. 90% of those who attended said that they are not using *Aristolochia* species in their remedies at all.

Discussion/ Conclusions

Epidemiological and laboratory studies have shown the toxicity of herbal remedies containing plant species of the genus *Aristolochia*. Herbal compounds containing *Aristolochia* are classified as a Group 1 carcinogen by the International Agency for Research on Cancer. In July 1999, two cases of nephropathy associated with the use of Chinese botanical preparations have been reported in the United Kingdom. Researchers have observed that those preparations were shown to contain Aristolochic acid. Biopsy samples have shown extensive loss of cortical tubules with interstitial fibrosis.

Aristolochia clematitis is most notable for containing toxic Aristolochic acid, sometimes in quantities fatal to humans. "Birthwort" has been used in childbirth to expel the placenta.

In 1993, a series of end-stage renal disease cases have been reported from Belgium associated with a weight loss treatment, where *Stephania tetrandra* in a herbal preparation was suspected of being substituted with *Aristolochia fangchi*. More than 105 patients have been identified with nephropathy following the ingestion of this preparation from the same clinic from 1990-1992. Many of them have been reported to require renal transplantation or dialysis. Subsequent follow up of these patients had shown that they are at an increased risk of urological cancer. Contamination of grain with European Birthwort (*Aristolochia clematitis*) has been implicated in the aetiology of Balkan nephropathy, a severe renal disease occurring in parts of southeastern Europe.

In Sri Lanka, about 66 Ayurvedic prescriptions which contain *Aristolochia* (Sapsanda/ Sasanda) are available for the treatment of more than 20 diseases. As per the focus group discussions conducted, there was no evidence to suggest any variations in the prescription and usage patterns of herbal medicines across the country. *Aristolochia* species are mainly used in remedies to cure snakebites and other poison bites. *Aristolochia indica*, known as Sapsanda or Sasanda, is the major species used in remedies by Sri Lankan Ayurvedic practitioners. There are many remedies that contain *Aristolochia indica* in Ayurvedhic literature. Further studies are required to objectively evaluate whether ayurvedic practitioners are currently using these remedies to treat patients and if so to ban/dissuade their use.

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SECTION 4

Impact of Research results

Relevance of results achieved to scientific advancement

Several studies had been carried out over the past decade to find the cause/s of CKDu by individual teams according to different study proposals resulting in duplication and lack of coherence. Such piece-meal efforts are unlikely to provide information that can guide policy action to address this major public health problem. In order to generate insight into the pathogenesis of CKDu and to develop appropriate preventive strategies, it is absolutely essential that epidemiological, environmental, socioeconomic and analytical studies be linked and the data subjected to a comprehensive analysis through a well coordinated research effort such as the one elaborated here.

Compared to previous studies conducted on CKDu, this research effort had several strengths:

- A stringent definition was used to define CKDu
- Range of biological samples were analyzed from CKDu subjects mainly at an international reference laboratory
- Control groups within and outside the endemic area provided comparison
- Sensitive analytical techniques were used

Studies conducted hitherto to determine the prevalence and etiology of CKDu relied on dipstick method to identify kidney disease and did not use a case definition. This is also the first study in which there have been comprehensive analyses of heavy metals, metalloids and other elements in environmental samples and food and findings compared with those from a non endemic area. Pesticide residues in urine were also analyzed.

The project has also conducted an ethnobotanical survey to document the species of *Aristolochia* plants that grow in Sri Lanka particularly in the North Central province and their usage in traditional/herbal remedies used in Sri Lanka. Results show that leaf, root, fruit or vine with leaves of *Aristolochia indica* are part of the remedies against more than twenty diseases and poison bites and that there are nearly 66 prescriptions which contained *Aristolochia indica* as an ingredient.

Results of these studies advance the understanding of the pathogenesis of CKDu. Results indicate that long term exposure to low levels of Cd and As is playing an important role in the aetiology of CKDu. Even though the individual levels of Cd and As are below levels hitherto thought to be safe, the concurrent chronic exposure combined with a deficiency of protective factors such as selenium and simultaneous exposure to nephrotoxic pesticides constitute a triple insult leading to kidney damage in vulnerable individuals. Nephrotoxic pesticides may be aggravating the progression of the disease.

Relevance of results achieved to national/ socio-economic development

The information gathered from the above studies show that households affected by CKDu are often poor. Livelihoods are agricultural, with uncertain and low incomes. Individuals affected with CKDu present with end stage renal disease leading to death typically around the age of 40 - 60 years. Most of them are heads of households and leave behind a number of dependents so that the loss of income and labour has major adverse impacts on socio economic development and national poverty alleviation efforts.

Even though the majority of CKDu patients mainly access public health care services which are provided free there are many costs related to regular treatment regimes that are a burden to the household. They include:

- Costs of channeling specialists, blood tests and scans for confirming the original diagnosis of CKD
- Cost of treatment, drugs, special appliances and special food for kidney disease
- Costs of alternative medicine, rituals and religious functions
- Such costs contribute to the economic burden, often resulting in indebtedness including pawning or sale of assets. Hence CKDu has two major long term economic implications i) through loss of physical assets and ii) through potential loss of human capital.

The exact number of affected people is unknown but more than 8000 people are currently undergoing treatment. Given the low socioeconomic profile of individuals affected by CKDu treatment from the government hospital is the preferred form of care for the majority.

The need for health care, dialysis services and kidney transplantation in the Government Health Sector has increased as a result. In 2005, about 4.6% of the health budget (350 million rupees) had been spent for the management of patients with kidney disease and the current trend predicts a large increase in this amount over the next decade. This coordinated series of research activities have provided evidence regarding the aetiology of CKDu to make prevention an option. If results of the clinical trial are positive it will help to reduce the dialysis costs and services loads and guide the design and implementation of national prevention programs.

Analysis of incomes and livelihoods provide direction to policy decisions that need to be taken by the Government to provide timely, close to client healthcare services and social welfare services targeted at the family, particularly geared to safeguarding the educational opportunities of children.

Dissemination/application of research output

Results of this project are published in a peer reviewed international medical science journal for wide dissemination. Based on the findings of these studies public health policies are required to be strengthened to ensure access to safe drinking water, regulatory control to ensure appropriate use of agrochemicals including fertilizer, hazardous waste remediation, and regulatory control to prevent pollution of environment from discarded

batteries containing heavy metals, tobacco control and reduction of air pollution can reduce exposure to heavy metals. Please see annex 1

A literature review has been done and all publications, articles, power point presentations have been compiled on to a literature repository (please see separate publication).

Based on the findings of this study, the Government of Sri Lanka has already initiated collaborative action with the Ministries of Health, Agriculture, Irrigation, Scientific Affairs and Social Services to identify preventive action to mitigate the exposure of people to nephrotoxic substances which includes high level interministerial committees as well as establishment of subcommittees

The response from the government of Sri Lanka to the research findings of CKDu



Several initiatives are going on in different ministries and has resulted in policy level decisions already been made and has resulted in cabinet papers also being submitted. The details of the different ministerial response is summarised below.

Ministry of Health Cabinet Memorandum – March 2013

- Water purification schemes to be scaled up
- Strengthen the regulatory framework to improve quality control of imported agrochemicals
- Implement and monitor comprehensive public health measures to reduce the exposure of farmers to harmful health effects of agrochemicals
- Improve service provision for early detection of CKDu, hypertension and diabetes and appropriate treatment
- Increase the financial assistance provided to farmer families affected by CKDu
- Increase awareness among Ayurvedic practitioners of the nephrotoxic effects of *Aristolochia Indica* (sapsanda)
- Facilitate research to promote the use of alternative fertilizers, reduce heavy metals in soil, develop rice strains which require less fertilizer/resistant to pests, reduce environmental pollution

Ministry of Agriculture

- Parliamentary Advisory Committee on Agriculture appointed
- Priority actions for minimizing the usage of Agro-chemicals
- Avoidance of misuse, overuse & abuse of chemical inputs in Agriculture
- Identification of research needs by *National Committee on Post Harvest Technology & Human Nutrition* of the **Sri Lanka Council for Agricultural Research Policy (SLCARP)**
- Updated Fertilizer Recommendations for paddy documented
- Banned importation of 4 pesticides -**Carbaryl, Chlorpyrifos, Carbofuran, Propanil**

15 Recommendations Submitted as a cabinet paper :

1. Establishment of Statutory Technical Council to promote environmentally friendly agriculture
2. Establishment of new Sri Lankan Standards (SLS) on pesticides and agrochemicals
3. To make orders under the Pesticide Control Act to retain heavy metals and impurities to a minimum possible level
4. Establishing methodology for controlling under-growth (weeds) of paddy cultivation & encouraging farmers to cultivate alternate crops for minimizing the use of pesticide

5. Strengthening legal framework to authorize state officials including the health sector & Grama niladhari to take legal action against those resorting to indiscriminate use of pesticides and those supporting the same
6. To prohibit the use of **Propane, Glyphosate, Carbayl** and **Chlorpyrifos** which have been identified as harmful pesticides in areas where kidney diseases are spreading
7. In view of the health risk, taking measures to minimize the use of all chemical fertilizers while encouraging farmers to adopt alternative methods
8. Minimise the use of imported phosphate and increase production and use of local phosphates
9. Testing all fertilizer varieties with health risk posed due to heavy metal and toxic ingredient content and establishment of revised standard for the same
10. Strengthening of legal background & establishment of laboratory facilities for frequent testing of agro-chemical impurities
11. Educate the public on the harmful effects on human health due to the use of agro-chemicals and their safety and efficient use
12. Prohibit pesticide and agro-chemical fertiliser advertising over electronic & print media
13. Establishment of a safety method for recycling/disposal of empty pesticide containers/bottles and fertilizer bags
14. Providing people in Kidney disease prone areas with drinking water free of insipid water
15. Impose a 10% health safety cess on all imported pesticide varieties and the levied amount to be used for welfare of the kidney patients and research activities

Minister (Senior) for Rural Affairs & Chairman of the Committee to look into the indiscriminate usage of chemical fertilizer & Agrochemicals

SHORT TERM RECOMMENDATIONS

1. Launch an islandwide program to identify CKDu patients with special attention to NCP & take action to declare CKDu as a notifiable disease
2. Carry out surveys using GIS to identify all CKDu hotspots upto Grama Niladhari Division
3. Declare CKDu hotspots and take all initiatives, to establish casual factors and to mitigate CKDu in the prevalent areas
4. Establish a high powered policy implementation body to carry out further research on establishing the exact causal factors of CKDu and to control CKDu and CKD under an appropriate ministry and to coordinate and implement the recommendations
5. Launch a multidisciplinary further research program to cover all spectrum of CKDu and to strongly establish the causal factor for CKDu
6. Further analyze the fertilizer recommendation scheme while paying special attention to the environmental consequence of the scheme
7. Implement an integrated awareness program to address all important aspects of CKDu and to promote suitable agricultural practices
8. Include the impact of heavy metals on human health & environment and safe use of pesticides and fertiliser into curricular of Geography, Agriculture, Health Science and science in secondary schools
9. Establish an independent accredited laboratory & upgrade the existing laboratories with facilities such as trained staff & sophisticated equipments to analyse trace elements (Cd, As, Pb, Fe, Mn etc) pesticide residues & other elements related to CKDu
10. Regulate the promotional activities related to fertilisers & pesticides carried out by the agrochemical companies/institutions carried out by mass media
11. Establishment of legal provisions for mandatory requirements in relation to standards
12. Provide drinking water with low or no hardness to communities in CKDu endemic areas by way of providing effective filters and/or delivering portable water with acceptable quality
13. Promote & implement rain water harvesting structures with quality monitoring systems and make regulations for all new buildings in CKDu areas to be equipped with rain water harvesting units

14. Select high priority CKDu hotspots & establish “Green Zones” that are free of major potential CKDu casual inputs
15. Provide subsidy & marketing facilities for the farmers who make attempts to move from agrochemicals to alternate farming
16. Establish a fund for the welfare of CKDu patients, for carrying out research and financing for fund through economic instruments based on the polluter pay principles and producer responsibility as well as CSR
17. Enhance the medical facilities for CKDu patients with immediate effects in the affected areas
18. Facilities of the traditional medical practitioners to carry out their treatments for the affected people based on the patient interest & demand
19. Expedite the establishment of proposed chemical fertiliser manufacturing plant to produce fertiliser with minimum/standard limits of heavy metals using Eppawella rock phosphate

LONG TERM RECOMMENDATIONS

1. Establish procedures for examination of quality of agrochemicals at boarder poits, Factory outlets, wholesale & retail shops in the districts
2. Establish long term water quality monitoring system by an accredited agency under direct supervision of a government institution.
3. Capacity building of grass root level officers to educate farmers on use of minimum pesticides and fertilisers
4. Prepare necessary maps indicating zones for active, potential and prone to agrochemical contamination
5. Redesign land use pattern, crop & land implementation plans covering soil & water drainage engineering aspect & climatic parameters
6. Establish river banks, green manure banks, neem avenues, herbal gardens, compost bays and strict declaration of non toxic zones
7. Identify farmers/farmer groups and designate them as responsible agents/agri environment guard with authority to regulate the inputs used in agriculture
8. Introduce programmes for organic and sustainable certification to receive premium prices for farm products

9. Establish appropriate CSR avenues through Banks, Insurance companies, NGOs, local institutions for possible subsidy or incentives for proposed curative and corrective measures
10. Conduct extended cost benefit analysis for the use of agrochemicals in consideration of their impact on environmental & social effects

Ministry of Water Supply & Drainage

- Parliamentary Sub committee appointed to coordinate mitigation measures
- Concept paper and action plans have been prepared for supplying safe drinking water to all affected areas
- District wise action items/sub projects have been identified
- Implementation Plans

SHORT TERM

- Water for drinking and cooking using small RO (Reverse Osmosis) plants
- Rain water harvesting

MEDIUM TERM

- Medium sized water supplies based on surface water
- Water Supply extensions

LONG TERM

- Major Integrated Water Supply projects

Ministry of Social Services

Draft Cabinet paper prepared for following:

- To adhere to the Ministry of Health-World Health Organization criteria in order to diagnose the disease
- To pay monthly assistance of **Rs 1500** each for kidney patients who do not require dialysis (Stated in Grade 2/3)
- To pay monthly assistance of **Rs 3000** each for kidney patients who require dialysis (Stated in Grade 3/4)
- At present a monthly assistance is paid for only a few patients through Provincial social Services Department and ranges from Rs 500 - 1000

SECTION 5

Miscellaneous

List of publications/communications arising from the project and/or presentations made at seminars, workshops etc.

- a) Prevalance Study Database (CD)
- b) Literature Repository (Book & CD)
- c) **Annexure 1-** Research Article in BMC Nephrology
- d) **Annexure 2 –** Mission & Progress reports submitted by Dr Shanthi Mendis, Management of Non Communicable diseases, World Health Organisation
 - Mission Report - 6-8 June 2011
 - Mission Report - 5 -7 October 2011
 - Progress Report - 13 February 2012
 - Mission Report - 25 - 28 June 2012
- e) **Annex ure 3 –** Joint Press statement of the Ministry of Health and the World Health Organisation June 2011
- f) **Annexure 4-** Publications done by the epidemiology unit on CKDu: November – December 2009
- g) **Annexure 5 –** Publications done by the Ministry of Health and World Health Organisation on CKDu : December 2009 & June 2011
- h) **Annexure 6-** WHO Sri Lanka publications : January 2009 & February 2009
- i) **Annexure 7 –** Powerpoint Presentation on content of the final report including methodologies and results as well as work done upto now

RESEARCH ARTICLE

Open Access

Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country

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Abstract

Background: This study describes chronic kidney disease of uncertain aetiology (CKDu), which cannot be attributed to diabetes, hypertension or other known aetiologies, that has emerged in the North Central region of Sri Lanka.

Methods: A cross-sectional study was conducted, to determine the prevalence of and risk factors for CKDu. Arsenic, cadmium, lead, selenium, pesticides and other elements were analysed in biological samples from individuals with CKDu and compared with age- and sex-matched controls in the endemic and non-endemic areas. Food, water, soil and agrochemicals from both areas were analysed for heavy metals.

Results: The age-standardised prevalence of CKDu was 12.9% (95% confidence interval [CI] = 11.5% to 14.4%) in males and 16.9% (95% CI = 15.5% to 18.3%) in females. Severe stages of CKDu were more frequent in males (stage 3: males versus females = 23.2% versus 7.4%; stage 4: males versus females = 22.0% versus 7.3%; $P < 0.001$). The risk was increased in individuals aged >39 years and those who farmed (chena cultivation) (OR [odds ratio] = 1.926, 95% CI = 1.561 to 2.376 and OR = 1.195, 95% CI = 1.007 to 1.418 respectively, $P < 0.05$). The risk was reduced in individuals who were male or who engaged in paddy cultivation (OR = 0.745, 95% CI = 0.562 to 0.988 and OR = 0.732, 95% CI = 0.542 to 0.988 respectively, $P < 0.05$). The mean concentration of cadmium in urine was significantly higher in those with CKDu (1.039 $\mu\text{g/g}$) compared with controls in the endemic and non-endemic areas (0.646 $\mu\text{g/g}$, $P < 0.001$ and 0.345 $\mu\text{g/g}$, $P < 0.05$) respectively. Urine cadmium sensitivity and specificity were 70% and 68.3% respectively (area under the receiver operating characteristic curve = 0.682, 95% CI = 0.61 to 0.75, cut-off value $\geq 0.397 \mu\text{g/g}$). A significant dose-effect relationship was seen between urine cadmium concentration and CKDu stage ($P < 0.05$). Urine cadmium and arsenic concentrations in individuals with CKDu were at levels known to cause kidney damage. Food items from the endemic area contained cadmium and lead above reference levels. Serum selenium was $<90 \mu\text{g/l}$ in 63% of those with CKDu and pesticides residues were above reference levels in 31.6% of those with CKDu.

Conclusions: These results indicate chronic exposure of people in the endemic area to low levels of cadmium through the food chain and also to pesticides. Significantly higher urinary excretion of cadmium in individuals with CKDu, and the dose-effect relationship between urine cadmium concentration and CKDu stages suggest that cadmium exposure is a risk factor for the pathogenesis of CKDu. Deficiency of selenium and genetic susceptibility seen in individuals with CKDu suggest that they may be predisposing factors for the development of CKDu.

Keywords: Arsenic, Cadmium, Chronic kidney disease, Kidney disease of uncertain aetiology, Heavy metals, Lead, Pesticides

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Background

The study reported here describes an apparently new form of chronic kidney disease, which cannot be attributed to diabetes, hypertension or other known aetiologies, that has emerged in the North Central region of Sri Lanka [1]. Chronic kidney disease of uncertain aetiology (CKDu) is slowly progressive, probably starting in the second decade of life, and asymptomatic until advanced. Peripheral oedema and hypertension are late features. The main histopathological features include tubular atrophy, interstitial mononuclear cell infiltration and interstitial fibrosis [2]. These histological features suggest that nephrotoxins play a key role in the aetiology of CKDu.

Potential nephrotoxins are widely distributed in the environment. Exposure to environmental and other nephrotoxins, such as herbal medicines and analgesics, are known to play a role in the aetiology of chronic kidney disease. Defining their exact role in the aetiology of kidney disease is a challenge. Environmental toxins implicated in kidney damage include heavy metals, such as arsenic, cadmium, lead and uranium; mycotoxins produced by fungi in improperly stored foods; air pollutants, such as tobacco smoke; and pesticides, such as chlorpyrifos, diazinon and propanil [3-9].

Over the last 8 years, several studies have been carried out to determine the prevalence, nature and causes of CKDu in Sri Lanka [10-20]. These studies include hospital-based reviews of case series, in which high-risk areas in North Central Province were identified. The hospital studies gave rise to population-based surveys, which showed that the populations affected by CKDu are scattered in the North Central region of the country [14]. Some studies have reported the point prevalence of CKDu to be about 2-3% among those above 18 years of age [20]. Case-control and cross-sectional studies have provided some insight into associations with the condition. Specific evaluations of exposure to organophosphate and mycotoxins have been conducted. In a cross-sectional study, there was evidence of greater inhibition of acetyl cholinesterase among patients with chronic renal dysfunction in areas of high prevalence of CKDu [17]. Ochratoxin, a naturally occurring mycotoxin with nephrotoxic properties, was not found to be a contaminant of food in the region [13,16]. Some studies have shown high levels of environmental cadmium, lead, aluminium and fluoride in regions with high rates of the condition [14,15,17,19].

Recognising the gravity of the public health threat caused by CKDu, in 2010, the Ministry of Health Sri Lanka, in collaboration with the World Health Organization (WHO), launched a national research project with the aim of investigating the prevalence and aetiology of CKDu in Sri Lanka, with a view to developing appropriate preventive strategies.

The objectives of this study were to: determine the prevalence of and identify the risk factors for CKDu; compare CKDu cases and controls with regard to exposure to heavy metals/metalloids and pesticides; and analyse food, water, soil, fertilizers and weedicides for heavy metals, in order to determine whether the levels are above stipulated reference values.

A population prevalence study was conducted in three districts in the endemic area over the period 2010-2012 (Figures 1 and 2). Arsenic, cadmium, lead and other metals, elements and pesticide residues that are potential nephrotoxins [6-9,21-24], were analysed in biological samples. The results from individuals with CKDu were compared with those from controls in the endemic area and a non-endemic area (Hambantota where CKDu has not been reported). The demographic characteristics of the three groups are shown in Table 1. All individuals with CKDu ($n = 733$) had a blood pressure below 160/100 mmHg; 6.8% of these individuals were on treatment for high blood pressure and had a blood pressure below <140/90 mmHg. Three-quarters of those who were on treatment were on angiotensin-converting enzyme inhibitors. Others were on calcium channel blockers, beta-

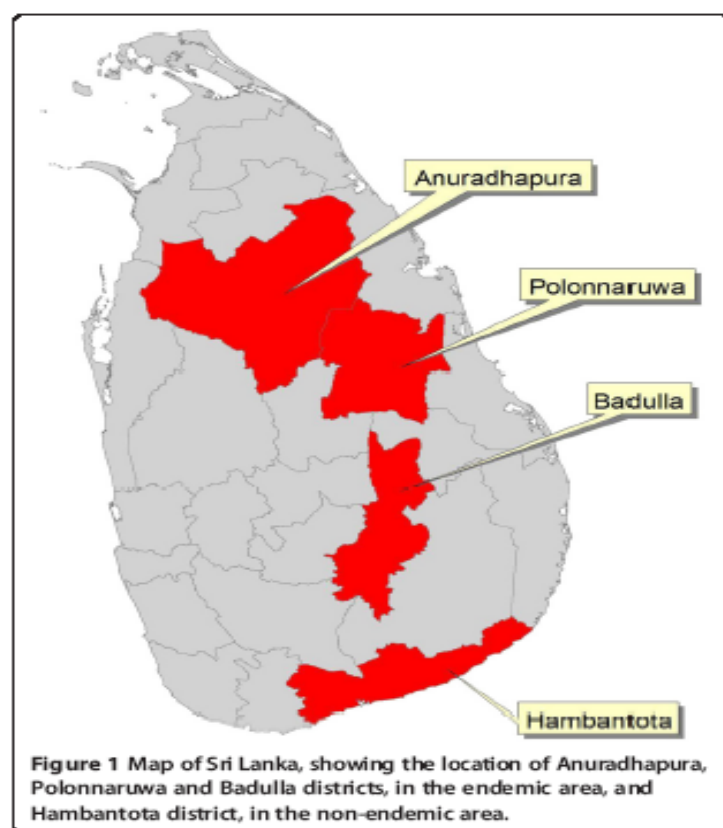


Figure 1 Map of Sri Lanka, showing the location of Anuradhapura, Polonnaruwa and Badulla districts, in the endemic area, and Hambantota district, in the non-endemic area.

Number invited to participate in the study from 220 randomly selected households

n=6698

Response rate 74% (n=4957)

ACR assay ≥ 30 mg/g on two occasions
and satisfy other criteria of CKDu
(n=733)

No diabetes, other kidney
disease, CKDu and snake bite=4044
(excluded=180, missing data n=25)

Urine arsenic, cadmium and lead n=495
Urine for other elements n=107
Serum selenium, strontium etc n=171
Hair/nails arsenic, cadmium lead n=80
Urine pesticide residues n=57

n=132
n=0
n=0
n=48
n=0

Figure 2 Flow chart of the study conducted in three districts (Anuradhapura, Polonnaruwa and Badulla) in the endemic area.
ACR = albumin-creatinine ratio.

blockers or diuretics, either alone or in combination with angiotensin-converting enzyme inhibitors.

In both endemic and non-endemic areas, water, food, tobacco, soil and agrochemicals were also analysed for heavy metals and metalloids, to determine whether they were within stipulated reference levels.

Methods

Case definition

The following case definition of CKDu was used. Participants who had persistent albuminuria, i.e. albumin-creatinine ratio (ACR) ≥ 30 mg/g in an initial urine sample and at a repeat visit, were considered to have CKDu if they satisfied the following criteria:

- no past history of glomerulonephritis, pyelonephritis, renal calculi or snake bite
- not on treatment for diabetes

Table 1 Demographic characteristics of CKDu cases in the endemic area, controls from the endemic area and controls from the non-endemic area

Characteristic	Endemic area		Non-endemic area
	CKDu cases	Controls	Controls
Total number	733	4044	250
Males, %	37.1	42.5	56
Age (years), mean (SD)	39.1 (14.2)	43.7 (13.9)	35.5 (14.0)
Farmer, %	38	43.9	18.3
BMI, kg/m ² , mean (SD)	22.3 (4.6)	21.1 (4.1)	21.7 (4.4)
ACR ≥ 30 mg/g	733	0	0

ACR albumin-creatinine ratio, BMI body mass index, SD standard deviation.

- normal glycosylated haemoglobin (HbA_{1c}; <6.5%)
- if on treatment for hypertension, blood pressure below <140/90 mmHg; if not on treatment for hypertension, blood pressure below <160/100 mmHg.

CKDu was graded as follows:

- *Stage 1*: persistent albuminuria (i.e. ACR ≥ 30 mg/g in initial and repeat urine sample) and estimated glomerular filtration rate (eGFR), using the Chronic Kidney Disease Epidemiology collaboration (CKD-EPI) equation [25] >90 ml/min/1.73 m²
- *Stage 2*: persistent albuminuria and eGFR 60–89 ml/min/1.73 m²
- *Stage 3*: persistent albuminuria and eGFR 30–59 ml/min/1.73 m²
- *Stage 4*: persistent albuminuria and eGFR <30 ml/min/1.73 m².

Population prevalence study

Ethical approval for the study was obtained from the Ethical Review Committee of the Sri Lanka Medical Association. All participants gave written consent for the study.

Six divisional secretariat areas (administrative divisions) were selected randomly from three districts in the endemic area. Twenty-two villages (Grama Niladari areas) were selected randomly from the six divisions. Using the electoral lists, 100 households from each village were randomly selected for the study. Males and females aged between 15 and 70 years ($n = 6698$), with no diagnosed diabetes, were invited to participate and 74% responded

(Figure 2, flow diagram). Trained interviewers used a survey questionnaire to gather information on age, sex, marital status, education, occupation, smoking, alcohol consumption, current residence, duration of residence in the study area, source of drinking water, storage containers for drinking water, exposure to agrochemicals, history of snake bite, glomerulonephritis, pyelonephritis, renal calculi, use of medications including herbal medicines, and past medical history. Height was measured to the nearest 0.1 cm. Weight was measured to the nearest 0.1 kg, using a calibrated weighing scale. Participants wore light clothes and no shoes. A medical officer verified the medical information gathered and measured the blood pressure after 15 minutes' rest, using a mercury sphygmomanometer. The average of two readings taken 5 minutes apart was used. Urine ACR, HbA_{1c} and serum and urine creatinine concentrations were also measured.

Analytical studies

Arsenic, cadmium and lead in urine, blood, hair and nails

Arsenic, cadmium and lead concentrations were analysed in urine in a randomly selected subset of CKDu cases ($n = 495$) and randomly selected matched controls from the endemic area, as well as from the non-endemic area ($n = 250$).

Urine sodium, potassium, calcium, magnesium, copper, zinc and titanium concentrations were analysed in a randomly selected subset of CKDu cases ($n = 148$). Their serum was also analysed for selenium, aluminium, strontium and chromium. Hair and nail samples were analysed for cadmium, arsenic and lead in a subset of CKDu cases ($n = 80$) and controls from the endemic area ($n = 48$).

Urine samples from CKDu cases ($n = 57$) and controls from the non-endemic area ($n = 39$) were analysed for pesticide residues (2,4-D, 2,4,5-T, 2,4,5-trichlorophenol, isopropoxyphenol, pentachlorophenol, 3,5,6-trichloropyridinol, *p*-nitrophenol, 1-naphthol, 2-naphthol, glyphosate, aminomethylphosphonic acid (AMPA)).

Arsenic, cadmium and lead in water, food, tobacco, pasture, weeds, soil, fertilizer, weedicides and pesticides

Arsenic, cadmium and lead were analysed in samples ($n = 234$) obtained from endemic and non-endemic areas. They comprised 99 sources of drinking water for individuals with CKDu (from ground wells, tube wells and natural springs), 123 other sources of water (from ground wells, tube wells, irrigation canals, reservoirs, natural springs) from the endemic area, and 12 from the non-endemic area.

Rice; pulses; vegetables, including leafy vegetables, coconut, yams and roots (e.g. kohila, lotus); freshwater fish; tobacco; pasture; and weeds obtained from endemic ($n = 119$) and non-endemic ($n = 32$) areas were analysed for arsenic, cadmium and lead.

Soil, phosphate fertilizer, pesticides and weedicides were analysed for arsenic, cadmium and lead. Soil samples were obtained from paddy fields, other types of cultivations, and reservoirs in the endemic ($n = 88$) and non-endemic ($n = 41$) areas.

Specimen handling and analysis

Samples were collected in uncontaminated collection vials and stored frozen (-20°C) until transfer to the laboratory. All analyses were performed in a contract laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium), which has an external quality control scheme for analysis of trace elements.

Measurements of arsenic, cadmium, lead and other elements in urine, water, vegetables, agrochemicals and soil, was performed by inductively coupled plasma mass spectrometry (MS).

Serum analyses were performed by electrothermal atomic absorption spectrometry. Limits of detection for aluminium, strontium, chromium and selenium were 0.1 $\mu\text{g/l}$, 0.5 $\mu\text{g/l}$, 0.01 $\mu\text{g/l}$ and 1 $\mu\text{g/l}$ respectively.

Determination of pesticide residues in urine

Samples were shipped in dry ice and stored at -18°C until analysis. Analysis used validated liquid chromatography with tandem MS (LC-MS/MS), gas chromatography-mass spectroscopy (GC-MS) and gas chromatography with tandem mass spectrometry (GC-MS/MS) methods.

Further details of sample preparation and analytical techniques are provided in the Additional file 1.

Statistics

The normality of data distribution was assessed with histograms. All data on metals had skewed distributions. After removal of a small number of outliers, log-transformations were used to normalise the data, in order to conduct statistical analyses. The mean, median, minimum and maximum values are reported on original data; *t*-tests of log-transformed values were used to test differences in quantitative variables. The results were also confirmed by non-parametric Wilcoxon rank-sum test.

A multiple logistic regression model was fitted for the CKDu definition. The model incorporated characteristics of interest, including age, sex, education, smoking, illicit alcohol consumption, occupation, type of agriculture, years of agriculture, source of drinking water, drinking water from paddy fields, exposure to fertilizer, exposure to weedicides and pesticides, type of water container, whether using protection against agrochemicals, and months living in the district. All were entered as categorical variables, except months living in the district. These data analyses were performed using Stata 11 and *P* values of less than 0.05 were considered statistically significant. A receiver-operating characteristic (ROC) curve was used to

calculate the area under the ROC curve (AUC), to determine the cut-off values for cadmium and selenium with the best sensitivity and specificity. A multinomial logistic regression was used to assess the dose–effect relationship between metal exposure and the outcome CKDu grade. The analyses were adjusted for age and sex.

Results

Population prevalence study

The age-standardised prevalence of CKDu was higher in females 16.9% (95% confidence interval [CI] = 15.5% to 18.3%) than in males 12.9% (95% CI = 11.5% to 14.4%; $P = 0.001$). About 37% of those with CKDu were male. The distribution of CKDu stages 1 to 4 in males was 27.0%, 27.9%, 23.2% and 22.0% and in females 53.3%, 32.0%, 7.4% and 7.3%, respectively. More severe stages of CKDu were seen more frequently in males (stage 3: males versus females = 23.2% versus 7.4%; stage 4: males versus females = 22.0% versus 7.3%; $P < 0.001$). In both sexes, the prevalence increased with increasing age ($P < 0.001$). The prevalence in the three districts was 15.1% in Anuradhapura, 20.6% in Polonnaruwa and 22.9% in Badulla.

There was a family history of kidney disease in parents or siblings in 20% of individuals with CKDu; 2.1% of individuals with CKDu had a history of ischaemic heart disease and/or cerebrovascular disease; 0.4% had a history of long-term use of herbal medicines for hypertension; 1.8% had a history of long-term use of aspirin; and 0.6% had a history of long-term use of analgesics. Being male reduced the risk of CKDu (odds ratio [OR] = 0.745, 95% CI = 0.562 to 0.988, $P < 0.05$), and being older than 39 years increased the risk of CKDu (OR = 1.926, 95% CI = 1.561 to 2.376, $P < 0.001$). When separate logistic regressions were run for each potential exposure, only occupation type (being a chena cultivation farmer increased the OR by 19.5%) and type of agriculture (engaging in paddy cultivation compared to cultivation of vegetables and other crops [chena cultivation] decreased the OR by 26.8%) were significant (Table 2).

Arsenic, cadmium, lead and other elements in urine

In CKDu cases, the concentration of cadmium in urine was significantly higher compared to controls, in both the endemic and the non-endemic areas (Table 3). Among CKDu cases, the concentration of cadmium in urine was positively correlated with lead ($r = 0.62$, $P < 0.001$) and arsenic concentrations in urine ($r = 0.28$, $P < 0.001$). There was no significant difference in urine arsenic and lead concentrations in CKDu cases compared to controls. The sensitivity and specificity for concentrations of cadmium in urine were 80% and 53.6% respectively (AUC = 0.682, 95% CI = 0.61 to 0.75, cut-off value ≥ 0.23 $\mu\text{g/g}$; Figure 3). At a cut-off value of ≥ 0.397 $\mu\text{g/g}$, sensitivity was 70% and specificity 68.3%. The sensitivity and specificity for the

Table 2 Summary results of logistic regression analysis for exposures

Exposure	OR	95% CI		P value	n
		Lower	Upper		
Education					
No education	Reference				174
School grades 1–9	0.900	0.612	1.323	0.594	4374
Higher	1.201	0.588	2.452	0.614	74
Smoking					
Never	Reference				3480
Current/former	1.072	0.813	1.415	0.619	1126
Illicit alcohol consumption					
Never	Reference				3701
Occasional/frequent/past	1.184	0.905	1.548	0.216	874
Occupation					
Other	Reference				2816
Farmer	1.195	1.007	1.418	0.041	1780
Agriculture type					
Non-paddy	Reference				315
Paddy	0.732	0.542	0.988	0.042	2620
Years working in agriculture					
<10	Reference				660
10–19	0.834	0.603	1.152	0.271	777
20–49	1.092	0.777	1.535	0.611	1182
≥ 50	1.322	0.462	3.785	0.602	22
Source of drinking water					
Not well	Reference				798
Well	0.971	0.785	1.202	0.793	3819
Water storage container					
Others	Reference				1741
Aluminium	1.03	0.87	1.22	0.715	2879
Protection from agrochemicals					
Yes	Reference				191
No	1.011	0.661	1.546	0.959	4271

Separate logistic regressions have been run per exposure variable; OR < 1 means protective, and OR > 1 means that the exposure increases the odds of CKDu. The total number (n) of observations varies per exposure, owing to missing data. All results are adjusted for sex and age. For all analyses, male sex was found to be protective and the risk increased with age. CI confidence interval, OR odds ratio.

Being male reduced the risk of CKDu (OR = 0.745, 95% CI = 0.562 to 0.988; $P < 0.05$), and being >39 years increased the risk of CKDu (OR = 1.926, 95% CI = 1.561 to 2.376, $P < 0.001$).

concentration of arsenic in urine were 90% and 23.2% respectively (AUC = 0.64, 95% CI = 0.58 to 0.71, cut-off value ≥ 88.57 $\mu\text{g/g}$). The concentration of lead in urine was a poor predictor of CKDu (AUC = 0.53, 95% CI 0.38 to 0.67). Dose–response analysis showed that cadmium exposure is a

Table 3 Urine concentration of arsenic, cadmium and lead for CKDu cases compared with controls from the endemic and non-endemic areas

	Mean, median (range) of concentration in urine (µg/g creatinine)		
	Arsenic	Cadmium	Lead
CKDu cases (n = 495)	45.447, 26.3 (0.4 to 616.6)	1.039, 0.695 (0.005 to 8.93)	1.153, 0.95 (0.04 to 8.53)
Controls from endemic area (n = 132)	92.443, 6.99 (0.2 to 966.29)	0.646, 0.18, (0.005 to 5.13) ^a	1.254, 0.793 (1.21 to 6.64)
Controls from non-endemic area (n = 250)	56.572, 42.025 (5.38 to 350.28)	0.345, 0.265 (0.005 to 20.79) ^b	2.099, 1.434 (0.277 to 20.9)

^a Urine cadmium concentration of cases compared to controls from endemic area $P < 0.001$.

^b Urine cadmium concentration of cases compared to controls from non-endemic area $P < 0.05$.

risk factor for the development of CKDu: $P = 0.019$ for stage 3 and $P = 0.024$ for stage 4. There was no significant dose-effect relationship between the concentration of arsenic, lead or selenium in urine and the stage of CKDu.

Urine concentrations of sodium, potassium, calcium, magnesium, copper, zinc, and titanium in CKDu cases were within normal limits (Additional file 2).

Serum aluminium, chromium, selenium and strontium in CKDu cases

Serum aluminium and chromium levels were within normal limits (Additional file 2). Serum selenium levels in subjects with CKDu ranged from 50.0 µg/l to 121.8 µg/l

(reference range = 54 µg/l to 163 µg/l). A serum selenium concentration of 90 µg/l is required to reach the maximum level of glutathione peroxidase [26]. About two-thirds (63%) of subjects had selenium levels below this cut-off value. Serum strontium levels were above normal limits (mean = 83.17 µg/l, standard deviation [SD] = 32.15 µg/l; reference range = 14 µg/l to 84 µg/l). The sensitivity and specificity for serum selenium were 80% and 60% respectively (AUC = 0.789, cut = off value ≥ 94.3 µg/l; Figure 3).

Cadmium and arsenic in hair and nails

A significantly higher cadmium concentration was also seen in the nails of CKDu cases ($n = 80$, mean = 0.017 µg/g,

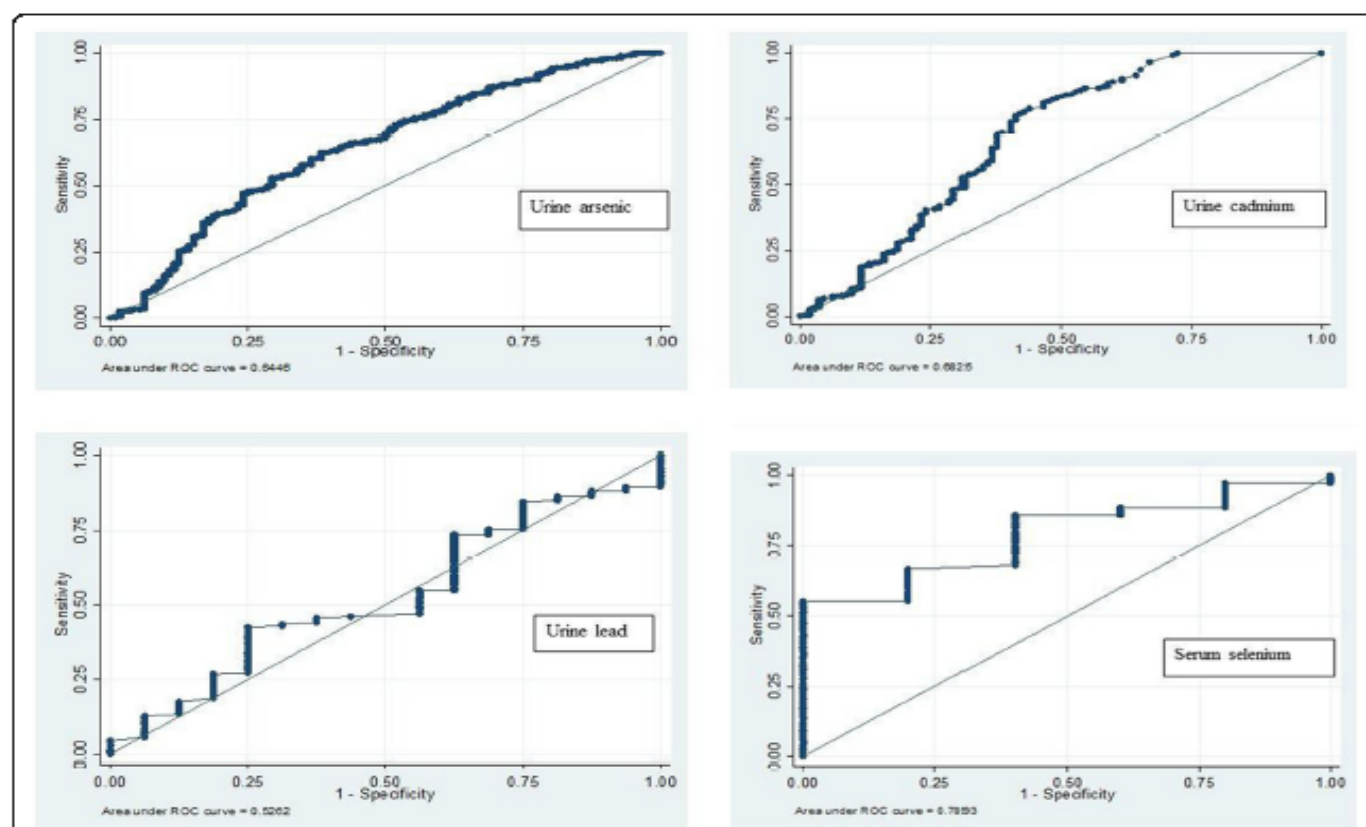


Figure 3 ROC curves generated with urine arsenic, cadmium and lead and serum selenium concentrations.

median = 0.007 $\mu\text{g/g}$, minimum = 0.001 $\mu\text{g/g}$, maximum = 0.347 $\mu\text{g/g}$) compared to controls ($n = 48$) from the endemic area (mean = 0.009 $\mu\text{g/g}$, median = 0.001 $\mu\text{g/g}$, minimum = 0.001 $\mu\text{g/g}$, maximum = 0.091 $\mu\text{g/g}$; $P < 0.05$).

Arsenic levels in hair were significantly higher in CKDu cases ($n = 80$; mean = 0.144 $\mu\text{g/g}$, median = 0.139 $\mu\text{g/g}$, minimum = 0.00 $\mu\text{g/g}$, maximum = 0.452 $\mu\text{g/g}$), compared to controls ($n = 48$) from the endemic area (mean = 0.125 $\mu\text{g/g}$, median = 0.103 $\mu\text{g/g}$, minimum = 0.006 $\mu\text{g/g}$, maximum = 1.214 $\mu\text{g/g}$; $P < 0.05$).

Arsenic, cadmium, lead and uranium in water (endemic area $n = 222$, non = endemic area, $n = 12$)

Levels of cadmium, lead and uranium in sources of drinking water (Figure 4) used by individuals with CKDu ($n = 99$) were within normal limits. Arsenic was borderline or raised in four samples (9.9 $\mu\text{g/l}$, 10.2 $\mu\text{g/l}$, 10.5 $\mu\text{g/l}$, 13.4 $\mu\text{g/l}$). Repeat analysis ($n = 32$) from the four sources showed normal arsenic levels.

In water samples from other sources, the arsenic concentration was 22.2 $\mu\text{g/l}$ and 9.8 $\mu\text{g/l}$ in two samples

taken from a canal and a reservoir, the cadmium concentration was 3.46 $\mu\text{g/l}$ in one sample from a reservoir and the lead concentration was 12.3 $\mu\text{g/l}$ in one sample from a reservoir in the endemic area. All other samples from wells, tube wells, irrigation canals, pipe-borne water, reservoirs and natural springs, including those taken from the non-endemic area, had normal arsenic, cadmium and lead levels.

Arsenic, cadmium and lead in food, tobacco leaves, pasture and weeds

Levels of cadmium in rice in both endemic and non-endemic areas were below the allowable limit (0.2 mg/kg; Figure 5). The maximum concentration of cadmium in vegetables in the endemic area and in the non-endemic areas was 0.322 mg/kg and 0.063 mg/kg respectively. Levels of cadmium in certain vegetables such as lotus root, and in tobacco, were high. Levels of cadmium in lotus and tobacco were higher in endemic than in non-endemic areas (lotus: mean = 0.413 mg/kg versus 0.023 mg/kg, median = 0.066 mg/kg versus 0.023 mg/kg,

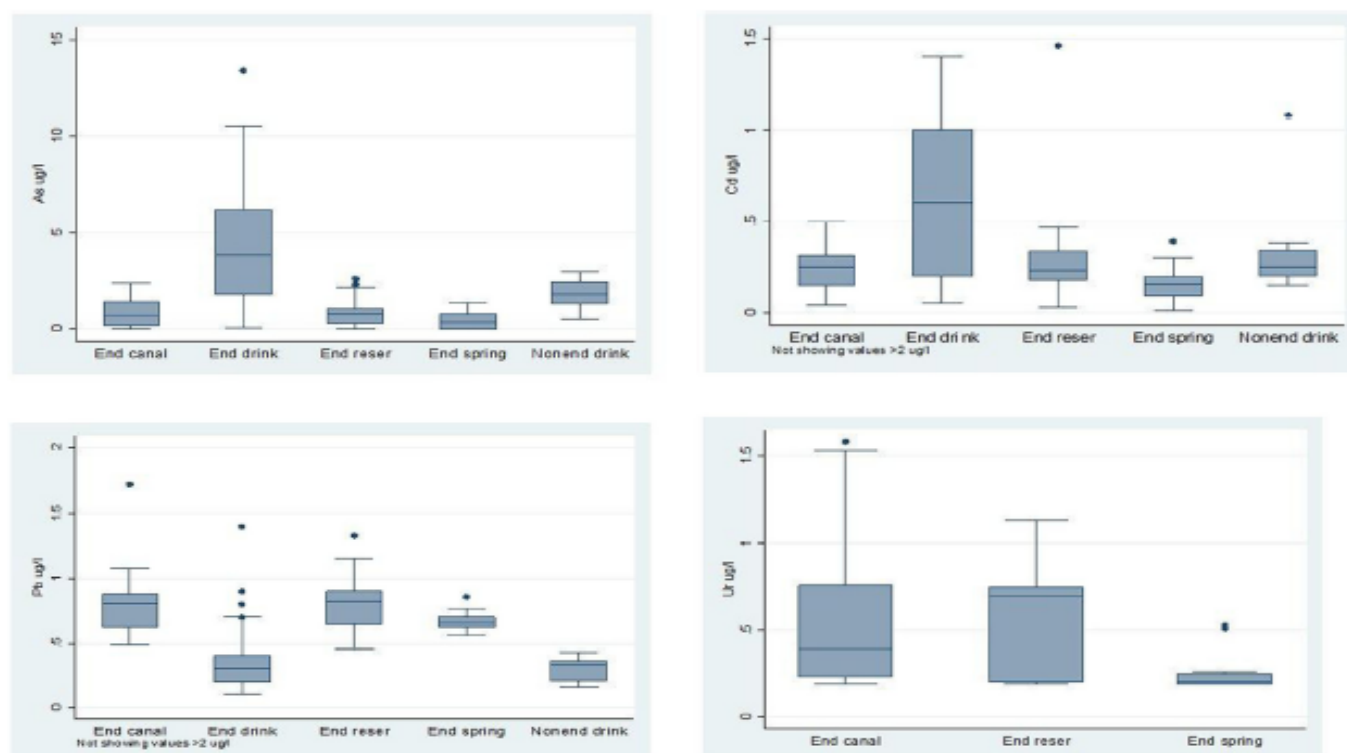


Figure 4 Concentration of arsenic, cadmium, lead and uranium in water^a in the endemic area ($n = 222$) and non-endemic area ($n = 12$). End canal = endemic area canal; End drink = endemic area drinking water; End reser = endemic area reservoir; End spring = endemic area spring; nonend drink = non-endemic area drinking water. Horizontal lines within the boxes represent the median values. The ends of the solid lines extending on either side of the boxes represent the minimum and the maximum. The dark dots are outliers; defined as being more than 1.5 interquartile ranges away from the box. The interquartile range is the distance between the upper part of the box and the lower part of the box.
^a Reference limits: arsenic <10 $\mu\text{g/l}$, cadmium <3 $\mu\text{g/l}$, lead <10 $\mu\text{g/l}$, uranium <2 $\mu\text{g/l}$ [21].

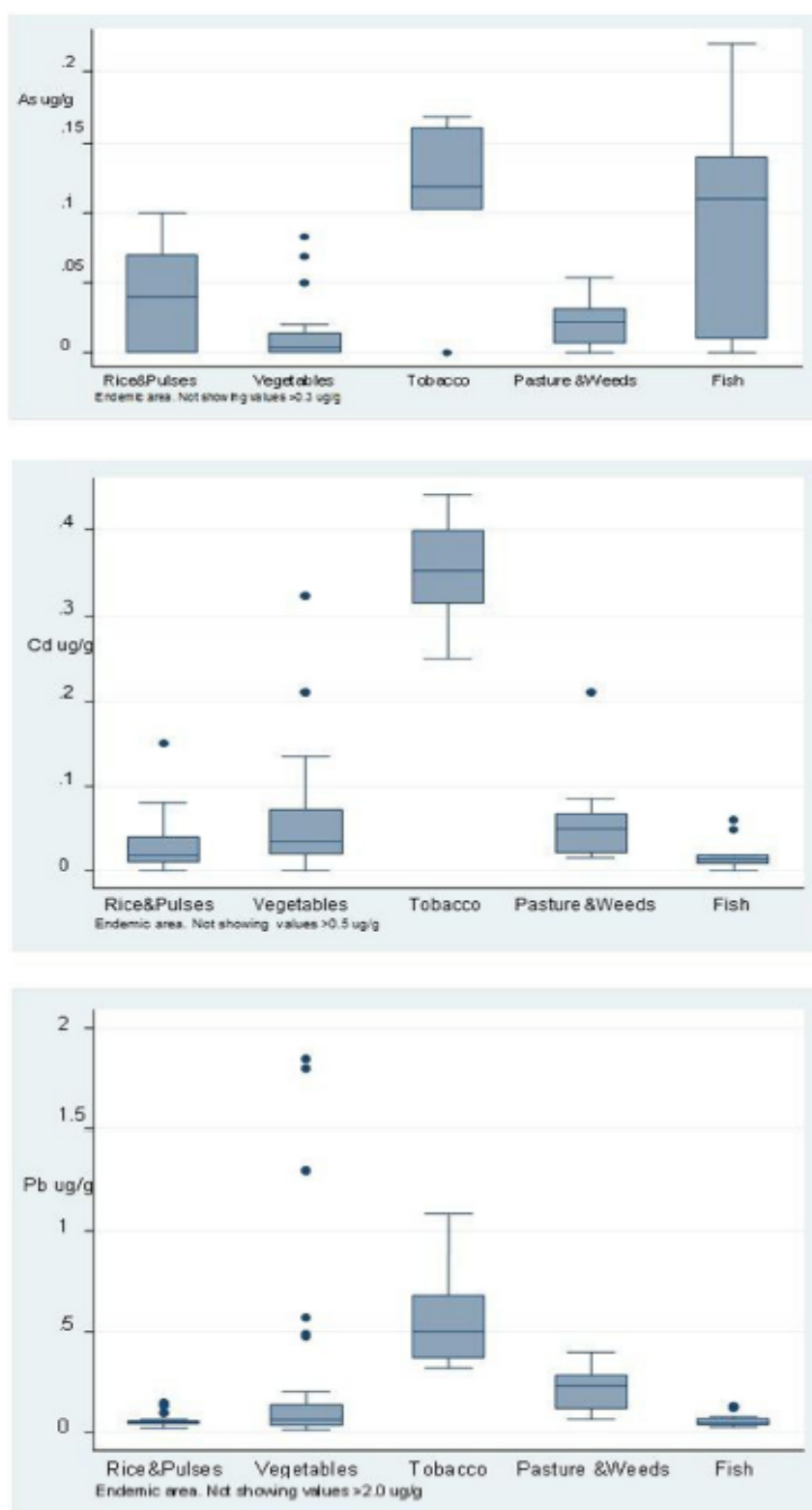


Figure 5 (See legend on next page.)

(See figure on previous page.)

Figure 5 Content of arsenic, cadmium and lead in food, tobacco leaves, pasture and weeds from the endemic area. Horizontal lines within the boxes represent the median values. The ends of the solid lines extending on either side of the boxes represent the minimum and the maximum. The dark dots are outliers; defined as being more than 1.5 interquartile ranges away from the box. The interquartile range is the distance between the upper part of the box and the lower part of the box. (The cadmium and lead content in certain food items exceeded the maximum stipulated reference value^a). ^a The maximum levels of cadmium permitted by the Codex Alimentarius for vegetables is 0.2 mg/kg [22,23] and by the Commission of the European Communities is 0.05 mg/kg [24]. The maximum concentration of cadmium stipulated for certain types of fish by the Commission of the European Communities is 0.05 mg/kg [24]. The maximum concentration of lead stipulated for vegetables by the Commission of the European communities is 0.10 mg/kg [24].

maximum = 1.50 mg/kg versus 0.03 mg/kg; tobacco: mean = 0.351 mg/kg versus 0.316 mg/kg, median = 0.351 mg/kg versus 0.316 mg/kg, maximum = 0.44 mg/kg versus 0.351 mg/kg in endemic versus non-endemic areas respectively).

Arsenic, cadmium and lead in soil and agrochemicals in the endemic and non-endemic areas

The level of cadmium in surface soil in the endemic area ($n = 94$, excluding samples from reservoirs), was 1.16 $\mu\text{g/g}$ compared to 0.49 $\mu\text{g/g}$ in the non-endemic area ($n = 45$, excluding samples from reservoirs) (Additional file 2).

Pesticide residues in urine

Pesticide residues were detected in the urine from individuals with CKDu ($n = 57$). The frequency of detection of 2,4-D, 3,5,6-trichloropyridinol, *p*-nitrophenol, 1-naphthol, 2-naphthol, glyphosate, AMPA was 33%, 70%, 58%, 100%, 100%, 65% and 28% respectively). Isopropoxyphenol, 2,4,5-trichlorophenol and pentachlorophenol were below detection limits. The proportions of CKDu cases with pesticide levels above reference values are shown in Table 4.

Discussion

The prevalence of CKDu found in this study (females 16.9%, males 12.9%) was higher than that reported previously (2% to 3%) [20]. Although the prevalence in females was higher, more severe stages of CKDu were seen more often in males. The reason for this discrepancy is not clear. Factors such as low iron stores in females in lower

socioeconomic groups may have an influence on the excretion of heavy metals and oxidative stress on the kidney. This would make the kidneys more vulnerable to CKDu, resulting in a higher prevalence in females. On the other hand, male sex has been reported to be a risk factor for progression to end-stage renal disease [27], and this may partly explain the occurrence of more severe stages of CKDu in men.

Previous studies have reported a family history of chronic kidney disease, ayurvedic treatment, and history of snake bite as significant predictors for CKDu [10,12,13]. In the present study, older age, being female and being a chena cultivation farmer increased the risk of CKDu. Family history was positive in one-fifth of those with CKDu, and a history of snake bite was one of the exclusion criteria. Long-term use of herbal medicines or analgesics was reported in only a very small percentage of those with CKDu. Fanconi syndrome and other hereditary kidney diseases have not been reported in communities in this region.

Previous studies have reported divergent information on the role of cadmium in the causation of CKDu [14,15,19,20]. In the present study, individuals with CKDu excreted significantly higher levels of cadmium compared to those in the control group, in both the endemic and non-endemic areas. Controls in the endemic area compared to those in the non-endemic area also had significantly higher urinary excretion of cadmium. The sensitivity and specificity for urine cadmium were 80% and 53.6% respectively (AUC = 0.682, cut-off value

Table 4 Pesticide residues in urine of CKDu cases ($n = 57$)

Parent compound	Biomarker	Reference limit ($\mu\text{g/l}$)	CKDu cases ($\mu\text{g/l}$), (minimum, maximum)	CKDu cases above reference limit (%)
2,4-D	2,4-D	<0.3	0.5, 0.62	3.5
Pentachlorophenol	Pentachlorophenol	<2	0.3, 2.2	1.7
Chlorpyrifos	3,5,6-trichloropyridinol	<11.3	0.5, 34.7	10.5
Parathion	<i>p</i> -nitrophenol	<25	0.5, 8.88	0
Carbaryl naphthalene	1-naphthol	<19.7	0.5, 45.1	10.5
Naphthalene	2-naphthol	<17.1	0.94, 47.88	10.5
Glyphosate	Glyphosate	<2	0.075, 3.36	3.5
Glyphosate	AMPA	<0.5	0.075, 2.65	14

$\geq 0.23 \mu\text{g/g}$). There was a dose–effect relationship between the concentration of cadmium in urine and the stage of CKDu. A significantly higher cadmium concentration was also seen in the nails of those with CKDu compared to controls from the endemic area. Cadmium is a known nephrotoxin and urinary excretion of cadmium is considered to be a reliable indicator of cumulative long-term exposure to cadmium [6]. The mean urine concentration of cadmium in CKDu cases was above the levels demonstrated in recent studies to cause oxidative stress and decreased glomerular filtration rate and creatinine clearance [28–33]. The results of this study indicate that cadmium exposure is a risk factor for CKDu.

The mean urine concentration of arsenic in CKDu cases was also above levels known to cause oxidative injury to the kidney [33]. In CKDu cases and controls from the endemic area, concentrations of arsenic in urine and in fingernails were higher than those reported in people living in low-exposure environments [34,35]. Urine is a major pathway for excretion of arsenic from the human body, so urine levels reflect exposure. In some studies, markers of oxidative stress have been demonstrated at urine arsenic concentrations as low as $3.95 \mu\text{g/g}$ [36]. The level of total arsenic in urine is associated with chronic kidney disease in a dose–response relationship, especially when the level is greater than $20.74 \mu\text{g/g}$ [36]. These findings support the contention that chronic exposure to low levels of cadmium may be a causative factor for CKDu in Sri Lanka. Co-exposure to cadmium and arsenic is known to produce additive effects on the kidney that are more pronounced than exposure to either metal alone [37,38].

Selenium has been shown to protect the kidney from oxidative stress [39]. A selenium concentration of 80–95 $\mu\text{g/l}$ is needed to maximise the activity of the antioxidant enzyme glutathione peroxidase and selenoproteins in plasma [40,41]. In this context, it is significant that serum selenium was below 80 $\mu\text{g/l}$ in 38% and below 90 $\mu\text{g/l}$ in 63% of individuals with CKDu. Low selenium levels may have been a contributory factor increasing the vulnerability of the kidneys to oxidative damage caused by heavy metals and metalloids.

The association of raised serum strontium levels with raised serum cadmium levels has been reported previously [42]. Strontium levels were not analysed in food or water. The most likely explanation is an alteration of strontium handling and excretion, owing to the effect of cadmium on renal tubular function.

Cadmium levels have previously been reported to be high in water sources in the domestic environment of people with CKDu, and 10–20 times the maximum stipulated level have been found in reservoirs in the endemic area [15]. The results of this study did not show

this to be the case. On the contrary, the cadmium content in all water samples analysed was within normal limits, except in one sample from a reservoir that had a borderline cadmium level ($3.45 \mu\text{g/l}$).

Drinking water is a major pathway for entry of inorganic arsenic into the human body. The arsenic content in 99% of water samples was below the WHO reference value of $10 \mu\text{g/l}$ [21]. However, it has recently been suggested that the concentration of arsenic in drinking water should be no more than $5 \mu\text{g/l}$ [43].

CKDu occurs in areas where groundwater is the main source of drinking water. Groundwater in this region is known to have a high content of fluoride and calcium. People living in the region for generations have used groundwater for drinking without ill effects. However, hardness of water, the high fluoride content, poor access to drinking water and inadequate intake of water in a warm climate may influence the body burden and/or the excretion of heavy metals and oxidative damage to the kidneys caused by heavy metals.

The maximum level of cadmium for vegetables permitted by the Codex Alimentarius is 0.2 mg/kg [22,23] and the level permitted by the Commission of the European Communities is 0.05 mg/kg [24]. The maximum levels in certain vegetables grown in the endemic area exceeded these safety levels. The maximum concentration of cadmium in fish ($0.06 \mu\text{g/g}$) also exceeded the European maximum limit of 0.05 mg/kg stipulated for certain types of fish [24]. The maximum level of lead in vegetables permitted by the Commission of the European Communities is 0.10 mg/kg [24]. The maximum level of lead in vegetables in the endemic area (0.476 mg/kg) exceeded this cut-off value. Levels of cadmium and lead in vegetables and cadmium in freshwater fish from the endemic area are above the maximum levels stipulated by certain Food Safety Authorities [22–24,44].

A provisional tolerable weekly intake (PTWI) for cadmium of $7 \mu\text{g/kg}$ body weight was established by the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) [45]. In 2011, the JECFA revised the PTWI for cadmium to $5.8 \mu\text{g/kg}$ body weight [46]. More recently, the PTWI for cadmium has been lowered to $2.52 \mu\text{g}$ cadmium/kg body weight, in order to ensure a high level of protection of all consumers, including exposed and vulnerable subgroups of the population [44]. Since the cadmium content of certain food items in the endemic area is above stipulated levels, the total weekly intake of cadmium in people living in the endemic area could exceed these safe limits, with detrimental effects on the kidneys, particularly in vulnerable people and those with predisposing factors.

Reported mean dietary exposure to inorganic arsenic in the United States of America (USA) and various

European and Asian countries ranges from 0.1 to 3.0 µg/kg body weight per day [45]. Recently, the PTWI for arsenic (0.015 mg/kg body weight per week) was withdrawn and environmental authorities are in the process of collecting more data for exposure assessment [46]. The current recommendation is that every effort should be made to keep concentrations of arsenic as low as reasonably possible. The PTWI for lead is set at 0.025 mg/kg body weight per week [45].

Previous studies have reported high levels of cadmium in fertilizer (mean 47 µg/g) [15]. The maximum cadmium, lead and arsenic concentrations in phosphate fertilizer from the endemic area in the present study were 30.8 µg/g, 823.4 µg/g and 0.19 µg/g respectively. The maximum acceptable levels for cadmium, lead and arsenic, in phosphate fertilizer product, at 1% of the nutrient level, are 4 µg/g, 20 µg/g and 2 µg/g, respectively [47].

The mean concentration of cadmium in soil from the endemic area was 0.4 µg/g. Surveys of agricultural soils in the USA and Sweden have reported lower soil cadmium levels (0.265 mg/kg and 0.23 mg/kg respectively) [48,49]. The concentration of cadmium, arsenic and lead in soil, and their impact on body burden and excretion, is known to be influenced by many environmental factors such as the pH of soil, buffering capacity, content of organic matter and water quality, among others [50-52]. Cadmium accumulation by plants, for example, is influenced by the reactive soil cadmium content and pH. It is decreased by high cation exchange capacity of the soil and increased by higher soil temperature [49-52]. The hardness and high content of fluoride in water in the endemic area may also influence the dynamics of cadmium in soil, absorption by plants [17] and excretion from the kidney.

Certain pesticide residues were above reference levels in 31.6% of CKDu cases. Residues are demonstrative of the extent of the environmental distribution of pesticides and certain pesticides are known to be nephrotoxic [4,5,53]. Simultaneous exposure of people to heavy metals and nephrotoxic pesticides may be a contributory factor in the pathogenesis and progression of CKDu.

Compared to previous studies conducted on CKDu, the present study has several strengths: (i) use of a consistent case definition for CKDu; (ii) analysis of a range of biological samples from individuals with CKDu; (iii) comparison of control groups within and outside the endemic area; and (iv) use of sensitive analytical techniques. Studies conducted hitherto to determine the prevalence and aetiology of CKDu [10,12,13,16,18,20] have relied on dipstick urinalysis to identify kidney disease. The present study is also the first in which heavy metals, metalloids and other elements in environmental and biological samples and pesticide residues in urine have been analysed.

There are several limitations in the study. Other kidney disease such as HIV nephropathy could fulfil the case-definition criteria used for CKDu. As HIV is not prevalent in Sri Lanka, it was not excluded through blood tests. The presence of glomerulonephritis was not excluded by biopsy but was based on past medical records and diagnosis cards. The sensitivity and specificity of the case definition relative to biopsy-proven CKDu is also not known. Stage 1 CKDu is defined by persistent microalbuminuria and may overestimate the prevalence of CKDu. The case definition required albuminuria. As a result, people with CKDu who have a low eGFR and no albuminuria were excluded from the study. In addition, the CKD-EPI equation used to estimate eGFR [25] has not been validated in people from South Asia. It is not known whether the albuminuria of CKDu responds to treatment for high blood pressure. If it does, an individual could then be excluded based on their ACR, despite having the disease.

CKDu has been reported in other populations as well [54-57]. Lessons learnt from other countries demonstrate that sound public health policies to ensure access to safe drinking water; regulatory control to ensure appropriate use of agrochemicals including fertilizer; hazardous waste remediation; regulatory control to prevent pollution of the environment from discarded batteries containing heavy metals; tobacco control; and reduction of air pollution can reduce exposure to heavy metals [58,59]. Based on the findings of this study, the Government and the Ministry of Health of Sri Lanka have already initiated multisectoral collaborative action with the Ministries of Agriculture, Irrigation, Scientific Affairs and Social Services, to mitigate the exposure of people to environmental nephrotoxic substances. Steps are being taken to strengthen the water supply scheme in the endemic area as well as the regulations related to procurement and distribution of fertilizers and pesticides. Further studies are ongoing to investigate the contributory role of infections in the pathogenesis of CKDu.

Conclusions

The results of this cross-sectional study indicate that multiple agents may play a role in the pathogenesis of CKDu. Herbal medicines and indiscriminate use of analgesics are unlikely to be causative factors of CKDu. Results show chronic exposure of people in the endemic area to low levels of cadmium through the food chain and also to pesticides. They may also be exposed to lead and arsenic through the food chain. Urine concentrations of cadmium and arsenic in individuals with CKDu were at levels known to cause kidney damage. Significantly higher urinary excretion of cadmium in individuals with CKDu, and the dose-effect relationship between urine cadmium levels and CKDu stages, indicate that cadmium

is a risk factor for the pathogenesis of CKDu in Sri Lanka. Deficiency of selenium and genetic susceptibility seen in individuals with CKDu suggest that they may be predisposing factors for the development of CKDu when people are exposed to nephrotoxins.

Additional files

Additional file 1: Details of sample preparation and analytical techniques.

Additional file 2: Table S1. Urine concentration of metals (sodium, potassium, calcium, magnesium, copper, zinc and titanium) in CKDu cases. **Table S2.** Serum concentration of aluminium, chromium, selenium and strontium in CKDu cases. **Table S3.** Concentration of arsenic, cadmium and lead in surface soil and in phosphate fertilizer, pesticides and weedicides, in the endemic area compared with a non-endemic area. Samples of soil from vegetable plots from the endemic area were obtained from the vicinity of households with CKDu patients.

Abbreviations

ACR: Albumin-creatinine ratio; AMPA: Aminomethylphosphonic acid; AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; CKD-EPI: Chronic kidney disease epidemiology collaboration; CKDu: Chronic kidney disease of uncertain aetiology; CV: Coefficient of variation; eGFR: Estimated glomerular filtration rate; FAO: Food and agriculture organization of the United Nations; GC-MS: Gas chromatography-mass spectroscopy; HbA_{1c}: Glycosylated haemoglobin; ICP-MS: Inductively coupled plasma mass spectrometry; JECFA: Joint FAO/WHO expert committee on food additives; LC-MS: Liquid chromatography with tandem mass spectrometry; MS: Mass spectrometry; OR: Odds ratio; PRWL: Provisional tolerable weekly intake; ROC: Receiver operating characteristic; SD: Standard deviation; USA: United States of America; WHO: World Health Organization.

Competing interests

None of the National Research Project Team members have declared any relationship with companies that may have a financial interest in the information contained in the manuscript.

Authors' contributions

SM led the development of the research proposal. She co-chaired the international advisory board and directed the execution and the technical aspects of the research project including analysis of results and drafting and finalization of the paper on behalf of the World Health Organization. FM was responsible for the implementation of the project at the country level and contributed to the paper. NJ and PM co-chaired the national CKDu research project committee on behalf of the Ministry of Health and contributed to the paper. All authors read and approved the final manuscript.

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Mission Report, 6-8th June 2011**Chronic Kidney Disease of Uncertain Aetiology (CKDu), Sri Lanka****Dr Shanthi Mendis, World Health Organization, Geneva, Switzerland****Background**

Chronic kidney disease has emerged as an important public health problem in some parts of Sri Lanka. Diabetes and hypertension contribute to this chronic kidney disease burden. However, a significant proportion of cases of chronic kidney disease that occur in the North Central and Uva Provinces are caused by a hitherto undetermined cause (Chronic Kidney Disease of Uncertain aetiology - CKDu). In order to address this public health issue, the Ministry of Health Sri Lanka in collaboration with the World Health Organization initiated a comprehensive National Research programme on CKDu in 2008/2009. Up to now this programme has been funded by the World Health Organization and the National Science Foundation of Sri Lanka.

Results of the National Research Programme

Results from Phase 1 of this research programme reveal, that in the North Central and Uva Provinces, a minimum of 15% of people in the age group 15-70 years are affected by CKDu. Men over the age of 40 years, who are engaged in farming for more than 10 years, are at higher risk of developing this disease. In addition, exposure to agrochemicals also increases the risk of developing CKDu. The majority of men and women suffering from this disease excrete raised levels of arsenic and/or cadmium in the urine. This indicates consumption of arsenic and cadmium in either water or food. Studies done so far on (drinking) water samples from Anuradhapura, Polonnaruwa and Badulla show that cadmium and lead levels are within normal limits. Few water samples, (3 out of 118 tested), showed slightly high arsenic levels and are been reanalyzed. Within the next 6 months data will be available on the cadmium and arsenic content in samples of a) human tissue, b) water from tanks and tube wells c) food items and d) soil and fertilizer collected from the North Central Province and control areas.

Conclusions

Exposure to a combination of factors that are toxic to the kidney (rather than one single factor) seems to cause this kidney disease. Toxic factors identified up to now include, nephrotoxic agrochemicals, arsenic and cadmium. Genetic factors and other known risk

factors of kidney disease appear to increase the individual susceptibility to this triple threat. Several other predisposing factors that may contribute to the development of this disease are under investigation. The social and economic impact of CKDu on impoverished households is grave.

Recommendations

Based on the above findings and the progressive nature of this serious disease for which there is no cure, the following interim measures are recommended:

1. Develop a regulatory framework to improve the quality control of imported fertilizer particularly with regard to nephrotoxic agents such as cadmium and arsenic.
2. Implement measures to reduce the exposure of farmers to the harmful health effects of agrochemicals through i) health education ii) compulsory provision of safety clothing , gloves and masks at the point of sale of agrochemicals and iii) control of the sale of agrochemicals which are known to be nephrotoxic e.g. propanil, chlopyrifos and others
3. Disseminate health education messages to people living in these areas e.g. to thoroughly wash vegetables and rice before cooking, to boil these food items in excess water and to discard the excess water once the food is cooked.
4. Increase the financial assistance provided to farmer families affected by CKDu to prevent them from getting more impoverished.
5. Provide more funds to expand and fast -track this National Research Programme of major public health importance.

It is imperative that the above steps are taken as soon as possible. Delaying action will cause further accumulation of toxic agents in the environment and result in cumulative damage to the health of the people living in these areas.

Mission Report, 5 -7 October 2011

Chronic Kidney Disease of Uncertain aetiology (CKDu), Sri Lanka

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Further to the report of June 2011 (attached annex A), during the last four months additional progress has been made in research on chronic kidney disease of uncertain aetiology (CKDu), in North Central and Uva Provinces in Sri Lanka within the framework of the National Research Programme.

As highlighted in annex A, long-term exposure to a combination of factors that are toxic to the kidney is causing kidney damage in people residing in North Central and Uva Provinces. Nephrotoxic agrochemicals, arsenic and cadmium as well as genetic factors and other known risk factors of kidney disease appear to increase the individual susceptibility to CKDu.

Analysis of water

As was outlined in annex A, arsenic and cadmium were analyzed in 118 water samples. 99 of these samples were taken from drinking water sources of people with features of CKDu. In 3 of these samples, arsenic levels were raised above WHO standard levels. Repeat analysis of new samples from the same sources did not show raised arsenic values. 118 Samples that were analyzed were obtained from 22 GN divisions in Anuradhapura, Polonnaruwa and Badulla Districts. 12 water samples taken from drinking water sources from Hambantota were also analyzed and were normal. These findings indicate that drinking water is unlikely to be the source of the Arsenic and Cadmium exposure that is causing CKDu. However it must be noted that as there is no central supply of water, and people are using water from a variety of different sources (Lakes, shallow wells, deep wells, springs outside the study area, tube wells, rain water and canals). Thus the findings of these analyses cannot be generalized to assume that arsenic and cadmium levels in water from all these sources are normal.

Agrochemicals

Analysis of 32 samples of agrochemicals showed that 10% were contaminated with arsenic and 20% were contaminated with lead.

Socioeconomic impact

The study to investigate the socioeconomic impact of CKDu was commenced. Preliminary findings from 200 patients interviewed indicate that in the advanced stages of the disease patients are too ill to continue in gainful employment.

Due to frequent shortage of medicines and laboratory tests in the public sector they are compelled to purchase private health services out-of-pocket. The government allowance currently provided to CKDu patients is inadequate.

Randomized controlled trial

The randomized controlled trial has been commenced to test the efficacy of an angiotensin converting enzyme inhibitor for slowing down/reversing the progression of CKDu. About 200 people who fulfill the diagnostic criteria of CKDu have been recruited to the study, up to now.

Recommendations

Cumulative nature of heavy metal exposure and progressive natural history of CKDu for which there is no known cure, demand urgent action to improve safe use and quality control of agrochemicals and quality control of fertilizer.

As advised by the Honourable Minister of Health, a multisectoral strategic plan need to be developed jointly with relevant ministries with short, medium and long-term measures by the end of 2011 and implemented as early as possible in 2012 to minimize the growing public health risks to the population.

1. Currently, the registrar of pesticides issues licenses to import pesticides if importers submit documents from any analytical laboratory certifying the efficacy of ingredients. A regulatory framework is needed to ensure that pesticides imported to the country are tested for toxic impurities (e.g. arsenic) in accredited laboratories selected by the Government.

Nephrotoxic agrochemicals such as propanil and chlopyrifos are heavily utilized by farmers. As they are already exposed to other renal toxins in the environment, more stringent measures need to be implemented to reduce harmful health effects of agrochemicals through i) health education ii) compulsory provision of safety clothing , gloves and masks at the point of sale of agrochemicals. Trained technical

assistants can perform these tasks at pesticide outlets. In addition, the legal support and capacity of the national entities for quality control of pesticides and fertilizer need to be strengthened.

2. Strategies need to be included in the plan to address the absence of quality control and regulations related to toxic impurities in fertilizer (e.g. cadmium, arsenic and others). They need to be developed and implemented by relevant officials of the Ministry of Agriculture particularly in the context of fertilizer subsidies. In the long-term alternative approaches to substitute or complement chemical fertilizer use need to be investigated.
3. Increase the financial assistance provided to farmer families affected by CKDu to prevent them from getting more impoverished due to their health care needs. In this regard if Rs. 1000 is given only to CKDu patients in Grade 3 and Grade 4, the cost per month for a population of 100,000 adults above the age of 30 years, would be two million rupees a month approximately. If the results of the ongoing RCT study demonstrate that progression of the disease can be slowed or prevented with drug treatment it would be essential to improve access to the relevant medicines for those in Grade 1 and Grade 2 so that larger numbers will not progress into Grade 3 and Grade 4.
4. The available scientific data of the national research project need to be published in the peer reviewed literature, at the latest by early next year so that the scientific basis of the strategic plan is documented and the impact of its implementation could be monitored and evaluated in the interest of accountability.

It is essential that the above steps are taken as soon as possible. Delaying action will cause further accumulation of toxic agents in the environment and result in cumulative damage to the health of the people living in these areas and with time also affects younger age groups. In the long-term there will also be severe social and economic consequences that will negatively impact the ongoing developmental and poverty alleviation efforts of this region.

Progress Report 13 Feb 2012

Chronic Kidney Disease of Uncertain Aetiology (CKDu) Sri Lanka

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Further to the previous reports (June & October 2011), during the last three months additional progress has been made in research on chronic kidney disease of uncertain aetiology, in North Central and Uva Provinces in Sri Lanka within the framework of the National Research Programme.

Overall, the results up to now indicate that long-term exposure to several risk factors toxic to the kidney in causing kidney damage in people residing in the North Central and Uva Provinces. While nephrotoxic agrochemicals and cadmium may have a direct toxic effect on the kidney, arsenic, lead, genetic factors, and others (calcium and magnesium) can have interactive effects which can indirectly damage the kidney.

In the urine analysis of 496 cases of CKDu, 56% had a urine cadmium excretion over 1 ug/g creatinine. Data from recent studies show that changes of early kidney damage occurs at cadmium excretion levels of even 0.6-1 ug/g creatinine. About 63% of CKDU patients had urine arsenic levels above 21 ug/g creatinine. Urine arsenic levels above 21ug/g creatinine have been shown to cause changes in kidney tissues that lead to chronic kidney disease. Approximately 88% of CKDu patients had urine cadmium >0.6 ug/g and/or urine arsenic >21 ug/g.

Arsenic was also analysed in hair and nails of people living in NCP including CKDu patients. In about 90% arsenic levels in hair were higher than those observed in developed countries (>0.02 ug/g). In about 94% arsenic levels in nails were higher than those observed in developed countries (>0.03 ug/g).

Our analysis did not find very high levels of cadmium exposure as reported in previous studies. The mean exposure for adults is at borderline of Recommended Total Weekly Intake (TWI) of 2.5 µg/kg body weight. Subgroups such as vegetarians, children, smokers and people living in highly contaminated areas may exceed the TWI. The data for arsenic are not available yet.

Among the patients with CKDu recruited for the clinical trial with a confirmed diagnosis of CKDu about 15% had a family history of CKDu in a sibling or parent. Although current knowledge has not evolved for direct public health application, there are several genes that confer tolerance to heavy metals which are responsible for both common and specific defence mechanisms which protect cells from arsenic and cadmium toxicity. Tolerance and detoxification mechanisms often involve extrusion of the toxic ions from the cell,

sequestration within internal organelles, chelation by metal-binding proteins, and reduction of uptake.

Water from 98 water sources used by patients with CKDu was analysed for hardness. 99% are hard to very hard. Hardness of water is known to affect heavy metal toxicity through antagonistic mechanisms and this may play a role in renal toxicity caused by cadmium and arsenic in the North Central Province.

The laboratory in Antwerp has experienced difficulties in digestion of soil and fertilizer samples to determine content of heavy metals accurately and reliably and results of these analyses are still not available.

Recommendations

1. Implement the recommendations in previous reports (June 2011 and October 2011)
2. Strengthening the institutional arrangements for the implementation, inter sectoral coordination, monitoring and evaluation of control of pesticides and fertilizer. Pollution of environment with agrochemicals cannot be controlled by a single agency. Control activities should include necessary amendments to existing legislation, regulation and processes and control measures should be monitored using sensitive indicators.
3. Increasing the public awareness of the adverse health effects of agrochemicals. The general public should be made aware of the actions taken to control agrochemicals and the importance of applying safety and control measures. Health education programmes should focus on high risk populations including farmers, vendors and also expanded to involve school children and the public at large.
4. Strengthen water purification schemes in the North Central Region: Some studies have shown a weak inverse relationship between water hardness and cardiovascular disease up to a level of 170 mg calcium carbonate per litre of water. The World Health Organization has reviewed the evidence and concluded the data were inadequate to allow for a recommendation for a level of hardness. Recommendations have been made for the maximum and minimum levels of calcium and magnesium in drinking water, and total hardness.
5. As there are 66 ayurvedhic prescriptions that contain Aristolochia. Aristolochia increase awareness of Ayurvedhic Practitioners and the public of renal toxicity of Aristolochia species.

Mission Report, 25 - 28 June 2012

Chronic Kidney Disease of Uncertain Aetiology (CKDu), Sri Lanka

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Further to the mission reports of June 2011 and October 2011 (attached annexes A and B respectively), steady progress has been made in research activities related to Chronic Kidney Disease of uncertain aetiology (CKDu) in the North Central and Uva Provinces in Sri Lanka within the framework of the National Research Programme.

The main conclusions based on the analysis and syntheses of the data obtained from studies conducted up to now are:

- The overall prevalence of CKDu in Anuradhapura, Polonnaruwa and Badulla Districts in people aged 15-70 years is 15%.
- There is evidence of long-term exposure of people in these districts to low levels of cadmium.
- There is also evidence of chronic exposure to low levels of arsenic.
- In susceptible individuals, co-exposure to low levels of cadmium and arsenic is giving rise to more pronounced renal damage than exposure to each element alone.
- The heavy metal content of the soil indicate that exposure is through the food chain. Water is not the source of exposure to heavy metals.
- Contamination of the soil appears to be mainly from fertilizer and also from agrochemicals.
- Exposure due to air pollution has not been investigated so far.

At a meeting of the Scientific Committee, convened by the Ministry of Health on the 25th of June 2012, the above conclusions and results on which they were based were presented and discussed. A press briefing followed.

The next day, 26th of June 2012, a meeting to share the results and conclusions was also held at Polonnaruwa, attended by the Hon. Minister of Health, Maithripala Sirisena. Government officials from administrative and health sectors from Provincial and District

levels attended the meeting including Grama Sevaka Niladaris responsible for Grama Sevaka Divisions in which the study was conducted.

On the 27th of June 2012, the Hon. Senior Minister of Scientific Affairs, Professor Tissa Vitharana and the officials of the National Science Foundation were given a briefing on the current status of the study and results and conclusions to-date.

On the 28th of June 2012, a high level meeting was convened by the Hon. Minister of Health to disseminate the results of the study to other relevant Ministries and discuss appropriate action. Hon. Ministers from Ministries of Agriculture, Scientific Affairs and Social Services attended the meeting together with respective Secretaries, Additional Secretaries and Directors of relevant divisions. The recommendations proposed for their consideration and action are listed below.

Recommendations

1. Since the determinants of CKDu lie outside the health sector, set up a high-level inter-ministerial committee chaired by the Hon. Minister of Health to actively engage Ministries of Agriculture, Water Supply, Irrigation and Social Services to implement multisectoral policy remedial actions proposed.
2. Scale-up water purification schemes and provide water to households in the endemic area for drinking and cooking purposes.
3. Strengthen the regulatory framework to improve quality control of imported agrochemicals, particularly with regard to nephrotoxic agents such as cadmium and arsenic i.e. amendments to existing legislation, capacity strengthening for implementation and monitoring.
4. Implement and monitor comprehensive public health measures to reduce the exposure of farmers to harmful health effects of agrochemicals through:
 - I. education on the appropriate use of fertilizer,
 - II. compulsory provision of safety clothing, gloves and masks at the point of sale of agrochemicals,
 - III. control of the sale of agrochemicals which are known to be nephrotoxic e.g. propanil, chlopyrifos and others,

- IV. education on cooking practices i.e. avoid the use of water from irrigation canals for cooking and drinking, discard water after boiling rice, reduce intake of lotus particularly in families with a history of kidney disease,
 - V. education on the importance of adequate fluid intake and nonsmoking.
5. Improve service provision for early detection of CKDu, hypertension and diabetes and appropriate treatment (avoiding nephrotoxic medications), including through close to client services.
 6. Increase the financial assistance provided to farmer families affected by CKDu to prevent them from getting more impoverished and malnourished. Inability to purchase food will cause iron, folate, antioxidant and trace metal deficiency which increase susceptibility to harmful effects of heavy metals on the kidney.
 7. Provide more funds to expand the National Research Programme on CKDu.
 8. Increase awareness among ayurvedic practitioners of the nephrotoxic effects of *Aristolochia indica* (sapsanda) and recommend not using it.
 9. In the long term, regulate as necessary and facilitate research to; promote the use of alternative fertilizers, reduce heavy metals in soil or make them less available, develop rice strains which require less fertilizer/resistant to pests, reduce pollution of the environment including air pollution.

A scientific paper on the synthesis of available results and a technical report will be prepared by October 2012. A joint Ministry of Health and WHO Press Statement was drafted to be released on the 30th of June 2012 (Annexure C). Further work is ongoing to investigate other causative factors of CKDu including pesticides and infections and treatment to prevent progression of CKDu.

**Joint Press Statement of the Ministry of Health and the World Health Organization –
June 2011**

For several years there has been mounting concern about the rising prevalence of chronic kidney disease of unknown aetiology in the North Central Region in Sri Lanka. Recognizing the gravity of the public health threat caused by CKDu, in 2009, the Ministry of Health, Sri Lanka with technical support from the WHO launched a comprehensive National Research Initiative to investigate the magnitude and aetiology of CKDu with a view to developing appropriate preventive strategies. The National Science Foundation and WHO provided funding for the research initiative.

The results of the studies while still ongoing indicate that about 15% of the people in the North Central Region are affected by CKDu. One of the causative factors of CKDu is co-exposure of susceptible individuals to a combination of nephrotoxic heavy metals (cadmium and arsenic) at low concentrations. Heavy metals enter the body mainly through the food chain and also through air pollution. Water is not the source of this exposure. However improving water quality as well as lowering the current levels of heavy metals in soil can help to reduce the body burden of heavy metals. Likewise, prevention of indiscriminate use of fertilizers and certain pesticides which have nephrotoxic properties can help to protect the kidney.

Today (29th June) the Honorable Minister of Health, Maithripala Sirisena, convened a high level meeting of the Ministries of Health, Agriculture, Social Sciences, Irrigation and Water Supplies and Science and Technology to discuss immediate and long term remedial measures to address the situation.



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A publication of the Epidemiology Unit

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Chronic Kidney Disease - A Global Public Health Problem

Chronic Kidney Disease is increasingly recognized as a worldwide public health problem for many reasons. It causes premature morbidity and mortality and lowers quality of life. Further, it places a large burden on patients, their families, society and the health system, a burden that is getting larger despite existing control efforts. A broad and coordinated public health approach is necessary to meet the burgeoning health, economic and societal challenges of chronic kidney disease, in addition to the clinical approaches to controlling it.

During the past three decades, the incidence and prevalence of chronic kidney disease (CKD) and end stage renal disease (ESRD), the form of CKD in which life can be sustained only by dialysis or transplantation, have risen progressively. In the US, 9.6% of adults are estimated to have CKD. Studies from Europe, Australia and Asia also confirm high prevalence of CKD. As a result, physicians, researchers and public health officials across the world now put more effort to study in detail the antecedents and outcomes of CKD, determine risk factors for its development and progression, and develop strategies for its detection, evaluation and treatment.

The explosion in the number of people with CKD has enormous economic implications. As the treatment modalities are expensive, patients with ESRD consume a disproportionate share of health care resources. This is well reflected by the fact that the incidence of patients with ESRD being treated by renal replacement therapy is high in affluent countries. However, if the present trend continues, treatment of ever-increasing burden of ESRD cannot be afforded, even in the wealthiest of countries. The world's disease profile is changing, and

chronic diseases now account for the majority of global morbidity and mortality, rather than infectious diseases. This change is reflected in the type of disease causing chronic kidney disease and in their presentation and progression. Today, the major cause of CKD is diabetes as a result of the global pandemic of type 2 diabetes.

In United States, 44% of all incident patients with ESRD are diabetic, while glomerulonephritis, cystic kidney disease and hypertension have remained relatively steady as causes of ESRD over the past decade. In Australia, incidence of ESRD due to diabetes is 25%, and in the European Registry Data number of diabetes entering ESRD treatment programme is between 15%-33%, while the numbers entering due to glomerulonephritis are 7%-20%. Countries throughout Asia also have large percentages of incident ESRD patients due to diabetes: Hong Kong 38%, Pakistan 42%, Taiwan 35%, Philippines 25% and Japan 37%.

The rate of increase in the prevalence of diabetes is extraordinary and this will lead to a corresponding increase in the number of patients with CKD. The global projection by the International Diabetes Federation predicts that the number of diabetics in the world will rise from 189 million today to 224 million in the year 2025, an increase of 72%. By region, over the next quarter of a century, an increase of 88% in South America, 59% in North America, 18% in Europe, 98% in Africa, 97% in the Middle East and 91% in Asia has been predicted. The additional burden of progressive CKD due to the diabetes pandemic will constitute one of the greatest medical challenges of the 21st century. The clinical manifestations and course of CKD depend on the cause and type, severity, rate of

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progression and co-morbid conditions. Outcomes of CKD include not only progression to ESRD but also increased risk of cardiovascular disease (CVD). Patients with CKD are far more likely to die, principally from CVD, than to develop kidney failure. Approximately 30% of patients with diabetic nephropathy eventually progress to ESRD and the rest usually die from cardiovascular disease before reaching end stage.

Prevention of CKD

There is requisite knowledge to prevent or at least delay its onset, its progression, and the co-morbidities that accompany it. Translating these advances to simple and applicable public health measures must be adopted worldwide. Although, there is still much to learn about the impact of treatments and their optimal combinations, it is not too early to begin implementation.

A key will be the early identification of individuals who are at risk. However, unfortunately, CKD is commonly "under-diagnosed" and/or "under-treated", resulting in lost opportunities for prevention. Many patients with CKD continue to receive suboptimal care. The reasons for this suboptimal care are complex, but people at risk because of diabetes or hypertension are often unaware that CKD can be caused by these conditions. Further, most individuals with CKD are unaware that they have this disorder.

Current preventive care practices include maintaining stringent control of blood pressure to a target of 130/80 mm Hg, using angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) in both diabetic and non-diabetic nephropathies, maintaining careful glycaemic control in individuals with diabetes, and following a low-protein diet. Additional reports indicate that treating dyslipidaemia, losing weight, quitting smoking, and managing anaemia may also help to delay progression of early CKD.

The Way Forward

The issue of CKD extends beyond a clinical problem addressed only by health care providers to a major public health issue requiring multilevel efforts. There is a great challenge to communicate the magnitude of CKD problem to governments worldwide, in order to influence global and national health policy and decision makers. Initiatives should be undertaken to make the general population more aware of the seriousness of CKD, its risk factors, and opportunities for screening. People identified with CKD should be provided appropriate educational materials to explain the treatment regimens and the benefits of undertaking therapy. Access to high-quality care should be ensured.

Public health policies for CKD must be coordinated with existing policies for non-communicable diseases as it is common in people with other chronic diseases and multiplies the risk for adverse outcomes and costs. Currently few countries have policies for CKD and most are unaware of the high prevalence of CKD, its contribution to other diseases, or its economic burden. Prevention, early detection and intervention are the more cost effective strategies for CKD.

Governments should support programmes for screening and surveillance of CKD. These activities would document the

prevalence, incidence, outcomes, care and education of the public and health care providers. Some of the specific recommendations for screening and surveillance are briefed below.

Screening for CKD

Screening is an activity, whereby patients in a defined population who are not aware of CKD are tested to detect the disease and, if present, are subsequently treated to reduce the risk of progression of CKD and its complications. However, it is not known whether screening the general population would be cost-effective. Generally, targeted screening is recommended, where screening is conducted in subgroups of the population who would derive the most benefit from CKD detection.

Target groups should include patients with hypertension, diabetes and cardiovascular disease. Other groups might include families of patients with CKD, individuals with hyperlipidaemia, obesity, metabolic syndrome, smokers, patients treated with nephrotoxic drugs, patients with some chronic infectious diseases and cancers, and age > 60 years. In these groups, screening for CKD could be implemented using existing facilities for detection of other chronic diseases. Tests for CKD screening should include a urine test for proteinuria and a blood test for creatinine to estimate GFR. Verification of proteinuria would require two out of three positive tests. In the absence of specific recommendations, screening need not be more frequent than once per year.

Surveillance for CKD

Surveillance refers to an activity to provide key information on CKD, such as time, location, magnitude and severity, in order to guide implementation of medical and public health measures to control progression of CKD and its complications. It is recommended that all countries should have a surveillance programme for CKD Stages 4-5 (ESRD) and strive to include earlier stages. Surveillance for ESRD would enable countries to monitor the magnitude and the care of this high-risk, high-cost population. If possible, data on risk factors for development and progression of CKD can be included.

Conclusion

The burden of CKD, in terms of human suffering and economic costs, is exploding as we move through the early years of the 21st century, making it a major public health issue. We know how to prevent or delay the onset of CKD and to limit its progression. Unfortunately, the extent to which we have applied this knowledge, which can effectively reduce the burden of CKD, is disappointing. A comprehensive public health approach will be needed to effectively address this major health problem.

Sources:

Position Statement from Kidney Disease Improving Global Outcomes (KDIGO), United States Renal Data System (www.usrds.org), www.ANZDATA.org.au, www.cdc.gov/pcd/issues/2006/apr/05_0105.htm

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Research Programme for Chronic Kidney Disease of Unknown Aetiology in Sri Lanka

Chronic Kidney Disease (CKD) is often combined with poor health outcomes and high economic cost. As discussed in the previous issue, it is now emerging as a global health problem. Sri Lanka is no exception to this trend. The aetiology of CKD varies between countries, but diabetes and hypertension are usually the leading factors, followed by glomerular and vascular causes. However, for a significant proportion of CKD cases reported from some parts of Sri Lanka, especially in North Central, North Western, Uva and Eastern Provinces, aetiology of the disease remains a mystery (CKD of Unknown Aetiology - CKDu).

To resolve this public health issue, the Government of Sri Lanka in collaboration with the World Health Organization has initiated a multisectoral and multidisciplinary research effort built upon on existing information. This coordinated series of research activities is designed to generate conclusive evidence regarding the aetiology within a specified time period to make prevention an option.

National Coordination Mechanism for CKDu Research

To ensure smooth functioning of the research programme, it is of vital importance to outline the functions and responsibilities of different stakeholders. In order to achieve this, three committees have been constituted at different levels namely the National Steering Committee, Management Committee and Scientific Committee with clearly defined terms of reference. In addition to these committees, there is a panel of International Experts providing technical inputs for the conduct of research. They also help in ensuring quality and ethical standards of research together with peer reviewing of protocols, reports and publications. The Epi-

demiology Unit, Ministry of Health has been given the responsibility of overall coordination.

CKDu - Case Definition

Adoption of a consistent case definition of CKDu will facilitate collaboration of study groups and, sharing and adoption research findings more readily. It is also essential for following trends over time and for cross region comparison. The following case definition has been agreed upon by the Scientific Committee of the National Research Programme. Accordingly, it will be used in future studies on CKD:

A case of CKDu should satisfy all the criteria stated below:

1. No past history of or current treatment for diabetes mellitus or chronic and/or severe hypertension, snake bite, urological disease of known aetiology or glomerulonephritis
2. Normal HbA1C (< 6.5%)
3. BP < 160/100 mmHg untreated or < 140/90 on up to two antihypertensive agents

The staging (Grade 1-4) of CKD will be based on the classification system recommended by the National Kidney Disease Outcomes Quality Initiative but modified for logistic and financial reasons.

A circular has been issued by the Ministry of Health with regard to the definition of CKDu (Circular No. Epid/392/2008/25 dated February 10th, 2009).

CKDu Study Groups

The National Research Programme for CKDu consists of a series of coordinated studies, each of which will potentially contribute to elucidating key determinants of CKDu. However, due to limited resources it is not possible to carry out all the studies listed in the study protocol simultaneously. Hence, the studies were consid-

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ered in order of priority and five studies have been commenced. An update on these studies is given below:

Population Prevalence study

The main purpose of this cross-sectional study is to identify the prevalence of CKDu in selected areas of Sri Lanka. This study is currently being conducted in Anuradhapura, Polonnaruwa and Badulla Districts. A total of 6698 subjects aged between 15 to 70 years (both inclusive) from 22 GN divisions were found to be eligible for this study according to the selection criteria. Representativeness of the study population was assured by strictly adhering to the scientifically sound methodology including sampling procedure. At the beginning of the study, all the selected households were mapped using the global positioning system (GPS). The field assistants were able to interview 6132 subjects (92% of the eligible). Early morning urine samples for albumin creatinine ratio (ACR) were obtained from 4941 subjects (74% of eligible). Those who found to be having urine ACR of equal or more than 30 mg/g were subjected to anthropometric measures, blood pressure measurement and biochemical investigations (serum creatinine and glycosylated haemoglobin).

All the field activities related to this research component have been completed and now we are in the process of identifying subjects with chronic kidney disease of unknown aetiology (CKDu) according to the case definition agreed upon. By identifying the prevalence of CKDu in different areas, this study will help to get an estimate of the diseases burden in the country. Further, the 'cases' identified from this study will be used for a case control study planned for this year and the serum specimens of the subjects currently stored at -70°C at the Epidemiology Unit will be subjected to further biochemical analysis (levels of cadmium, aluminium, lead, fluoride etc).

Hospital Based CKD Registry

The objectives of this registry are to characterize CKD/CKDu populations; to estimate prevalence and incidence of CKD/CKDu based on hospital data; to enable geographic mapping of CKD patients; to help in identifying new areas for special renal studies and to support investigator-initiated research. It has been established in four hospitals in the North-Central Province namely TH Anuradhapura, DGH Polonnaruwa, BH Medirigiriya and DH Medawachchiya. At present the registry is having the details of 1997 patients. For each patient in the registry, the database includes information on basic socio-demographics, primary medical diagnosis that led to CKD and treatment details.

Environmental Study

Details of 606 CKDu patients identified from the hospital-based registry were shared with the Environmental Study Group by the Epidemiology Unit of the Ministry of Health. Fifty patients from this list were randomly selected and their houses were visited for sample collection. From each household, 15 - 20 different types of samples were collected (e.g. soil, water, rice, pulses, vegetables, tobacco, fish, milk etc). They were analysed for Cadmium, Lead and Iron using internationally accepted, standard pre-preparation and analysing methods. A total of 670 samples were collected from above households and the analysis was done at the Department of

Chemistry, University of Kelaniya. GPS coordinates of the selected households were obtained. Entire dermal, dental and other variations among the patients were recorded and other information such as food habits and water usage were collected.

Pilot Analytical Study (Post-mortem Study)

As the metal analysis is very expensive, this component of the research programme will be conducted initially as a pilot study. The postmortem study is expected to give the direction for future studies on which particular element/s will be focused. Postmortem specimens (kidney cortex, liver and bone) are currently being collected from the following: CKD patients who had dialysis and were residents of Colombo, CKD patients who had dialysis and were residents of North Central Province, healthy adults aged between 40 and 60 years killed in accidents and were residents of North Central Province and healthy adults aged between 40 and 60 years killed in accidents and were residents of Colombo.

The specimens collected will be subjected to trace metal analysis at an international reference laboratory located at the University of Antwerp, Belgium. The "Collaboration and Material Transfer Agreement" between the Ministry of Health and the reference laboratory in Belgium has been already signed. The collected specimens are currently stored at -70°C at the Epidemiology Unit.

Sociology Study

The Disaster Management Centre (DMC) and United Nations Development Programme (UNDP) have supported a sociology study on behavioural patterns of CKD patients. This study also analysed the patterns of water and food consumption, consumption of liquor, smoking and chewing betel, and agricultural practices. Addressing the social and mental wellbeing of CKD patients and their families, improving patients' capacity to seek treatment and looking for practical alternatives for safe agricultural practices were some of the recommendations highlighted in this study.

Fund Mobilization for the National Research Programme

The collaborative national research effort is expected to cost around USD 1 million. To raise the necessary funds, two donor forums were organized by the World Health Organization with the participation of national and international donor agencies. These forums were chaired by the Hon. Minister of Healthcare & Nutrition. As the Ministry of health deemed this issue as a public health priority, the WHO Country Office has managed to raise USD 75,000 by re-programming some of the funded activities. In addition, WHO - SEARO (South East Asia Region) has contributed USD 240,000 up to December 2009. A proposal had been submitted to the Department of National Planning of the General Treasury through the National Science Foundation, which has a mandate to carry out research and development for socio economic development of Sri Lanka for further funding. This effort was successful in securing USD 700,000 for research activities in 2010.

Compiled by Dr. N. Janakan (Epidemiology Unit), Dr. Lanka Jayasuriya Dissanayake (Country Office, WHO) and Sumudu Hewawasam (Field Programme Officer, CKD Research)

Chronic Kidney Disease of Unknown Origin (CKDu)

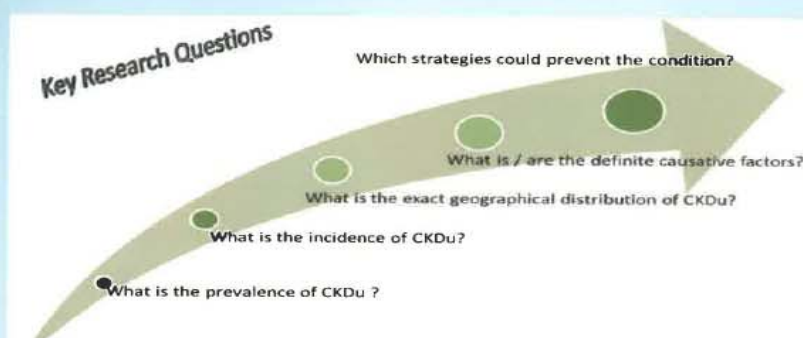
DECEMBER 2009

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National Research Programme for Chronic Kidney Disease of unknown origin (CKDu) in Sri Lanka

Chronic Kidney Disease (CKD) is an emerging health problem and is often combined with poor health outcomes and high economical cost on patient, family, community and health system. In recent years, a significant increase in CKD cases has been observed in some parts of the country especially in North Central, North Western, Uva and Eastern Provinces. For a significant proportion of CKD cases reported from these areas, aetiology of the disease remains a mystery. To resolve this public health issue, the Government of Sri Lanka requested the World Health Organization to coordinate a multisectoral, multidisciplinary research effort, which built upon on existing information. This coordinated series of research activities is designed to generate conclusive evidence within a specified time period to make prevention an option.



CKDu—Case Definition : Health Ministry Circular

A circular was issued by the Ministry of Health to all preventive and curative health institutions with regard to the definition of CKDu.

The aetiology of chronic kidney disease will be considered as "Uncertain or Unknown" only if all the criteria stated below are satisfied:

No past history of or current treatment for diabetes mellitus or chronic and/or severe hypertension, snake bite, urological disease of known aetiology or glomerulonephritis

Normal HbA1C (< 6.5%)

BP < 160/100 mm Hg untreated or < 140/90 mm Hg on up to two antihypertensive agents

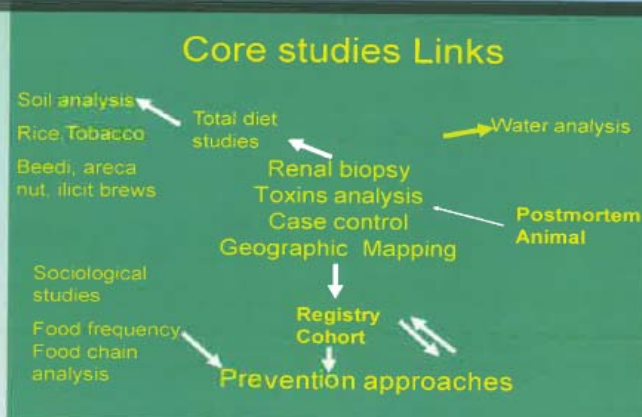
The staging of CKDu into Grades 1–4 will be based on the classification system recommended by the National Kidney Disease Outcomes Quality Initiative but modified for logistic and financial reasons.

CKDu Study Groups

The National Research Programme for CKDu consists of a series of coordinated studies, each of which will potentially contribute to elucidating key determinants of CKDu. However, due to limited resources it is not possible to carry out all the studies listed simultaneously. Hence, the studies were considered in order of priority as shown below and the first four studies have been commenced in the latter part of 2008.

- Systematic survey to identify low and high prevalence CKDu areas.
- Geographic mapping of cases and water sources and establish registry
- Preliminary studies to assist further prioritization; Pilot analytical study (post mortem), Retrospective study on histology, Pilot renal biopsy study (analytical and electron microscopy)
- Environmental studies: sub-sampling of all relevant local foods, water supplies, soil, etc for analyses of potential environmental toxins
- Comparison of high and low prevalence CKDu areas
- Case-control study
- Human renal biopsy analyses (electron microscopy and metal mapping)
- Human Post-mortem Studies
- Cohort study to commence with cases from the systematic survey
- Analytical studies on animal tissues

National CKDu Research Programme—Core Studies



National Coordination mechanism for CKDu

To ensure smooth functioning of the research programme, it is of vital importance to outline the functions and responsibilities of different stakeholders. In order to achieve this, three committees have been constituted at different levels namely the National Steering Committee, Management Committee and the Scientific Committee with clearly defined terms of reference. In addition to these committees, there is a panel of International Experts who has provided technical inputs into finalization of the research proposal. Further, this panel of experts will help to ensure quality and ethical standards of research together with peer reviewing of protocols, reports and publications.

National Steering Committee

This is chaired by the secretary of the Ministry of Healthcare & Nutrition and consists of Secretaries from different ministries inclusive of DM, Agriculture, Education, Higher education, Environment, Indigenous Medicine, Science & Technology, Public Administration & Home Affairs & Social Services & Social Welfare. In addition Chief Epidemiologist and WHO, UNDP Country Representative will also be present. The main aim of this committee is to advice on policy, technical, legal, scientific & administrative issues related to CKDu.

Management Committee

This is chaired by the DDG – PHS 1 and consists of the Regional Directors of Health Services of the affected areas, Heads of the Institutions under the different ministries like Central Environment Authority, Disaster Management Centre, National Science Foundation, Water supply & drainage Board, Registrar of pesticides. They are the implementers of the decisions taken at the National Steering committee and ensures multisectoral participation.

Scientific Committee

This is chaired by the chief epidemiologist and consists of group leaders of the different research groups including cohort study, Renal Biopsy study, Environmental study, Sociology & Diet study, Geographical mapping & Animal tissue study. This committee ensures execution of the studies at community level.

Population Prevalence study

The main purpose of this cross-sectional study is identifying the prevalence of chronic kidney disease of unknown origin (CKDu) in selected areas of Sri Lanka. This study is currently being conducted in Anuradhapura, Polonnaruwa and Badulla Districts.

A total of 6698 subjects aged between 15 to 70 years (both inclusive) from 22 GN divisions were found to be eligible for the study according to the selection criteria. Representativeness of this study population was assured by strictly adhering to the scientifically sound methodology including sampling procedure. At the beginning of the study, all selected households were mapped using the global positioning

system (GPS).

The field assistants were able to interview 6132 subjects (92% of the eligible). Early morning urine samples for albumin creatinine ratio (ACR) were collected from 4941 subjects (74% of eligible). Those who found to be having urine ACR of equal or more than 30 mg/g were subjected to anthropometric measures, blood pressure measurement and biochemical investigations (serum creatinine and glycosylated hemoglobin).

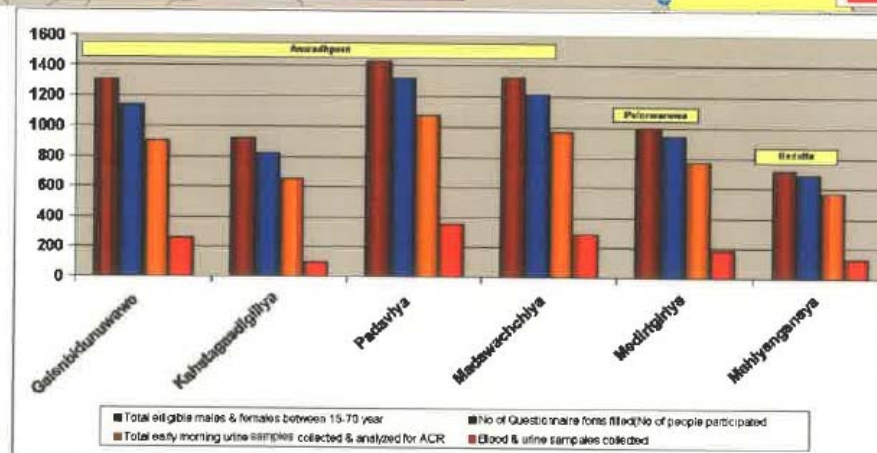
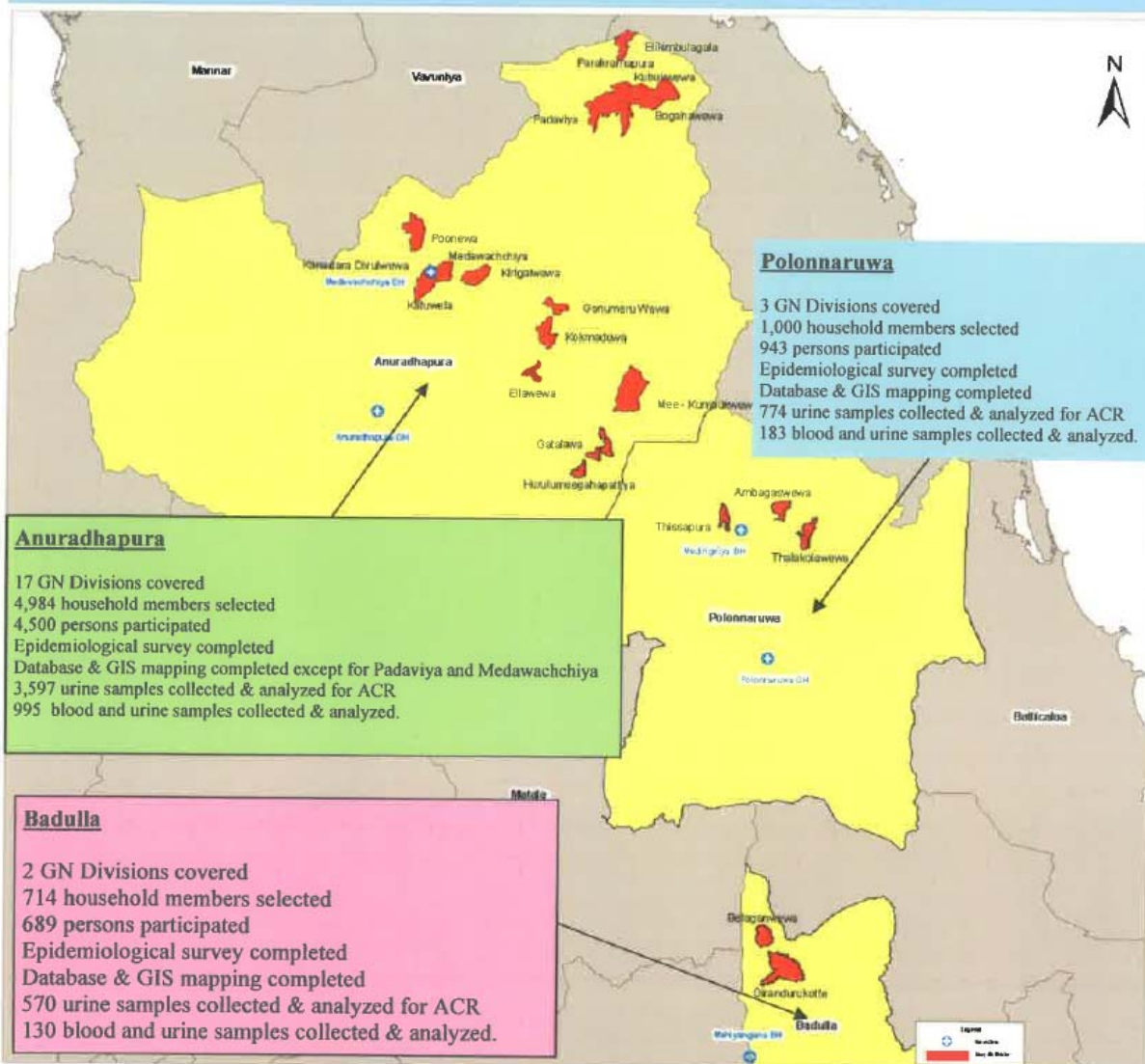
All the field activities related to this research component have been completed with the support of District & Divisional Secretaries, MOHs and Grama Niladaris, and now we are in the process of identifying subjects with chronic kidney disease of un-

known aetiology (CKDu) according to the case definition agreed upon.

By identifying the prevalence of CKDu in different areas, this study will help to get an estimate of the diseases burden in the country. Further, the 'cases' identified from this study will be used for a case control study planned for this year and the serum specimens of the subjects currently stored at -70°C at the Epidemiology Unit cold room complex will also be subjected to further biochemical analysis (levels of cadmium, aluminium, lead, fluoride etc).

The image shows a two-page questionnaire form. The left page is titled 'අනුරාධපුර ප්‍රදේශයේ CKDu ප්‍රචලය පරීක්ෂණය' (CKDu Prevalence Study in Anuradhapura District). It contains various sections for demographic data, medical history, and physical examination. The right page continues the form with more detailed questions and checkboxes. A yellow banner with the text 'Questionnaire form used for the survey' is placed diagonally across the center of the form.

Summary of CKD Prevalence Study - December 2009

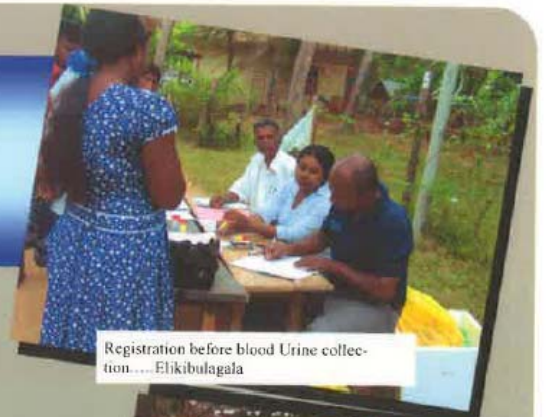


15 December 2009

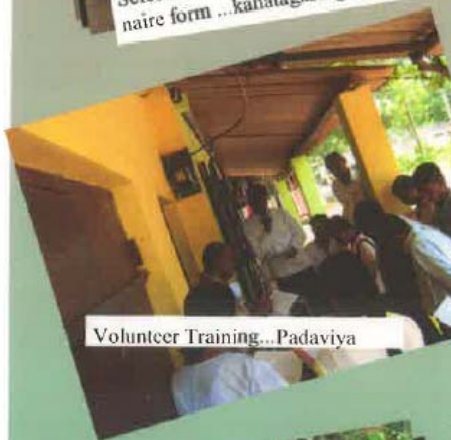
The Team at Work....



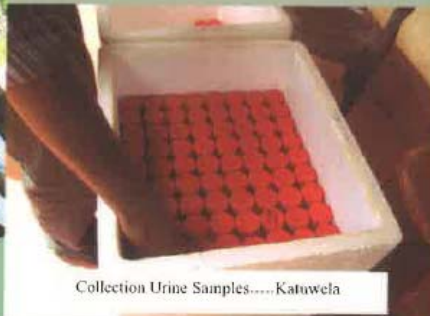
Selected field workers being trained on questionnaire formkahatagasdigiliya



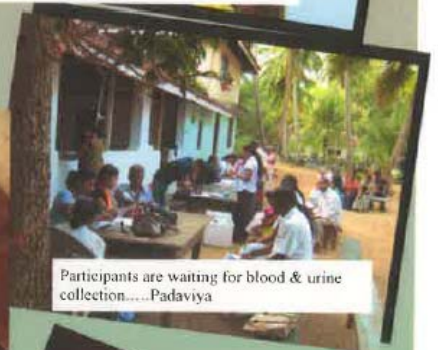
Registration before blood Urine collection.....Elakibulagala



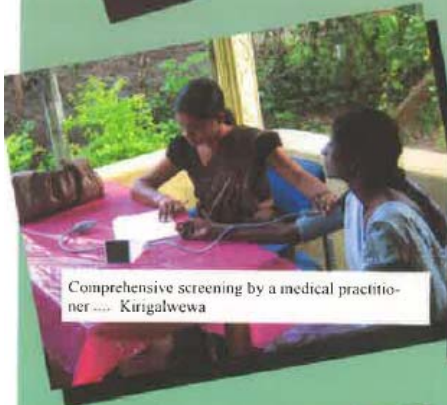
Volunteer Training...Padaviya



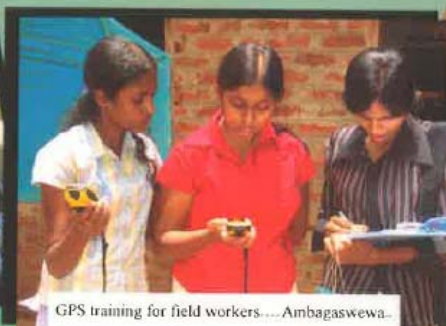
Collection Urine Samples.....Katuwela



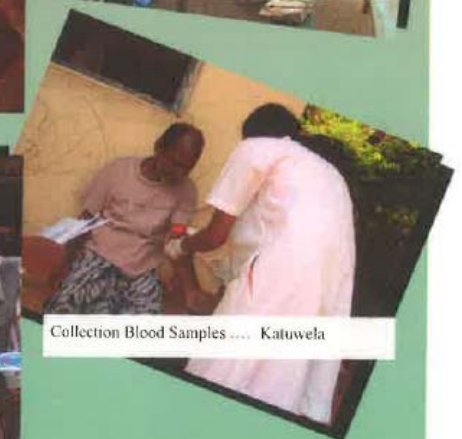
Participants are waiting for blood & urine collection.....Padaviya



Comprehensive screening by a medical practitioner Kirigalwewa



GPS training for field workers....Ambagaswewa...



Collection Blood Samples Katuwela



Summarizing days work.... Katuwela GN



Team at Gonumeruwewa GN....urine collection...



Visiting CKD patient households Ellawewa GN

Hospital Based CKD Registry

The main objectives of this registry are to characterize CKD/CKDu populations; to estimate prevalence and incidence of CKD/CKDu based on hospital data; to enable geographic mapping of CKD patients; to help in identifying new areas for special renal studies and to support investigator-initiated research.

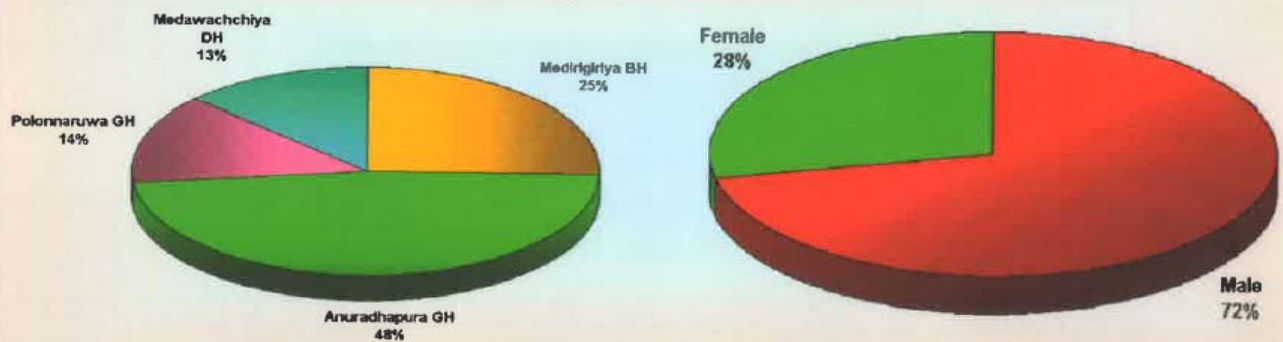
The hospital-based CKD registry has been established in four hospitals in

the North-Central Province namely TH Anuradhapura, DGH Polonnaruwa, BH Medirigiriya and DH Medawachchiya.

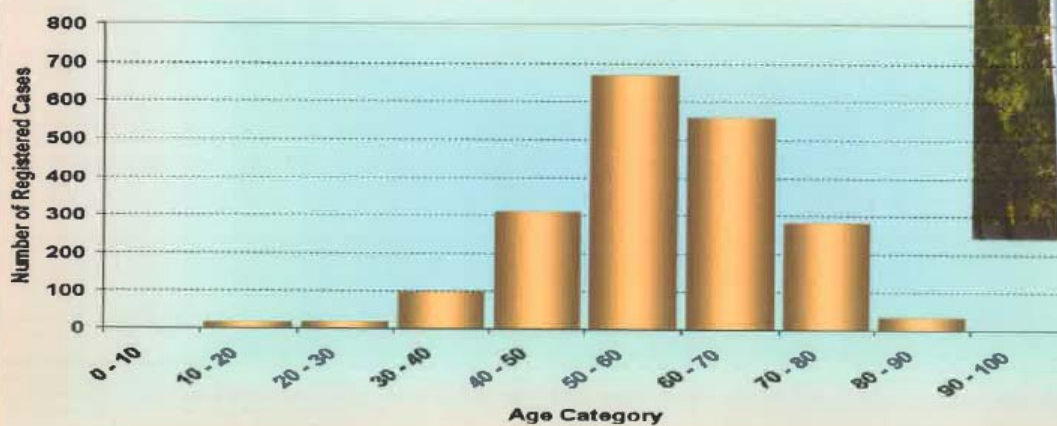
At present the registry is having the details of 1997 patients. For each patient in the registry, the database includes information on basic socio-demographics, primary medical diagnosis that led to CKD, treatment records and transplant information if available.

It is an ongoing activity and steps have been taken to expand this activity in a stepwise manner to other hospitals also (i.e. towards a national registry). The database will be linked with all renal centres in Sri Lanka. An annual report containing descriptive and analytic epidemiologic data on CKD patients will be published in future.

Cases registered in the hospital registry - 1,997 CKDu Cases—775(39%)



Age Breakdown of Registered CKD Cases



Environmental Study Group—Sample collection & analysis

Details of 606 CKDu patients identified from the hospital-based registry were shared with the Environmental Study Group by the Epidemiology Unit of the Ministry of Health. Fifty patients from this list were randomly selected and their houses were visited for sample collection. From each household, 15 -

20 different types of samples were collected. They were analysed for Cadmium (Cd), Lead (Pb) and Iron (Fe) using internationally accepted, standard pre-preparation and analysing methods. Samples were subjected to wet washing acid digestion prior to analyse by the flame and graphite furnace

Atomic Absorption Spectrophotometer. A total of 670 samples collected from above households and the analysis was done at the Department of Chemistry, University of Kelaniya.

Environmental Study

The samples collected consisted of following:

- * *Nelumbo nucifera* (Lotus)
- * Beetle
- * Sediments of reservoirs
- * Soils of agricultural lands
- * Soils of non agricultural lands
- * Irrigation water
- * Drinking well water
- * Agro-well water
- * Pipe borne water
- * Tube well water
- * Rice
- * Pulses - locally grown
- * Fish - Tilapia
- * Fish - Lula (Seasonal)
- * Pasture - onsite / from the farmers
- * Milk - cows and buffaloes
- * Milk - mothers
- * *Nelumbo nucifera* (Lotus)
- * Beetle
- * Tobacco
- * Leafy vegetable consumed in the region
- * *Lasia spinosa* (Kohila)
- * Urine
- * Weeds
- * Field products



GPS coordinates of the selected households were obtained. Entire dermal, dental and other variations among the patients were recorded and other information such as food habits and water usage were obtained.



Pilot Analytical Study (Post Mortem Study)

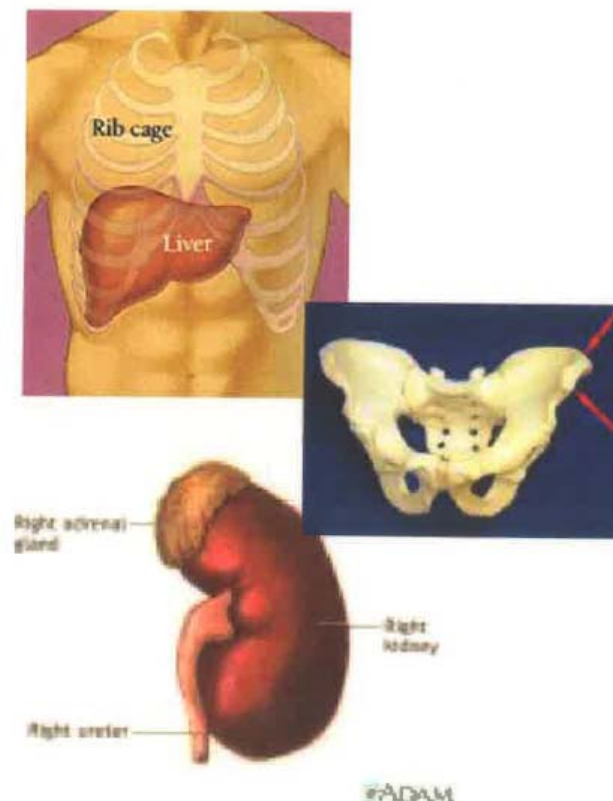
As the metal analysis is very expensive, this component of the research programme will be conducted initially as a pilot study. The postmortem study is expected to give the direction for future studies on which particular element/s will be focused.

Postmortem specimens (kidney cortex, liver and bone) are currently being collected from the following:

- * Six chronic kidney disease patients who had dialysis and were residents of Colombo
- * Six chronic kidney disease patients who had dialysis and were residents of North Central Province
- * Three apparently healthy adults aged between 40 and 60 years, killed in accidents and were residents of North Central Province
- * Three apparently healthy adults aged between 40 and 60 years, killed in accidents and were residents of Colombo

The specimens collected will be subjected to trace metal analysis at an international reference laboratory located at the University of Antwerp, Belgium. The "Collaboration and Material Transfer Agreement" between the Ministry of Health and the reference laboratory in Belgium has been already signed. The collected

specimens are currently stored at -70C at the Cold Room Complex, Epidemiology Unit.



Fund Mobilization — CKDu

The collaborative national research effort is expected to cost around USD 1 million. To raise the necessary funds, two donor forums were organized with the participation of national and international donor agencies. These forums were chaired by the Hon. Minister of Healthcare & Nutrition.

As the Ministry of health deemed this issue as a public health priority, the WHO Country Office has managed to raise USD 75,000 by re-programming some of the funded activities. In addition, WHO - SEARO (South East Asia Region) has contributed USD 240,000 up to December 2009.

WHO Country office has also supported the Ministry of Health to submit a proposal to Department of National Planning of the General Treasury, through the National Science Foundation, which has a mandate to carry out research and development for socio economic development of Sri Lanka. This effort was successful in securing USD 700,000 for research activities in 2010.

In 2005, 3.5 million USD (4.6%) of the annual health budget was spent on management of patients with renal disease

CKDu—What the papers say...



Way Forward

- * To analyse the results obtained from the population prevalence study and obtain prevalence rates for CKDu - January 2010.
- * To complete the pilot analytical studies - January 2010
- * Retrospective study - Review of Histopathology - January 2010
- * Pilot Renal Biopsy Study - Analytical & Electron Microscopy - January 2010
- * Comprehensive screening investigations to be extended to control group and to also include total diet study and socio-logical study
- * To complete analysis of priority & other studies - September 2010



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Epidemiology Unit
Ministry of Healthcare & Nutrition



Ministry of Health



Chronic Kidney Disease of Unknown Aetiology (CKDu)

June 2011

National Research Programme - CKDu

Chronic kidney disease is an emerging global health problem and Sri Lanka is no exception to this trend. The aetiology of CKD varies between countries, but diabetes and hypertension are usually the leading factors. However, for a significant proportion of CKD cases reported from certain parts of Sri Lanka, aetiology of the disease remains a mystery (CKD of Unknown Aetiology - CKDu).

To resolve this public health issue, the Ministry of Health in collaboration with the World Health Organization has initiated a multisectoral and multidisciplinary research effort built upon on existing information. This coordinated series of research activities is designed to elucidate key determinants of CKDu and ascertain feasible options for prevention.

Much work has been done with participation of many stakeholders including different ministries, academia, clinicians, public health specialists, civil society and other concerned parties.

Current Studies



Future Studies



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Due to limited resources it is not possible to carry out all the studies listed in the study protocol simultaneously.

As such the research activities were arranged according to priority. A series of future studies are currently being reviewed.

An update on the current and future studies is given in this newsletter.

Case definition based on the classification recommended by the National Kidney Disease Outcomes Quality Initiative was used for this study. .

Adoption of a consistent case definition of CKDu will facilitate collaboration of study groups and, sharing and adoption research findings more readily.

Population Prevalence Study

- Ethical approval obtained from Ethical Review Committee / Sri Lanka Medical Association
- Multi stage sampling: Random selection of 6 DS areas from 3 districts (Anuradhapura, Polonnaruwa & Badulla); Random selection of 22 GN divisions from these 6 DS areas; Complete household lists prepared for selected GN divisions; From each GN division, random selection of 100 households; All members aged 15 - 70 years (both inclusive) in the selected households recruited to the study (n = 6,698)
- Interviewing of participants & GPS Mapping: Subjects were interviewed by trained field assistants & GPS mapping of their residences done, Response rate was 92% (6,132/6,698)
- Biochemical investigation: Early morning urine samples collected for ACR, Response rate was 81% (4,941/6,132)
- Anthropometric measures & further biochemical investigations done for those with urine ACR ≥ 30 mg/g: height, weight & BP measured, samples collected - urine for repeat ACR & blood for serum creatinine & HbA1C, Response rate was 92% (1,308/1,416)
- Results of analysis (prevalence of CKD & CKDu with staging) are available
- Serum samples of 1308 subjects for whom the urine ACR ≥ 30 mg/g were stored in -70°C at the Medical Research Institute for further analysis, if necessary



Chronic Kidney Disease of Unknown Aetiology (CKDu)

Case Control Study Metal Analysis of Urine

- A sample of 94 CKDu cases in stage III & IV and 401 CKDu cases in stage I & II (as per the case definition of CKDu) identified from the population prevalence study
- Urine samples collected from these cases for ACR (repeat) & metal analysis. The results are available
- Urine metal analysis (cadmium, lead & arsenic) was done at Antwerp University, Belgium & the results are available
- Urine samples from controls (n = 132, M:F = 1:1) recruited from non-CKDu households in the study areas (22 GN divisions) sent to University of Antwerp, Belgium for metal analysis (awaiting results)

Case Control Study Analysis of Hair & Nail Samples for arsenic

- Hair & nail samples from 77 cases (stage I - 16, stage II - 19, stage III - 22 & Stage IV – 20) identified from the population prevalence study sent to University of Antwerp, Belgium for arsenic analysis (awaiting results)
- Hair & nail samples from controls (n = 50, M:F = 1:1) recruited from non-CKDu households in the study areas (22 GN divisions) sent to University of Antwerp, Belgium for arsenic analysis (awaiting results)



Chronic Kidney Disease of Unknown Aetiology (CKDu)

Environmental Study

Phase I

- Drinking water samples of 99 CKDu cases in stage III & IV (identified in the population prevalence study) sent to Belgium for metal analysis (cadmium, lead & arsenic). Results are available.
- Environmental samples (sediments of reservoirs, irrigation water, drinking well water, agro-well water, pipe borne water, tube well water, soils of agricultural & non-agricultural lands, locally grown pulses, onsite pasture, rice, maize, tamarind, beetle, tobacco, weeds, vegetables consumed in the region, lotus, kohila, field products, freshwater fish) from CKDu high prevalent areas sent to Antwerp University, Belgium for metal analysis (awaiting results). In addition, 10 rice samples from CKDu patients' residences also sent to Belgium (awaiting results)
- From Hambantota (control area), environmental samples (sediments of reservoirs, irrigation water, drinking well water, agro-well water, pipe borne water, tube well water, soils of agricultural & non-agricultural lands, locally grown pulses, onsite pasture, rice, beetle, tobacco, weeds, manioc, mushroom, leafy vegetables, lotus, kohila, field products, freshwater & sea fish) from CKDu high prevalent areas sent to Belgium for metal analysis (awaiting results)
- Completed GPS mapping of tube wells in 22 GN divisions selected for population prevalence study

Phase II

- Soil (from paddy field, vegetable plots & chena cultivation) & fertilizer/ pesticides samples collected from 22 GN divisions (a total of 88 soil & 22 fertilizer/ pesticides samples). Samples dispatched to Belgium for metal analysis
- Soil & fertilizer samples (n = 50) from control area (Hambantota) collected. Samples dispatched to Belgium for metal analysis
- A comprehensive list of pesticides used in study and control areas has been prepared.



Chronic Kidney Disease of Unknown Aetiology (CKDu)

Study on Nephrotoxic Herbal Remedies

- A group of investigators from the Bandaranayake Memorial Ayurvedic Research Institute are involved in this study.
- Expected outputs: List of aristolochic acid containing herbal remedies & their prescription pattern in Sri Lanka especially in CKDu high prevalent areas.

Aristolochic Acid Nephropathy (AAN) is a rapidly progressive renal interstitial fibrosis. Clinically, the initial presentation is silent and the renal failure is discovered by routine blood testing. There are reports of AAN cases due to use of herbal remedies.

In Sri Lanka, where use of herbal preparations is common, there is a risk of AAN due to ingestion of aristolochic acid containing remedies.

Postmortem Study

Analysis at International Reference Laboratory (University of Antwerp, Belgium)

Phase I (Pilot study)

- Material Transfer Agreement (MTA) signed with University of Antwerp, Belgium and the ethical approval was obtained from the SLMA Ethical Review Committee
- Postmortem specimens of 06 CKDu patients & 03 dead due to accidents from North Central Province, and 01 CKD patient (known aetiology) & 02 dead due to accidents from Western Province were sent to Belgium for metal analysis. The results are available.

Phase II

- Permission for extension of study obtained from SLMA Ethical Review Committee
- Postmortem specimens of 20 CKDu patients & 11 dead due to accident from NCP & Uva Provinces sent to Antwerp University, Belgium for metal analysis (awaiting results)
- Postmortem specimens included kidney, liver and bone tissues

Analysis at University of Peradeniya

- Postmortem specimens of 06 CKDu patients & 03 controls will be analyzed for aluminium, lead, cadmium, arsenic and fluoride
- Postmortem specimens include kidney and bone tissues & the study to be started shortly

Chronic Kidney Disease of Unknown Aetiology (CKDu)

Hospital-based Chronic Kidney Disease Registry

- Database has information on basic socio-demographics, lifestyle factors, environmental factors, health status, anthropometry & laboratory investigations for 1997 patients registered in selected hospitals (TH Anuradhapura, DGH Polonnaruwa, BH Medirigiriya & BH Medawachchiya)
- It will serve as a resource to the academic & clinical medicine communities
- Need to be expanded further to include newly diagnosed CKD patients and other hospitals in the region
- Computerization & linking of data to a central database to be done

Randomised Clinical Trial

- A double blind clinical trial to examine the renal effects of an Angiotensin Converting Enzyme Inhibitor (enalapril) in CKDu patients (Hypothesis: Enalapril would significantly reduce progression of renal disease in CKDu patients)
- Purpose of the study is to examine the renal effects of enalapril versus placebo in CKDu patients by comparing & evaluating the effect of enalapril to a placebo on: estimated GFR, albuminuria & change in stage of CKDu
- Ethical approval obtained from Ethical Review committee / Medical Research Institute. Sub-Committee on Clinical Trial, Drug Regulatory Authority has issued "no objection" letter for the trial

Socioeconomic & Productivity Impact Study

- Objective is to estimate the socio-economic impacts of CKDu & recommend mitigation measures (Estimation of costs of CKDu to the affected households & communities and the health system; Description of modes of coping adapted to mitigate adverse socio-economic impacts; Estimation of economic impact of CKDu on the GDP; and Evaluation of different mechanisms of social support & recommend the best options for implementation)
- Study to be started shortly (Sociological aspects have been studied to some extent)

Chronic Kidney Disease of Unknown Aetiology (CKDu)

Future Studies

Renal Biopsy Study

- Immunofluorescence & electron microscopy, and metal mapping of renal tissues will be done (Biopsies will be obtained from CKDu patients followed at TH Anuradhapura)

Study on Early Disease Markers

- Proposal to be finalized

Animal (Slaughter House) Study

- Histopathology study (metal analysis) of slaughterhouse samples will be done at a local University
- Metal analysis of randomly selected slaughterhouse samples will be done at University of Antwerp, Belgium

Cyanobacteria Study

- As per the decisions taken at the Scientific Committee meeting held on January 18, 2011, awaiting for a joint proposal from the study group

Ochratoxin, Polyaromatic Hydrocarbons (PAH) and aristolochic acid analysis

- Awaiting for more details on lab procedures and cost price from refer-

Chronic Kidney Disease of Unknown Aetiology (CKDu)



WHO Sri Lanka

::BIANNUAL NEWSLETTER OF THE WHO COUNTRY OFFICE FOR SRI LANKA::

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World Health Day 2009 :: Health Facilities in Emergencies

The first World Health Assembly, called for the creation of a "World Health Day" to mark the founding of the World Health Organization (WHO) in 1948. Since 1950, World Health Day has been customarily celebrated annually on the 7th of April and is considered an opportunity to focus on key public health issues of national and international importance. Every year a theme is selected which highlights a priority area of concern.

The theme for World Health Day 2009 is identified as "Health Facilities in Emergencies". This message is in parallel with the focus of the biennial World Disaster Reduction Campaign (2008-2009) which is "Hospitals Safe from Disasters: Reduce Risk, Protect Health Facilities, Save Lives." The slogan for World Health Day 2009 has been identified as "Save lives: Make hospitals safe in emergencies"

Safe health facilities are those that are accessible and function at maximum capacity immediately after a disaster event. Health facilities, large or small, urban or rural, are the focus of this work and are not just the work of the health sector and health professionals alone. They need to work together with other sectors and experts from other fields such as urban planners, architects, engineers to bring not just awareness, but more importantly action.

The goal of raising awareness in this issue is to effect changes that will ensure that health facilities and services are able to function in the aftermath of emergencies and disasters, protect the lives of patients, serve the affected population and keep health workers safe. This means:

Several activities were held in Sri Lanka by the World Health Organization Country Office (WCO) in collaboration with the Ministry of Healthcare and Nutrition to mark this event. Media seminar held on 3 April 2009 was well attended by media persons from both electronic and press media. A supplement was also published on the 7th April in leading national newspapers in English, Sinhalese and Tamil.

Ensuring the structural resilience of health structures with existing technologies;

Keeping the equipment and supplies of these health facilities intact should an emergency happen;

Improving the preparedness and risk reduction capacity of health workers; and ;

Involving communities in this effort



"National Conference on Hospital Safety in time of Disasters" was conducted on 7th April as the main event with the objective of creating awareness and enthusiasm among the different stakeholders. Professionals including health administrators, public health experts, health planners, trainers, service providers participated in the conference representing Central / Provincial / District Health authorities. Professionals such as urban planners, architects, engineers, academics made the participation more meaningful.

WHO South East Asia Regional Director's message on World Health Day was telecasted in both these, which grabbed audience attention. WHO Representative to Sri Lanka, Dr Firdosi Rustom Mehta addressed both highlighting the origin of the World Health Day and importance of the theme with special reference to Sri Lankan experiences. Hon. Nimal Siriipala De Silva, Minister of Healthcare and Nutrition made the key note speech in both highlighting the role of different stakeholders in bringing the changes in order to provide quality health services for people even during disasters and emergencies.

This World Health Day theme is appropriate and timely to generate more momentum that will help sustain and mainstream disaster risk reduction into health sector initiatives. WCO Sri Lanka will continue to work with all the partners and stakeholders to build and sustain efforts to ensure that health facilities can function during and in the aftermath of disasters.

Chronic Kidney Disease of Unknown Aetiology (CKDu)- Progress

The new form of CKDu which has emerged in several areas of Sri Lanka, is characterized by the slow progressive, asymptomatic development, with characteristic changes of kidney tissues (Tubulo Interstitial Nephritis), compatible with the effects of an environmental toxin.

Preliminary studies have investigated the prevalence, aetiology, clinical and histopathological features of this CKDu. Several possible aetiological determinants have been identified including Cadmium, Flouride, Aluminium, Pesticides, Snake Bite & Ayurvedic Medicine Ingestion.

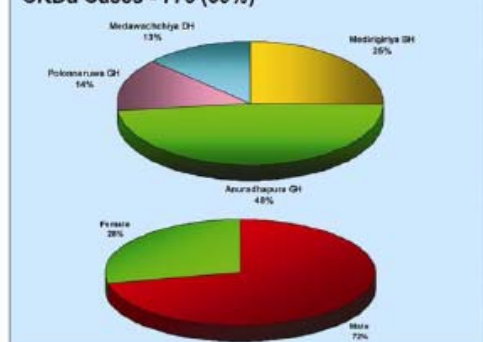
“The research proposal for investigation & evaluation of chronic kidney disease of uncertain aetiology in Sri Lanka” which was prepared by Co-Chairs of the International Steering Committee, Prof. Neil R.Poulter, Consultant Physician & Epidemiologist, International Centre for Circulatory Health (ICCH) , Imperial College, London & Dr. Shanti Mendis, Senior Adviser/Coordinator, Chronic Disease Prevention & Management , WHO Geneva – has been submitted to the Ministry of Healthcare and Nutrition (MoH) by the WHO Country Office(WCO) in June 2009.

A coordinated & integrated series of activities are proposed in this research proposal which is built upon currently available evidence, to determine the aetiology of CKDu, having first established its prevalence. The diagnosis of CKDu is now based on the modified classification system recommended by the National Kidney Disease Outcomes Quality Initiative. The parameters that are used, defines the CKDu into Grade 1-4.

The prevalence and environmental studies commenced since with systematic survey of randomly selected 2200 household in 12 Grama Niladhari(GN) divisions of the Anuradhapura, Polonnaruwa & Badulla districts. In order to monitor a significant change in CKDu throughout Sri Lanka a computerized database has been created with data obtained from hospital registries where renal clinics are conducted. Analysis of environmental samples from randomly selected 50 households with CKDu patients including water, soil, fertilizers etc begun and are being analyzed for 5 metals. Geographical mapping has completed for all cases of CKDu identified in the population. A pilot post mortem study will be conducted to analyze bone, liver & kidney biopsy samples from 18 individuals for metals. Pending studies including Retrospective study on histopathology, Analytical studies on Human & Animal tissues, Cohort Study to be conducted once successful resource mobilization is done.

These national research efforts are spearheaded by the National Steering Committee with input from the Scientific & Management Committees. International support is provided by the International Steering Committee.

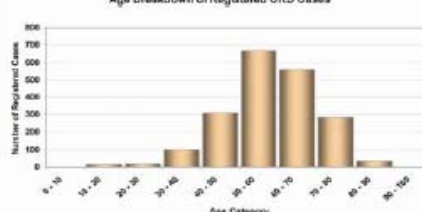
**Cases registered in the hospital registry - 1,997
CKDu Cases - 775 (39%)**



The complete research effort entails the following different research programmes:

- Case Control Study
- Cohort Study
- Renal Biopsy Study
- Environmental Study Group for Case Control Phase of the Study
- Environmental Study Group for Analysis of Water for Case Control Study
- Post Mortem Study
- Human Tissue (post mortem), Urine and Blood Analysis Study
- Chronic Kidney Disease Registry and GIS Mapping Study
- Analysis of Animal Tissues Study
- Nutrition and Sociology Study

Age Breakdown of Registered CKD Cases





**World Health
Organization**

COUNTRY OFFICE FOR **Sri Lanka**

Chronic Kidney Disease of Unknown Aetiology (CKDu); A New Threat to Health

Introduction

At the beginning of the 21st century, an apparently new form of chronic kidney disease of unknown aetiology (CKDu) had emerged in several areas of Sri Lanka.

The CKDu is not related to diabetes, hypertension, snake bite or any other known causes of traditional chronic kidney disease. The disease is characterized by a slow, progressive, asymptomatic development, frequently starting at a younger age group. There is a possible propensity for it to be more prevalent among men engaged in agriculture, typically around the age of 40-60 years.



History of CKDu in Sri Lanka

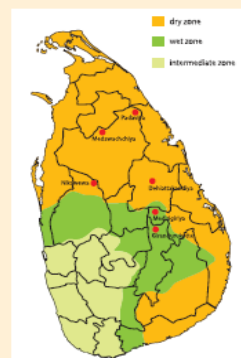
A range of studies of varying types have been carried out over the last 8 years with a view to elucidating the prevalence, nature & causes of CKDu in several parts of Sri Lanka. According to the data reported in the Annual Health Bulletin 2005, the hospital mortality rate for diseases of the genitourinary system has doubled during the period 1980 to 2005. Several studies have investigated the prevalence of this type of CKDu. However from the studies done so far over a period of 8 years, there has been no concrete evidence to support a particular environmental nephrotoxin.

Presence of high levels of fluoride, widespread use of agrochemicals such as pesticides and heavy metals (e.g. cadmium, lead, uranium) in soil and water sources could be postulated as contributing factors to the high prevalence of CKDu in certain areas.

As demonstrated in some studies, mycotoxins, use of herbal / ayurvedic medicines, smoking and history of snake bite are some other factors to be considered. A combination of two or more of the above factors, possibly a synergistic effect, could also be responsible

Geographical distribution of CKDu

The geographical distribution of CKDu appears to be biased towards the North Central Region (NCR) of the country in which North Central, part of North Western and part of Uva provinces are included. The populations at risk are scattered in the North Central Region with high prevalence observed at Medawachchiya, Padaviya, Dehiattakandiya, Girandurukotte, Medirigiriya and recently Nikawewa



Impact of CKDu

The total number of affected individuals is unknown, however speculations suggest that in excess of 6000 people are currently undergoing treatment for this condition.

In 2005, Anuradhapura Teaching Hospital alone recorded 742 live discharges and 140 deaths due to CKDu. Mortality due to genitourinary diseases was the leading cause of death in many districts, being the 11th leading cause of Mortality in the country. In 2005, about 350 million rupees (4.6% of the Annual Health Budget) was spent on the management of patients with Renal Diseases.



Initiation by Hon. Minister of Healthcare and Nutrition

A request was made to WHO headquarters in Geneva, in January 2008 by the Minister of Healthcare & Nutrition Hon. Nimal Siripala De Silva, to assist in elucidating the exact cause for the high prevalence of CKDu in the country. This was done as medical studies done so far have failed to establish a concrete link to any aetiological factor. In response to this request, WHO pledged to send a team to Sri Lanka to carry out a pragmatic & feasible research to elucidate a causative agent.



World Health Organization

COUNTRY OFFICE FOR **Sri Lanka**

Chronic Kidney Disease of Unknown Aetiology (CKDu); A New Threat to Health

CKDU research seminar

As an initial step towards achieving these objectives, the Epidemiology Unit of the Ministry of Healthcare and Nutrition in association with the World Health Organization organized a seminar on "Unusual Occurrence of Chronic Kidney Disease in Sri Lanka" on 7th - 8th May 2008 in Colombo. The main objective of this seminar was to review all available information, with a view to providing technical assistance for developing a research proposal to address prevention issues. A panel of International experts was in attendance in addition to all the local researchers and related stakeholders.

Development of the research proposal

A draft research proposal was prepared by the team of experts following this meeting. This research proposal provides a framework for program of research activities, the main arm of which is to identify the prevalence and main determinant(s) of chronic kidney disease. This coordinated series of activities is built upon evidence generated by a body of smaller research projects, but was designed to provide a more methodical approach and thereby generate more conclusive evidence regarding the aetiology of the problem. Once the aetiology is known, preventive strategies can be developed and implemented.

Feedback on the research proposal & stakeholder meeting



This draft research proposal was shared amongst the relevant stakeholders including the researchers, academics, consultants & local authorities for necessary feedback. A three day consultative meeting was held in Polonnaruwa on 3rd, 4th & 5th August 2008.

The complete research effort entails the following different research programmes

- Case Control study
- Cohort study
- Renal biopsy study (tissue and data collection)
- Environmental study group for case control phase of the study
- Environmental study group for analysis of water for case control study
- Post mortem study group (collection of organs and data)

- Human tissue (post mortem), urine and blood analysis study
- Chronic Kidney Disease registry and Geographical Mapping study
- Study group for analysis of animal tissues
- Nutrition and Sociology Study

Partners meeting on CKDU

A partners meeting was organized by the WHO Country Office (WCO) Sri Lanka in collaboration with the Ministry of Healthcare and Nutrition on 2nd October 2008. The main objective of this meeting was to highlight the importance of the issue of CKDu and request assistance from development partners to come forward to help in this emerging public health issue which is of great concern to the country. UNICEF, UNDP, USAID, JICA, AmeriCare and Oxfam GB were the developmental partner agencies who were present.



WHO SEARO provided USD 40,000 for initial activities. The total cost for the two year period for the research would be approx USD 1,000,000. WCO has re programmed funds for CKD activities amounting to USD 100,000 with SEARO pledging a further USD 100,000 together with the Embassy of Poland contributing USD 50,000 through SEARO.

Way forward

There is a need for a comprehensive public health effort to effectively address this problem of CKDu. This should be taken as a National Priority with joint responsibility resting on Health and Developmental Partners. Ground level preparatory work has already been done which includes recruitment of field programme officer, selection of households and data collection as well as the formulation of a hospital based disease registry.

In addition, Terms of References were developed for the National Steering Committee on CKDu with addition of high level members representing the multi-sectoral agencies involved in this effort. A Management Committee, Scientific Committee & an International Steering Committee was also formed to assist in the implementation of this national research effort into CKD of unknown origin.

Investigation and Evaluation of Chronic Kidney Disease of Uncertain Aetiology

CONTENT OF THE PRESENTATION

1. **Background**
2. **Study Components and research findings**
 - I. Prevalence and Causative Factors for CKDu in Sri Lanka
 - II. Socioeconomic and productivity impact of CKDu
 - III. Nephrotoxic herbal remedies used in Sri Lanka
 - IV. Randomized Clinical trial to examine the renal effects of an Angiotensin Converting enzyme Inhibitor (Enalapril) in adults with CKDu
3. **Recommendations**
4. **Future Studies**

Background



- Increase in a new form of CKD which is **NOT** attributed to DM, HT, GN or other known aetiologies observed
- Case load more in certain areas i.e. **regional clustering**
- **Insidious onset** which probably starts in second decade of life
- Slowly **progressive** and asymptomatic until very advanced
- High **economical cost** for patient, family & state

Global Situation



Source: Centre for Public Integrity, Washington DC

INVOLVEMENT OF WHO -2008

- Technical assistance requested by Minister of Health to WHO HQ
- For review of available data
- To initiate a coordinated, multisectoral research effort

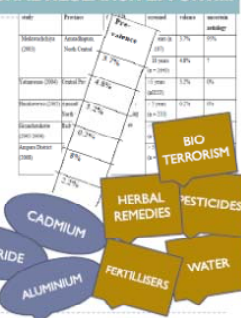
As this problem appears to be getting worse, I would appreciate if WHO can provide technical assistance from HQ to develop a properly designed research study to investigate this priority health issue as soon as possible.

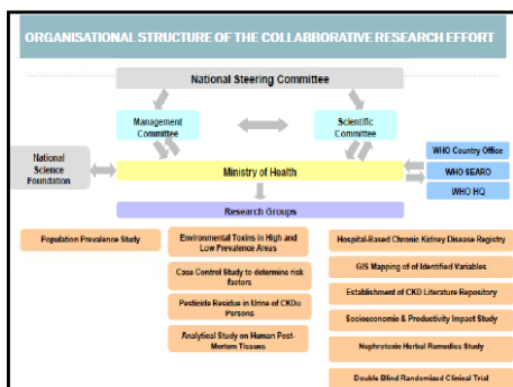


JUSTIFICATION FOR A NATIONAL RESEARCH EFFORT....

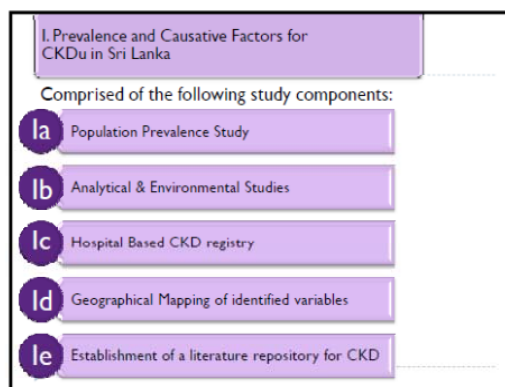
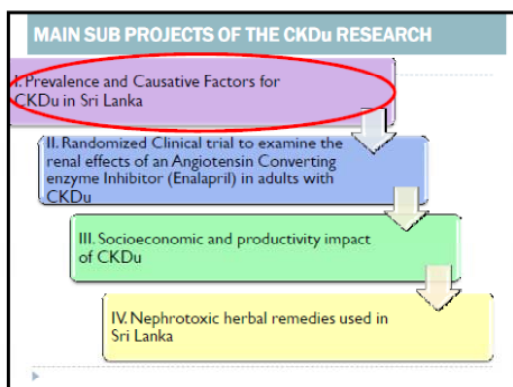
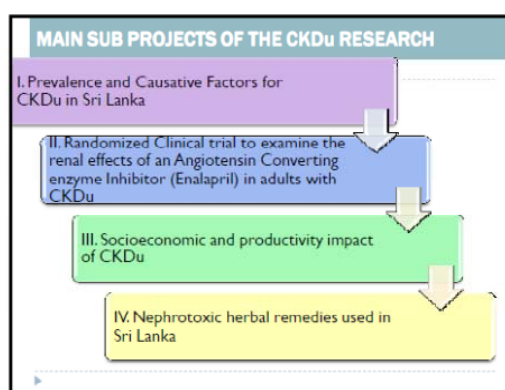
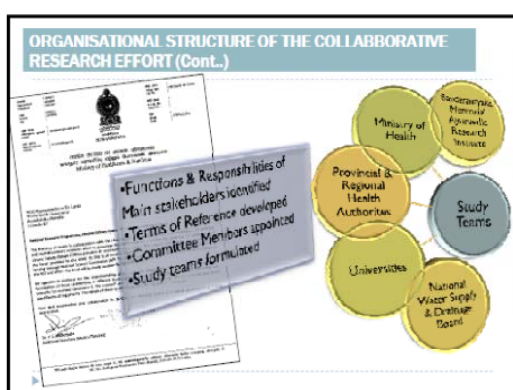
Multiple Prevalence Rates!
Multiple Causative Agents!

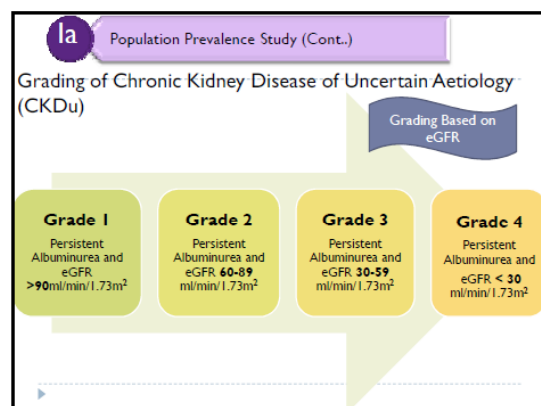
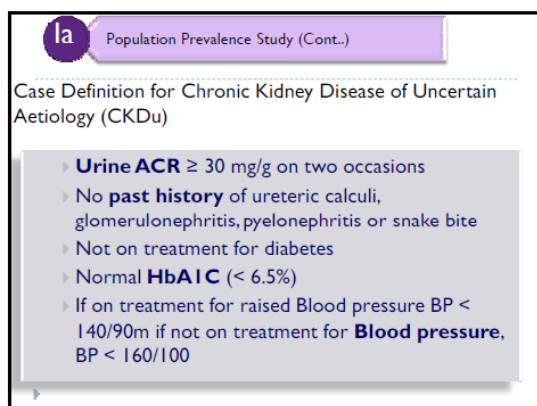
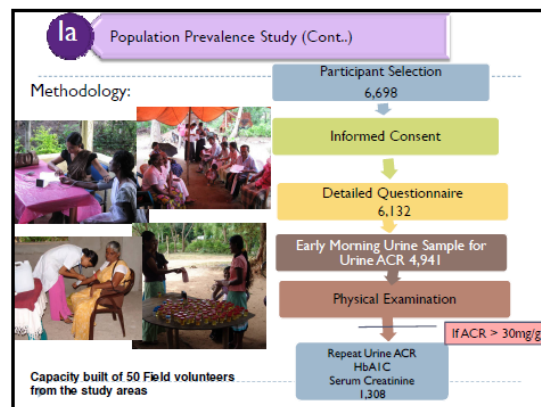
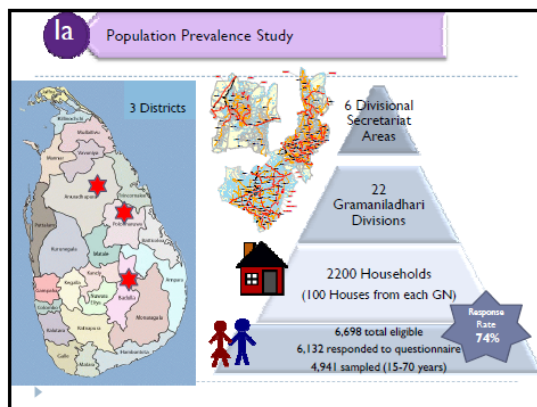
- Definition of CKDu to be established and used as a standard screening tool
- Representativeness and nature of populations screened unclear
- Geographical mapping piece meal
- Little coordination of epidemiological, analytical & environmental studies





- ### STRENGTHS OF THE STUDY
1. Use of consistent case definition of CKDu
 2. Analysis of a range of biological samples from CKDu subjects and controls
 3. Comparison of control groups within and outside the endemic area
 4. Use of sensitive analytical techniques
 5. Heavy metals, metalloids and other elements in environmental samples were analysed





RESULTS PREVALANCE OF CKDu

Age standardized prevalence of CKDu was higher in Females **16.9%** (95% CI = 15.5% to 18.3%) than Males **12.9%** (95% CI = 11.5% to 14.4%)

	Males	Females
Grade 1	27.0%	53.3%
Grade 2	27.9%	32.0%
Grade 3	23.2%	7.4%
Grade 4	22.0%	7.3%

Advanced grades (severe) of CKDu seen more among males ($p < 0.001$)

In both sexes the prevalence increased with increasing age ($p < 0.001$)

RESULTS PREVALANCE OF CKDu

Why is there a difference in Male & Female prevalence?

Low iron stores in females in lower socio economic groups has influence on excretion of heavy metals and oxidative stress on the kidney – making kidneys more vulnerable to CKDu – resulting in *higher prevalence in females*

Male sex has been reported to be a risk factor for progression to end-stage renal disease, and this may partly explain the occurrence of more severe stages of CKDu in men

RESULTS

PREVALANCE OF CKDu

- Family history of kidney disease in parents or siblings in **20%** individuals with CKDu
- From individuals with CKDu
 - 2.1% had ischaemic heart disease and/or cerebrovascular disease
 - 0.4% had long term use of herbal medicine for hypertension
 - 1.8% had a history of long term use of Aspirin
 - 0.6% had a long term use of Analgesics
- Being up Male **reduced** the risk of CKDu (OR=0.745, 95% CI=0.562 to 0.988, P<0.05)
- Being older than 39 years **increased** the risk of CKDu (OR=1.926, 95% CI=1.561 to 2.376, P<0.001)

RESULTS

SUMMARY RESULTS OF LOGISTIC REGRESSION ANALYSIS FOR EXPOSURE

Occupation Type - Being a chena cultivation *increased* OR by **19.5%**

Type of Agriculture - Engaging in paddy cultivation compared to cultivation of vegetables and other crops(chena cultivation) *decreased* OR by **26.8%**

Older Age, being female, being a farmer and being engaged in non-paddy cultivation increased the odds of CKDu

RESULTS

DEMOGRAPHIC CHARACTERISTICS OF CKDu CASES

Characteristic	Endemic Area		Non Endemic Area
	CKDu cases	Controls	Controls
Total Number	733	4044	250
Males, %	37.1	42.5	56
Age (years), mean (SD)	39.1 (14.2)	43.7 (13.9)	35.5 (14.0)
Farmer,%	38	43.9	18.3
BMI,kg/m2, mean (SD)	22.3 (4.6)	21.1 (4.1)	21.7 (4.4)
ACR \geq 30 mg/g	733	0	0

ACR=Albumin-Creatinine ratio, BMI Body Mass Index, SD standard deviation

Ib

Analytical & Environmental Studies

This comprised of the following Components:

- Case-Control Studies: Comparing newly diagnosed cases of CKDu and matched controls to identify risk factors for CKDu
- Cross Sectional Comparison: Comparison of potential environmental routes in endemic and non endemic areas for CKDu
- Determination of pesticide residues
- Analytical Studies of human postmortem tissues

Ib

Analytical & Environmental Studies

Response Rate 74% (n=4957)

ACR \geq 30mg/g on two occasions & other criteria satisfied (n=733)

No diabetes, kidney diseases, CKDu & snake bite (n=4044)

Urine Arsenic, Cadmium & Lead	n=495	n=132
Urine for other elements	n=107	N=0
Serum Selenium, Strontium etc	n=171	N=0

SPECIMEN HANDLING AND ANALYSIS

- Samples were collected in uncontaminated collection vials and stored frozen (-20°C) until transfer to the laboratory.
- All analyses were performed in a contract laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium), which has an external quality control scheme for analysis of trace elements.
- Measurements of **Arsenic, Cadmium, Lead** and other elements in urine was performed by inductively coupled plasma mass spectrometry (MS).
- Serum analyses were performed by electrothermal atomic absorption spectrometry.
- Limits of detection for Aluminium, Strontium, Chromium and Selenium were 0.1 $\mu\text{g/l}$, 0.5 $\mu\text{g/l}$, 0.01 $\mu\text{g/l}$ and 1 $\mu\text{g/l}$ respectively.

RESULTS OF URINE – Arsenic, Cadmium & Lead								
	Arsenic (ug/g creatinine)			Cadmium (ug/g creatinine)			Lead (ug/g creatinine)	
	CKDu Cases	Controls from Endemic Area (EA)	Controls from Non Endemic Area (NEA)	CKDu Cases	Controls from Endemic Area (EA)	Controls from Non Endemic Area (NEA)	CKDu Cases	Controls from Endemic Area (EA)
	n=495	n=132	n=250	n=495	n=132	n=250	n=495	n=132
Mean	45.447	92.443	56.572	1.039	0.646	0.345	1.153	1.254
Median	26.3	6.99	42.025	0.695	0.18	0.265	0.95	0.793
Range	0.4 - 616.6	0.2 - 966.29	5.38 - 350.28	0.005 - 8.93	0.005 - 5.13	0.005 - 2.079	0.04 - 8.53	1.21 - 6.64

The sensitivity & specificity for concentrations of Cadmium in urine were 80% and 53.6% (AUC=0.682, 95% CI=0.61 to 0.75, cut-off value = 0.23 ug/g).
At a cut-off value of 0.397 ug/g, sensitivity was 70% and specificity 68.3%.

The sensitivity and specificity for the concentration of arsenic in urine were 90% and 23.2% respectively (AUC = 0.64, 95% CI = 0.58 to 0.71, cut-off value = 88.57 ug/g).

The concentration of lead in urine was a poor predictor of CKDu (AUC = 0.53, 95% CI 0.38 to 0.67)

RESULTS OF URINE

- In Subjects with CKDu urine **Cadmium** excretion was significantly higher compared to control in both endemic and non endemic areas
- Controls in the endemic area compared to those in the non endemic area also had significantly higher urinary excretion of **Cadmium**.
- The sensitivity and specificity for Urine **Cadmium** were 80% and 53.6% respectively*
- Dose-response analysis showed that **Cadmium** exposure is a risk factor for the development of CKDu* **

*AUC=0.682, cut-off value =0.23 ug/g **P = 0.019 for stage 3 and P = 0.024 for stage 4.

RESULTS OF URINE

- The sensitivity and specificity for concentration of **Arsenic** in urine was 90% and 23.2% respectively*
- The mean urine concentration of **Arsenic** in CKDu cases was above levels known to cause oxidative injury to kidneys
- There was no significant dose-effect relationship between the concentration of **Arsenic**, **Lead** or **Selenium** in Urine and the stage of CKDu

*AUC = 0.64, 95% CI = 0.58 to 0.71, cut-off value =88.57 ug/g

RESULTS OF URINE

- Among CKDu cases, the concentration of Cadmium in Urine was positively correlated with **Lead** and **Arsenic**** concentrations in urine
- There was no significant difference in urine **Arsenic** and **Lead** concentrations in CKDu cases compared to controls

**Lead (p=0.62, p<0.0001)
Arsenic (p=0.25, p<0.001)

RESULTS OF URINE – Other Metals

Metals mg/g creatinine in CKDu subjects n=107	Mean	Median	Minimum	Maximum
Sodium	4105.5	3544.00	425.00	17458.00
Potassium	917.94	800.00	243.00	2469.00
Calcium	80.45	67.00	4.00	368.00
Magnesium	79.89	80.00	2.00	169.00
Copper	13.34	11.00	3.70	91.10
Zinc	229.99	235.99	31.00	510.00
Titanium	0.26	0.24	0.03	0.88

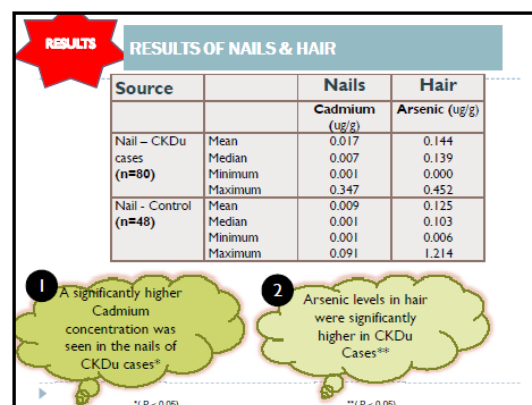
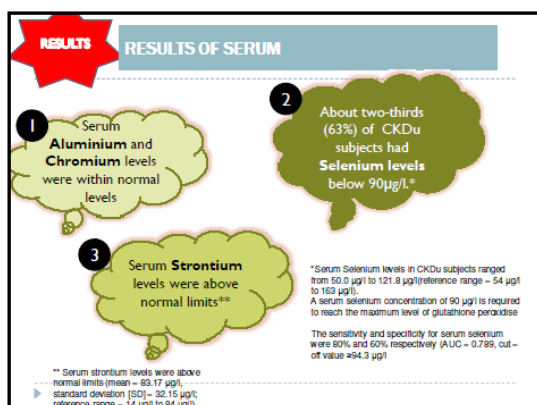
Urine concentrations of sodium, potassium, calcium, magnesium, copper, zinc, and titanium in CKDu cases were within normal limits

RESULTS OF SERUM

Concentration of metals in serum of subjects with CKDu n= 171

	Serum Concentration (ug/l)			
	Mean	Median	Minimum	Maximum
Aluminium	4.13	3.00	1.00	12.00
Chromium	0.118	0.06	0.01	1.15
Selenium	88.27	84.5	50.0	121.8
Strontium	83.17	82.00	29.00	198.00

Serum selenium reference range 54-163 ug/l.
Serum strontium reference range 14 - 84 ug/l.



KEY MESSAGES **CADMIUM**

- ▶ Cadmium is a known nephrotoxin
- ▶ Urinary Excretion of Cadmium is a reliable indicator of cumulative long-term exposure to cadmium
- ▶ The mean urine concentration of cadmium in CKDu cases was above the levels demonstrated in recent studies to cause oxidative stress and decreased glomerular filtration rate and creatinine clearance
- ▶ A significantly higher cadmium concentration was also seen in the nails of those with CKDu compared to controls from the endemic area.
- ▶ The results of this study indicate that cadmium exposure is a risk factor for CKDu.

KEY MESSAGES **ARSENIC**

- ▶ The mean urine concentration of arsenic in CKDu cases was also above levels known to cause oxidative injury to the kidney
- ▶ In CKDu cases and controls from the endemic area, concentrations of arsenic in urine and in fingernails were higher than those reported in people living in low-exposure environments.
- ▶ Urine is a major pathway for excretion of arsenic from the human body and so urine levels reflect exposure.
- ▶ In some studies, markers of oxidative stress have been demonstrated at urine arsenic concentrations as low as 3.95 µg/g

KEY MESSAGES **ARSENIC**

- ▶ The level of total arsenic in urine is associated with chronic kidney disease in a dose-response relationship, especially when the level is greater than 20.74 µg/g.
- ▶ Co-exposure to cadmium and arsenic is known to produce additive effects on the kidney that are more pronounced than exposure to either metal alone

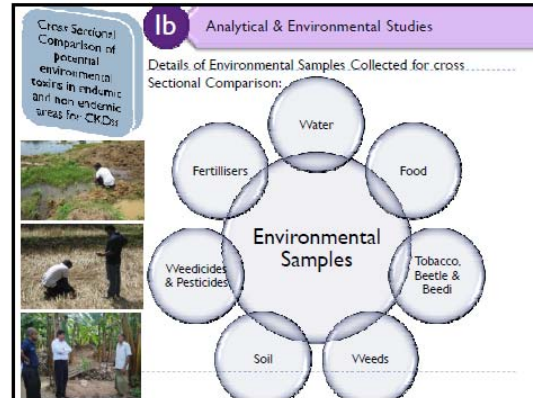
KEY MESSAGES **SELENIUM**

- ▶ Selenium has been shown to protect the kidney from oxidative stress
- ▶ A selenium concentration of 80–95 µg/l is needed to maximise the activity of the antioxidant enzyme glutathione peroxidase and selenoproteins in plasma
- ▶ Serum Selenium was below 80 µg/l in 38% and below 90 µg/l in 63% of individuals with CKDu.
- ▶ Low selenium levels may have been a contributory factor increasing the vulnerability of the kidneys to oxidative damage caused by heavy metals and metalloids.

KEY MESSAGES

STRONTIUM

- ▶ The association of raised Serum strontium levels with
- ▶ raised serum cadmium levels has been reported previously
- ▶ Strontium levels were not analysed in food or water.
- ▶ The most likely explanation is an alteration of Strontium handling and excretion, owing to the effect of Cadmium on renal tubular function.



SPECIMEN HANDLING AND ANALYSIS

- ▶ Samples were collected in uncontaminated collection vials and stored frozen (-20°C) until transfer to the laboratory.
- ▶ All analyses were performed in a contract laboratory (Laboratory of Pathophysiology of the University of Antwerp, Belgium), which has an external quality control scheme for analysis of trace elements.
- ▶ Measurements of **Arsenic, Cadmium, Lead** and other elements in water, vegetables, agrochemicals and soil, was performed by inductively coupled plasma mass spectrometry (MS).

RESULTS

RESULTS OF WATER ANALYSIS

99

- Sources of drinking water for individuals with CKDu in **Endemic Area**
- (from ground well, tube wells and natural springs)

123

- Other sources of water from **Endemic Area**
- (From ground wells, tube wells, irrigation canals)

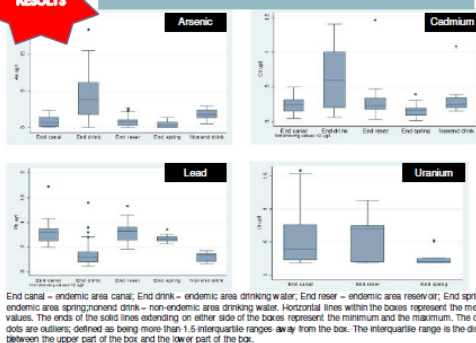
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- **Non Endemic Area**



RESULTS

RESULTS OF WATER ANALYSIS



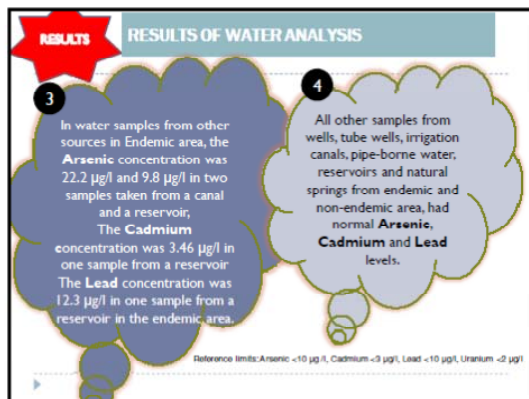
RESULTS

RESULTS OF WATER ANALYSIS

- 1 Levels of Cadmium, Lead and Uranium in sources of drinking water used by individuals with CKDu were within normal limits.
- 2 Arsenic was borderline or raised in four samples* of drinking water used by individuals with CKDu repeat analysis from the four sources showed normal Arsenic levels.

Reference limits: Arsenic <10 µg/l, Cadmium <3 µg/l, Lead <10 µg/l, Uranium <2 µg/l

* (9.9 µg/l, 10.2 µg/l, 10.5 µg/l, 13.4 µg/l).



KEY MESSAGES **DINKING WATER**

- ▶ The **Cadmium** content in all water samples analysed was within normal limits, except in one sample from a reservoir that had a borderline cadmium level (3.45 µg/l).
- ▶ Drinking water is a major pathway for entry of inorganic **Arsenic** into the human body.
- ▶ The arsenic content in 99% of water samples was below the WHO reference value of 10 µg/l.
- ▶ However, it has recently been suggested that the concentration of arsenic in drinking water should be no more than 5 µg/l.

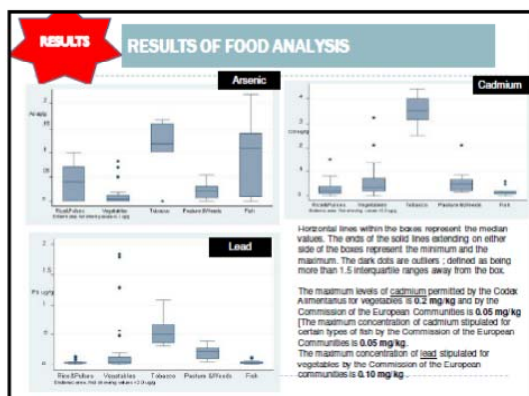
KEY MESSAGES **DINKING WATER**

- ▶ CKDu occurs in areas where groundwater is the main source of drinking water. Groundwater in this region is known to have a high content of **Fluoride** and **Calcium**.
- ▶ People living in the region for generations have used groundwater for drinking without ill effects.
- ▶ However –
 - ▶ hardness of water; the high fluoride content,
 - ▶ Poor access to drinking water
 - ▶ Inadequate intake of water in a warm climate
 may influence the body burden and/or the excretion of heavy metals and oxidative damage to the kidneys caused by heavy metals.

RESULTS **RESULTS OF FOOD ANALYSIS**

119 • Rice, Pulses, Vegetables including leafy vegetables, Coconut, Yams & roots (eg. Kohila, Lotus), Fresh Water fish, Tobacco, Pasture & Veds from **Endemic area**

32 • Rice, Pulses, Vegetables including leafy vegetables, Coconut, Yams & roots (eg. Kohila, Lotus), Fresh Water fish, Tobacco, Pasture & Veds from **Non Endemic area**



RESULTS **RESULTS OF FOOD ANALYSIS**

Levels of **Cadmium** in Rice in both Endemic & Non Endemic areas were below the allowable limit (0.2mg/kg)

The maximum concentration of **Cadmium** in vegetables in the endemic area was 0.322 mg/kg and in the non endemic areas it was 0.063 mg/kg

Levels of **Cadmium** in certain vegetables such as lotus root, and in tobacco, were high. Levels of Cadmium in lotus and tobacco were higher in endemic than in non-endemic areas

Source		Cadmium (mg/kg)	
		Endemic Area (EA)	Non-Endemic Area (NEA)
Lotus	Mean	0.413	0.023
	Median	0.066	0.023
	Maximum	1.50	0.03
Tobacco	Mean	0.351	0.316
	Median	0.351	0.316
	Maximum	0.44	0.351

KEY MESSAGES FOOD TOBACCO

- ▶ The maximum level of **Cadmium** for vegetables permitted by the Codex Alimentarius is 0.2 mg/kg
- ▶ The level of **Cadmium & Lead** permitted by the Commission of the European Communities
Cadmium - 0.05 mg/kg.
Lead - 0.10 mg/kg
- ▶ The maximum levels in certain vegetables grown in the endemic area exceeded these safety levels.
Fish - Cadmium (0.06 µg/g)*
Vegetables in the endemic area - Lead (0.476 mg/kg)
- ▶ Levels of cadmium and Lead in vegetables and Cadmium in freshwater fish from the endemic area are above the maximum levels stipulated by certain Food Safety Authorities

* also exceeded the European maximum limit of 0.05 mg/kg stipulated for certain types of fish

KEY MESSAGES FOOD TOBACCO

- ▶ A provisional tolerable weekly intake (PTWI) established by the Joint Food and Agriculture Organisation of UN (FAO) / WHO Expert committee on Food Additives (JECFA) for body weight per week
- ▶ **Cadmium** - 5.8(ug/g) ➡ **2.52(ug/g)***
- ▶ **Arsenic** - 0.015(mg/kg) ➡ **Level withdrawn – To keep low as possible**
- ▶ **Lead** - 0.025(mg/kg)

Since the Cadmium content of certain food items in the endemic area is above stipulated levels, the total weekly intake of cadmium in people living in the endemic area could exceed these safe limits, with detrimental effects on the kidneys, particularly in vulnerable people and those with predisposing factors.




RESULTS RESULTS OF SOIL ANALYSIS

88

• Soil samples were obtained from paddy fields, other types of cultivations and reservoirs from **Endemic area**

41



• Soil samples were obtained from paddy fields and other types of cultivations from **Non Endemic area**

RESULTS RESULTS OF SOIL ANALYSIS

Source		Arsenic (ug/g)		Cadmium (ug/g)		Lead (ug/g)	
		Endemic Area (EA)	Non Endemic Area (NEA)	Endemic Area (EA)	Non Endemic Area (NEA)	Endemic Area (EA)	Non Endemic Area (NEA)
Paddy EA (n=45) NEA (n=21)	Mean	0.16	0.17	0.49	0.45	16.54	14.49
	Median	0.11	0.08	0.43	0.40	15.75	16.95
	Minimum	0.00	0.01	0.16	0.01	5.03	0.02
	Maximum	0.85	0.99	0.56	1.61	34.54	39.95
		0.06	0.40	0.40	0.59	15.41	14.84
Chena EA (n=20) NEA (n=10)	Mean	0.06	0.29	0.36	0.55	13.82	13.93
	Median	0.00	0.09	0.17	0.34	8.25	5.42
	Minimum	0.22	1.57	1.27	0.93	28.33	26.1
	Maximum	0.11	0.27	0.48	0.47	17.46	18.01
		0.07	0.24	0.37	0.41	16.76	18.03
Vegetable Plot EA (n=23) NEA (n=10)	Mean	0.00	0.08	0.16	0.29	6.69	5.57
	Median	0.46	0.53	70.00	0.84	41.02	32.87
	Minimum	0.05	0.13	0.60	0.28	20.55	7.96
	Maximum	0.06	0.13	0.5	0.28	20.29	7.96
		0.00	0.09	0.17	0.24	9.98	3.15
Crop land EA (n=4) NEA (n=2)	Mean	0.01	0.18	1.47	0.33	32.1	12.77
	Median	0.60		0.66		19.16	
	Minimum	0.50		0.52		17.16	
	Maximum	0.17		0.15		7.11	
		0.43		1.36		33.49	
Reservoir EA (n=4) NEA (n=3)	Mean						
	Median						
	Minimum						
	Maximum						

RESULTS RESULTS OF SOIL ANALYSIS

The mean Cd Concentration of soil from the endemic area was 0.4µg/g.

The level of Cadmium in surface soil in the endemic area (n = 94, excluding samples from reservoirs), was 1.16 µg/g compared to 0.49 µg/g in the non-endemic area (n = 45, excluding samples from reservoirs)

KEY MESSAGES SOIL

- ▶ The mean concentration of **Cadmium** in soil from the endemic area was 0.4 µg/g.
- ▶ Surveys of agricultural soils in the USA and Sweden have reported lower soil cadmium levels (0.265 mg/kg and 0.23 mg/kg respectively)
- ▶ The concentration of **Cadmium, Arsenic and Lead** in soil, and their impact on body burden and excretion, is known to be influenced by many environmental factors:
 - ▶ pH of soil
 - ▶ Buffering capacity
 - ▶ Content of organic matter
 - ▶ Water quality

KEY MESSAGES

SOIL

- ▶ Cadmium accumulation by plants, for example, is influenced by the reactive soil cadmium content and pH.
- ▶ It is decreased by high cation exchange capacity of the soil and increased by higher soil temperature
- ▶ The hardness and high content of fluoride in water in the endemic area may also influence the dynamics of cadmium in soil, absorption by plants and excretion from the kidney.

RESULTS

RESULTS OF WEEDICIDES & PESTICIDES

	Arsenic (ug/g)		Cadmium (ug/g)		Lead (ug/g)	
	Endemic Area (EA) n=26	Non Endemic Area (NEA) n=8	Endemic Area (EA) n=26	Non Endemic Area (NEA) n=8	Endemic Area (EA) n=26	Non Endemic Area (NEA) n=8
Mean	6.73	3.81	0.77	0.76	40.62	15.65
Median	1.68	1.38	0.31	0.3	1.79	1.89
Minimum	0.01	0.01	0.05	0.05	0.83	1.01
Maximum	94.93	13.15	9.34	2.0	930.81	56.39



A total of 26 samples analyzed from endemic areas

RESULTS

RESULTS OF PHOSPHATE FERTILIZERS

	Cadmium (ug/g)		Lead (ug/g)		Arsenic (ug/g)	
	Endemic Area (EA) n=13	Non Endemic Area (NEA) n=6	Endemic Area (EA) n=13	Non Endemic Area (NEA) n=6	Endemic Area (EA) n=13	Non Endemic Area (NEA) n=6
Mean	2.98	0.49	94.23	20.29	0.06	0.43
Median	0.04	0.03	1.42	0.65	0.04	0.19
Minimum	0.01	0.01	0.17	0.09	0.00	0.00
Maximum	30.79	1.28	823.41	98.52	0.19	1.22

The maximum acceptable levels for Cadmium, Lead and Arsenic, in phosphate fertilizer product, at 1% of the nutrient level, are 4 µg/g, 20 µg/g and 2 µg/g, respectively

A total of 19 samples analyzed (TSP - 6, MOP - 3, Urea - 7, Mixed - 3)

Determination of pesticide residues

Ib

Analytical & Environmental Studies

SPECIMEN HANDLING AND ANALYSIS

- ▶ Samples were shipped in dry ice and stored at -18°C until analysis. Analysis used validated liquid chromatography with tandem MS (LC-MS/MS), gas chromatography-mass spectroscopy (GC-MS) and gas chromatography with tandem mass spectrometry (GC-MS/MS) methods

RESULTS

RESULTS OF PESTICIDE RESIDUES

Parent Compound	Bio Marker	Reference Range (µg/l)	CKDu cases (µg/l) (Minimum, Maximum)	CKDu cases above reference limit (%)
2,4-D	2,4-D	<0.3	0.5, 0.62	3.5
Pentachlorophenol	Pentachlorophenol	<2	0.3, 2.2	1.7
Chlorpyrifos	3,5,6-trichloropyridinol	<11.3	0.5, 34.7	10.5
Parathion	P-nitrophenol	<25	0.5, 8.88	0
Carbaryl	1-naphthol	<19.7	0.5, 45.1	10.5
Naphthalene	2-naphthol	<17.1	0.5, 47.88	10.5
Glyphosate	Glyphosate	<2	0.075, 3.36	3.5
Glyphosate	AMPA	<0.5	0.075, 2.65	14

RESULTS

RESULTS OF PESTICIDE RESIDUES

Pesticide residues were detected in the urine from individuals with CKDu

Pesticide Residue	Frequency of detection
2,4-D	33%
3,5,6-trichloropyridinol	70%
P-nitrophenol	58%
1-naphthol	100%
2-naphthol	100%
Glyphosate	65%
Aminomethyl phosphonic acid (AMPA)	28%


1b Analytical & Environmental Studies

Analytical Studies of Human postmortem tissues

Postmortem tissues (kidney cortex, liver & bone) of 40-60 years

- 26 CKDu patients
- 16 accident victims

Analyzed for Arsenic, Cadmium & Lead



RESULTS RESULTS OF POST MORTEM TISSUE

		Arsenic (ug/g)	Cadmium (ug/g)	Lead (ug/g)
Kidney	Mean	885.54	4.04	0.89
	Median	152.62	2.34	0.6
	Minimum	19.28	0.0384	0.01
	Maximum	7458.54	14.16	2.54
Liver	Mean	165.39	5.38	4.56
	Median	117.19	2.42	3.93
	Minimum	22.22	0.13	0.98
	Maximum	1471.41	26.16	13.33
Bone	Mean	8.68	6.47	64.04
	Median	4.87	4.34	47.13
	Minimum	0.82	0.47	2.11
	Maximum	70.66	28.84	233.92

- Cadmium & Lead contents in bone tissues of known CKDu patients were higher than that for controls
- No significant difference in levels of Arsenic in bones of cases & controls
- No significant difference in levels of all 3 metals in kidney cortex & liver tissues of cases & controls

1b Analytical & Environmental Studies


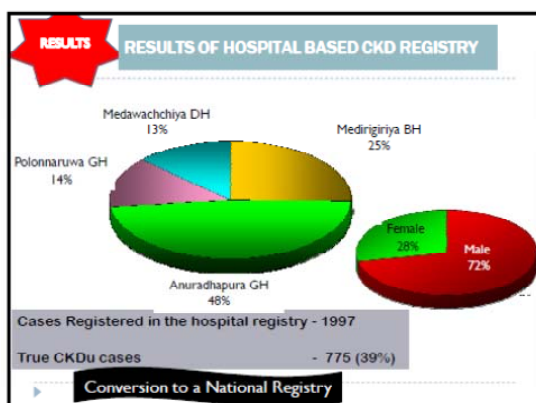
Completed....

- Case-Control Studies comparing newly diagnosed cases of CKDu and matched controls to identify risk factors for CKDu
- Cross Sectional Comparison of potential environmental causes in high and low prevalence areas for CKDu
- Determination of pesticide residues
- Analytical Studies of Human postmortem tissues

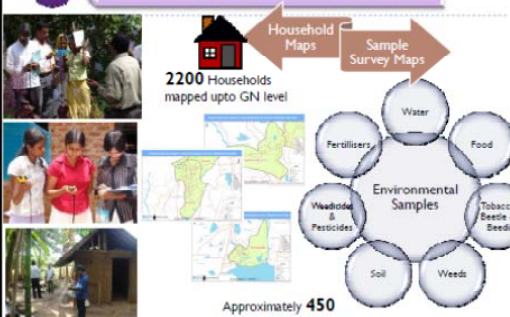
1c Hospital Based CKD registry

Main objectives:

- To characterize CKD / CKDu population attending renal clinics in :
 - Medawachchiya DH
 - Medirigiriya BH
 - Anuradhapura GH
 - Polonnaruwa GH
- Database created with following:
 - Basic socio-demographics
 - Lifestyle
 - Environmental factors,
 - Anthropometry
 - Results of lab investigations

1d Geographical Mapping of identified variables



2200 Households mapped upto GN level

Household Maps

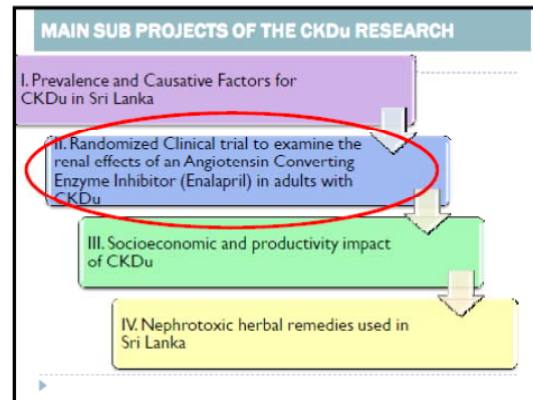
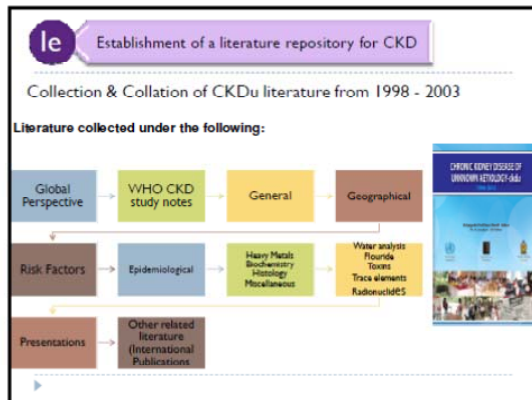
Sample Survey Maps

Environmental Samples

- Water
- Food
- Tobacco, Beetle & Beedi
- Weeds
- Soil
- Weedicide & Pesticides
- Fertilisers

Approximately 450 sampling sites mapped

Capacity of 50 field volunteers built from the area



II. Randomized Clinical trial to examine the renal effects of an Angiotensin Converting enzyme Inhibitor (Enalapril) in adults with CKDu

To examine renal effects of Enalapril versus placebo in adults with CKDu by comparing and evaluating the effect of Enalapril to placebo on:

- Estimated GFR
- Albuminuria
- Change in stage of CKDu

• Randomized, double blind, placebo controlled clinical trial

• Study settings are special clinics organised in

- Anuradhapura TH
- Padaviya BH
- Medirigiriya BH

Analysis of Results Awaited

• A total of **266** participants recruited and randomized

RESULTS

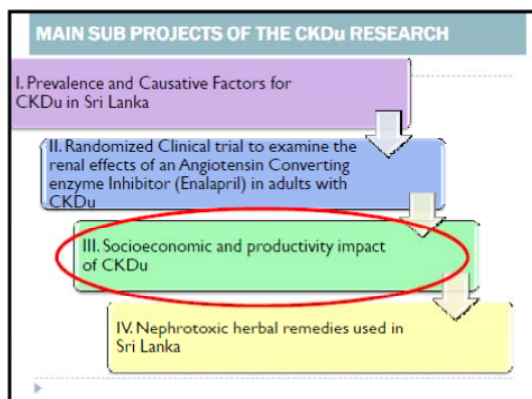
RESULTS OF RANDOMISED CLINICAL TRIAL

Levels of **Cadmium** in Rice in both Endemic & Non Endemic areas were below the allowable limit (0.2mg/kg)

The maximum concentration of **Cadmium** in vegetables in the endemic area was 0.322 mg/kg and in the non endemic areas it was 0.063 mg/kg

Levels of **Cadmium** in certain vegetables such as lotus root, and in tobacco, were high. Levels of Cadmium in lotus and tobacco were higher in endemic than in non-endemic areas

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	Median	0.066	0.023
	Maximum	1.50	0.03
Tobacco	Mean	0.351	0.316
	Median	0.351	0.316
	Maximum	0.44	0.351



III. Socioeconomic and productivity impact of CKDu

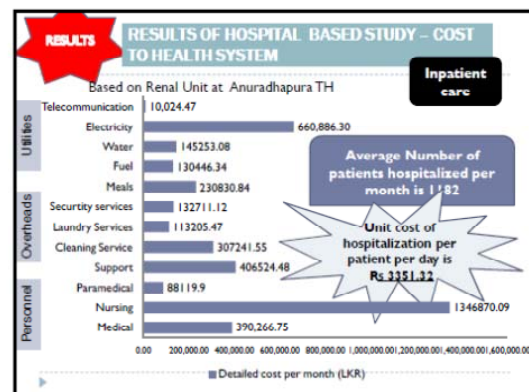
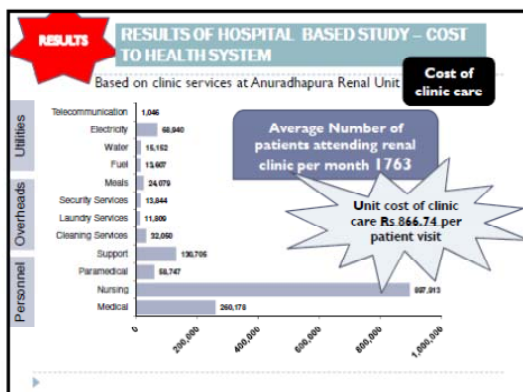
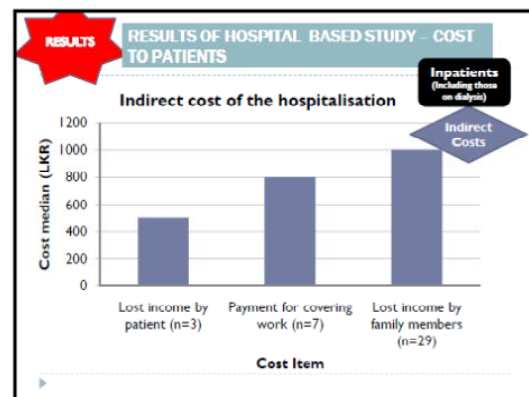
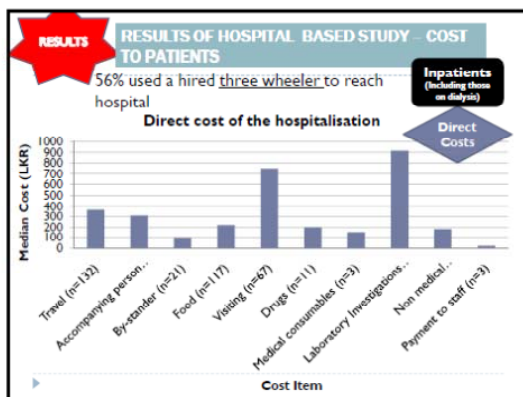
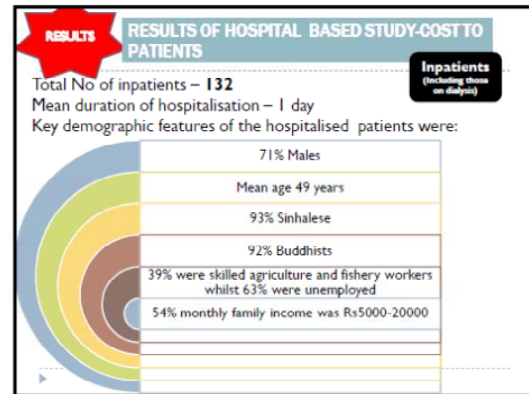
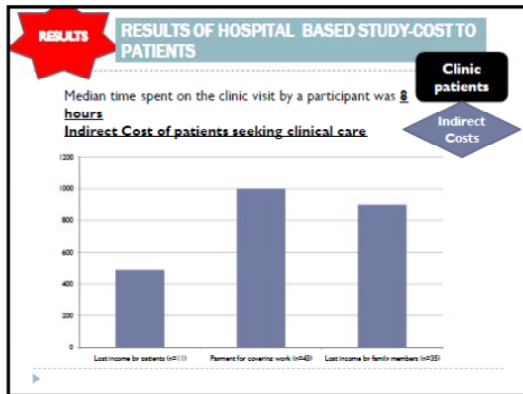
Consisted of two research components:

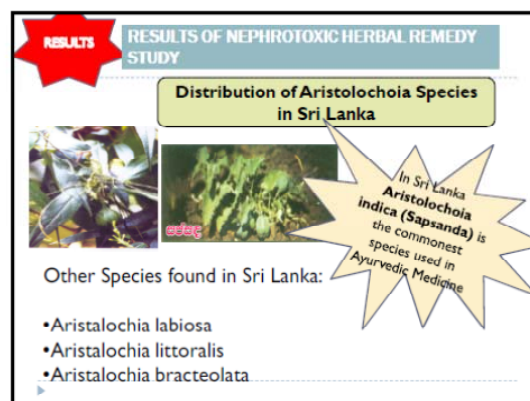
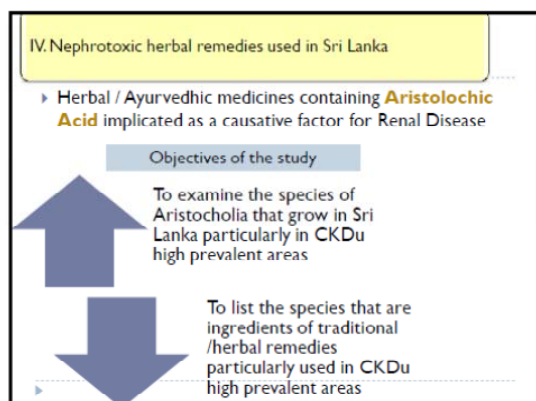
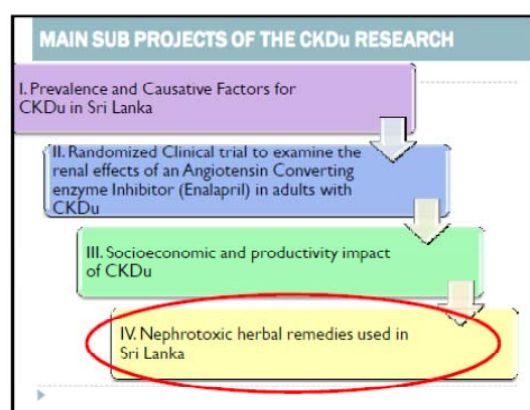
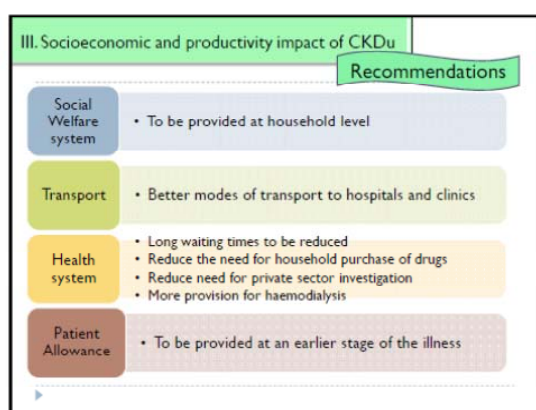
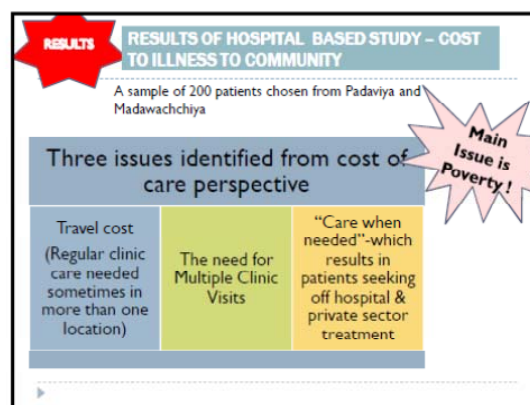
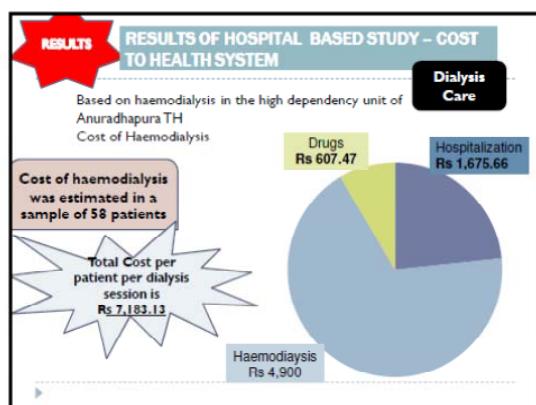
- To estimate costs of CKDu to individual, household & communities
- To understand psychosocial impact
- Describe modes of coping at all levels
- Evaluate impact of existing coping mechanisms

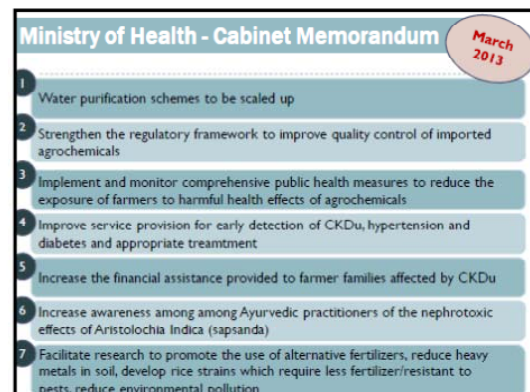
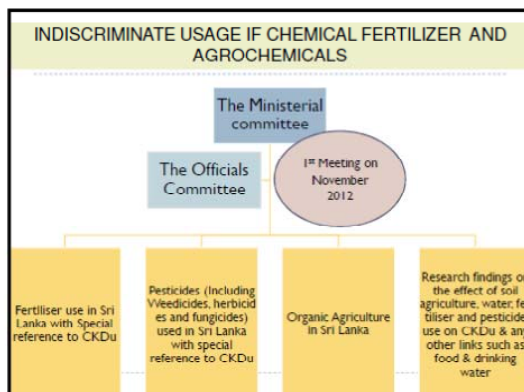
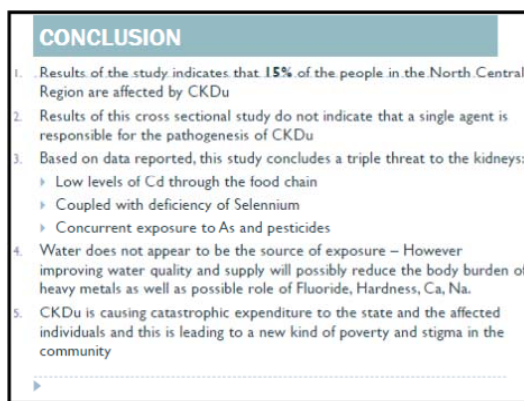
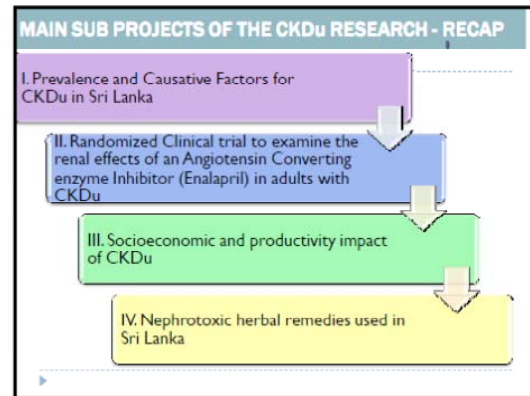
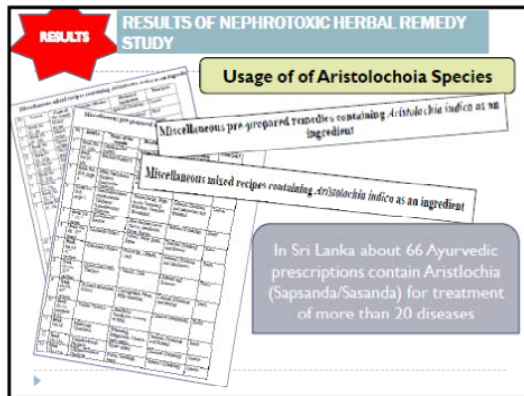
IIIa Community Based Study

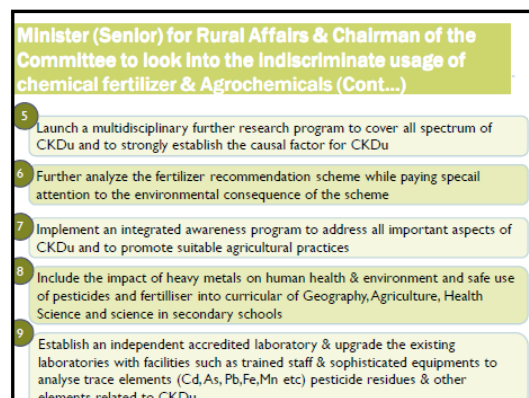
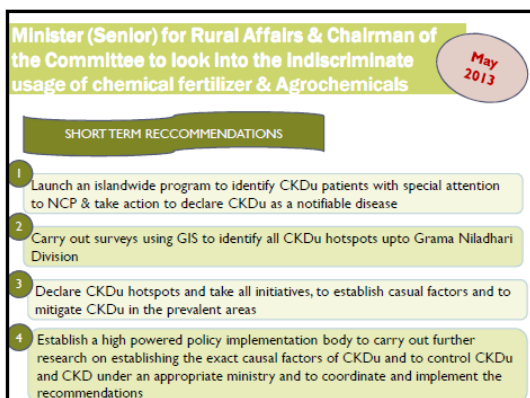
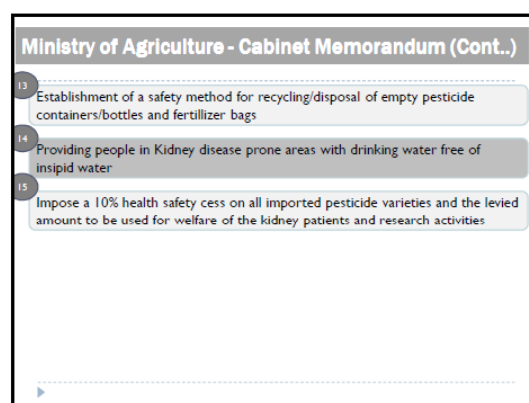
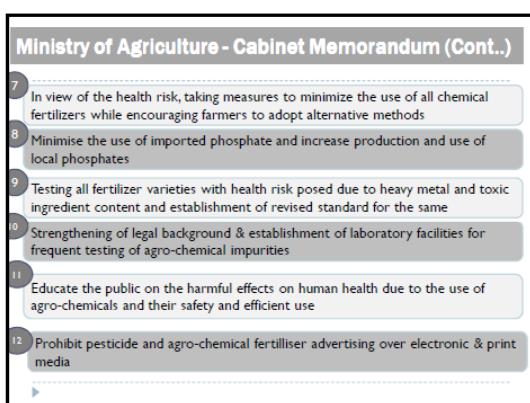
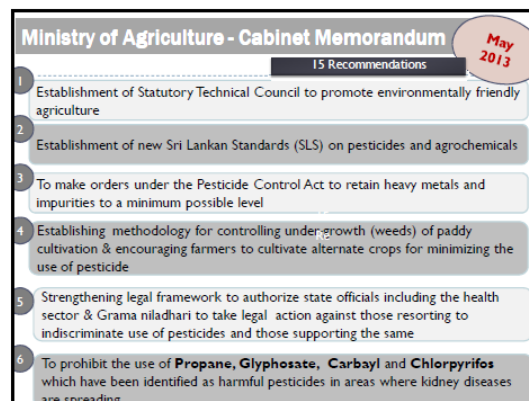
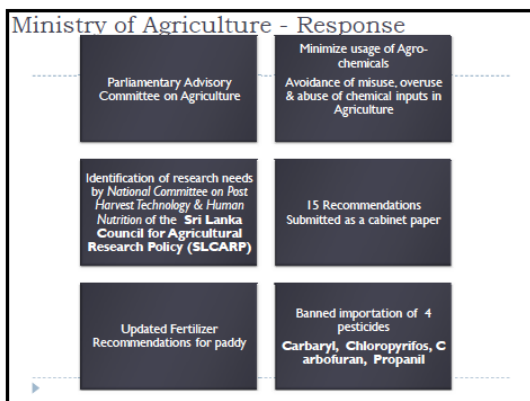
IIIb Hospital Based Study

- To estimate the socioeconomic impacts of CKDu & to identify methods of easing burden









Minister (Senior) for Rural Affairs & Chairman of the Committee to look into the indiscriminate usage of chemical fertilizer & Agrochemicals (Cont...)

10. Regulate the promotional activities related to fertilisers & pesticides carried out by the agrochemical companies/institutions carried out by mass media
11. Establishment of legal provisions for mandatory requirements in relation to standards
12. Provide drinking water with low or no hardness to communities in CKDu endemic areas by way of providing effective filters and/or delivering portable water with acceptable quality
13. Promote & implement rain water harvesting structures with quality monitoring systems and make regulations for all new buildings in CKDu areas to be equipped with rain water harvesting units
14. Select high priority CKDu hotspots & establish "Green Zones" that are free of major potential CKDu casual inputs

Minister (Senior) for Rural Affairs & Chairman of the Committee to look into the indiscriminate usage of chemical fertilizer & Agrochemicals (Cont...)

15. Provide subsidy & marketing facilities for the farmers who make attempts to move from agrochemicals to alternate farming
16. Establish a fund for the welfare of CKDu patients, for carrying out research and financing for fund through economic instruments based on the polluter pay principles and producer responsibility as well as CSR
17. Enhance the medical facilities for CKDu patients with immediate effects in the affected areas
18. Facilities of the traditional medical practitioners to carry out their treatments for the affected people based on the patient interest & demand
19. Expedite the establishment of proposed chemical fertiliser manufacturing plant to produce fertiliser with minimum/standard limits of heavy metals using Eppawella rock phosphate

Minister (Senior) for Rural Affairs & Chairman of the Committee to look into the indiscriminate usage of chemical fertilizer & Agrochemicals

LONG TERM RECOMMENDATIONS

20. Establish procedures for examination of quality of agrochemicals at boarder points, Factory outlets, wholesale & retail shops in the districts
21. Establish long term water quality monitoring system by an accredited agency under direct supervision of a government institution.
22. Capacity building of grass root level officers to educate farmers on use of minimum pesticides and fertilisers
23. Prepare necessary maps indicating zones for active, potential and prone to agrochemical contamination
24. Redesign land use pattern, crop & land implementation plans covering soil & water drainage engineering aspect & climatic parameters

Minister (Senior) for Rural Affairs & Chairman of the Committee to look into the indiscriminate usage of chemical fertilizer & Agrochemicals (Cont...)

25. Establish river banks, green manure banks, neem avenues, herbal gardens, compost bays and strict declaration of non toxic zones
26. Identify farmers/farmer groups and designate them as responsible agents/agri environment guard with authority to regulate the inputs used in agriculture
27. Introduce programmes for organic and sustainable certification to receive premium prices for farm products
28. Establish appropriate CSR avenues through Banks, Insurance companies, NGOs, local institutions for possible subsidy or incentives for proposed curative and corrective measures
29. Conduct extended cost benefit analysis for the use of agrochemicals in consideration of their impact on environmental & social effects

Ministry of Water Supply and Drainage

National Water Supply & Drainage Board

1. Parliamentary Sub committee appointed to coordinate mitigation measures
2. Concept paper and action plans have been prepared for supplying safe drinking water to all affected areas
3. District wise action items/sub projects have been identified
4. Implementation Plans

SHORT TERM:

- Water for drinking and cooking using small RO (Reverse Osmosis) plants
- Rain water harvesting

MEDIUM TERM:

- Medium sized water supplies based on surface water
- Water Supply extensions

LONG TERM:

- Major Integrated Water Supply projects

Ministry of Social Services


Draft Cabinet paper prepared for

1. To adhere to the Ministry of Health-World Health Organization criteria in order to diagnose the disease
2. To pay monthly assistance of **Rs 1500** each for kidney patients who do not require dialysis (Stated in Grade 2/3)
3. To pay monthly assistance of **Rs 3000** each for kidney patients who require dialysis (Stated in Grade 3/4)

At present a monthly assistance is paid for only a few patients through Provincial social Services Department and ranges from Rs 500 - 1000

Follow-up of Recommendations	
Ministry of Health	• Strengthening of the Health Services as per the recommendations (In progress)
Ministry of Agriculture	• Regulations on Indiscriminate use of Fertilizers /Pesticides (Cabinet Subcommittee - 15 priority areas)
Ministry of Water Supply & Drainage	• Improvement of Water Quality (Already in place)
Ministry of Indigenous Medicine	• Regulatory mechanism to be initiated for reduction of use of Aristolochia (Sapsanda/Sasanda)
Ministry of Environment	• Contribution towards reduction of causative factors
Ministry of Science & Technology	• Supported the National Research effort together with WHO • Continue research in identified areas
Ministry of Social Services	• Strengthening the social service component and facilitating the provision of patient allowance at an earlier stage

CONCLUSION



Sri Lanka has done work in the area of CKDu over many years. With a coordinated research initiative over a period of **27 months** funded by NSF and WHO has yielded evidence to initiate policy dialogue which has resulted in the highest political commitment translated into action by different stakeholders and ministries.

Thank You

SECTION 6

Summary Statement of Expenditure (indicate under Personnel, Equipment, Consumables, Travel and Subsistence and Miscellaneous)

Management Financial Report of Funds Awarded to World Health Organisation By National Science Foundation

(As of 31 December 2012)

	Funds Allocated (First Year)	Funds Allocated (Second Year)	Total NSF Allocation (2 years)	WHO Commitment (1/11/10 to 31/12/12)
(1) Personnel	LKR	LKR		LKR
Coordinator, Field Coordinator x1 - CKDu Project, GIS assistant, Data Entry Operator	2,460,000	2,460,000	4,920,000	4,633,100
Sub Total (Personnel)	2,460,000	2,460,000	4,920,000	4,633,100
(2) Equipment & Consumables				
Analysis of urine & blood samples for heavy metals	3,400,000	1,000,000	4,400,000	4,398,916
Analysis of food & diet studies	3,200,000	374,159	3,574,159	3,515,293
Analysis of metals in bone & tissue	3,000,000	2,000,000	5,000,000	4,794,336
Analysis of environmental samples for heavy metals	4,000,000	1,500,000	5,500,000	5,497,150
Sub Total (Consumables)	13,600,000	4,874,159	18,474,159	18,205,695
(3) Travel & Shipments				
Cost of sample collection (urine, blood, food, soil and water)	5,000,000	2,000,000	7,000,000	7,082,855
Shipments	200,000		200,000	105,342
Allowances for research personnel	1,000,000	1,000,000	2,000,000	2,188,701
Sub Total (Travel & Subsistence)	6,200,000	3,000,000	9,200,000	9,376,898
(4) Project Activities				
Consultations & Meeting Costs (In country)	1,000,000	500,000	1,500,000	1,647,192
Operational Costs for Follow up and Intervention Studies (Cohort Studies)	4,700,000	300,000	5,000,000	6,644,483
Special studies, Sociology and economic impact of CKDu and sociological studies, herbal remedies (intervention study emerged as priority research during the progress of research study)	4,000,000	1,200,000	5,200,000	9,771,531
Screening Tests	5,000,000		5,000,000	4,908,738
Renal Biopsy Study & Slaughter house study	1,000,000	230,000	1,230,000	1,296,048
National Renal Registry (CKD Registry)	172,743	300,000	472,743	450,000
Preparation of Final Report		2,500,000	2,500,000	2,590,205
Printing and publication of Final Report		750,000	750,000	1,000,501
Communication Strategy for public education	7,000,000	700,000	7,700,000	
Sub Total (Project Activities)	22,872,743	6,480,000	29,352,743	28,308,698
Total Cost	45,132,743	16,814,159	61,946,902	60,524,391

SUMMARY

1st installment received by World Health Organisation CO - SRL	19,000,000
2nd installment received by World Health Organisation CO - SRL	16,000,000
3rd installment received by World Health Organisation CO - SRL	16,000,000
4th installment received by World Health Organisation CO - SRL	14,000,000
Total Amount	65,000,000
Less: Project Support Cost	7,868,171
Net Available	57,131,829
Less: Expenditure as of 31 Dec 2012	60,524,391
Balance as at 31 Dec 2012 (LKR)	(3,392,561)

Note: The information in this report is drawn from the internal financial monitoring records. This is an informational report for the Donor. Uncertified financial statement issued by Budget & Finance Officer, WHO Regional Office, New Delhi on Quarterly basis

(1 USD = 111.1 LKR)

Further Details on the expenditure statement

(1) Personnel for screening and identification of cases

Personnel recruited through this project was a GIS assistant who assisted from the inception to the completion of the project. The ToR of this person is already included in the report and his work area covered data collection, data entry, training, field work in addition to the mapping exercise.

(2) Screening tests

The original proposal indicates that for screening tests which comprised of Urine ACR an allocation of Rs 4,950,000 is made for analyzing approximately 10,000 samples at a unit rate of Rs 450. However as per the final report we have analysed the following numbers of samples 4941(initial analysis for population prevalence study) + 1308(urine ACR>30) and 1840 (follow up). In addition samples from the case control study 496(cases) + 600(controls) were also analysed. The total analysis was therefore 9185 and also the unit price for analysis increased from Rs 450 upto Rs 550 during various stages of the study.

(3) Analysis of food and diet studies

The details of the food and diet studies are indicated in the body of the report and the annexure

(4) Analysis of Blood & Urine Samples

In the original proposal the budget allocation was for 1000 urine and 1000 blood samples each at a unit cost of Rs3500. Hence the total allocation for both was Rs 7,000,000. In the statement of expenditure however the allocation was Rs 4,400,000. The metal analysis was done at an international reference lab as there were minimal facilities in SriLanka to test this. The total number of urine samples collected was 878 and the total number of serum samples were 171. Although the initial unit cost of this was anticipated at Rs 3500 – The unit cost for analyzing urine for heavy metals was Rs 3690 (Eur 22.5) and for blood it was Rs 6560 (Eur 40)

(5) Analysis of metals in bone & tissue

In the original proposal there was only analysis of bone indicated for 500 samples at a unit rate of Rs 4000. In the statement of expenditure however the allocation was Rs 5,000,000. In addition to bone analysis of liver and renal tissues were also done as part of the postmortem study of the analytical study. A total of 135 tissues were examined and they were analysed at an international reference laboratory due to their expertise and international quality control. The unit cost for each sample analysis however was Rs 10218 (Eur 62)

(6) Analysis of Environmental Samples for heavy metals

The total numbers of environmental samples analysed and the list are all included in the final report as well as the annexures. In the original proposal the budget allocation was for 1500 samples at a unit rate of Rs 3500. The environmental analysis

was done both in Sri Lanka and at Antwerp university – which is an international reference laboratory

(7) Renal biopsy study and slaughter house study

In the original proposal the renal biopsy study came in as part of an analytical study which included the post mortem and the renal biopsy as well as the slaughter house study. There is a budget allocation of Rs 1,750,000 allocated in the original proposal for the renal biopsy study. In the statement of expenditure however the budget line “renal biopsy study & slaughter house study” has an allocation of Rs 1,230,000. Only the post mortem component was done. These funds have been used for analysis components of the studies – especially in relation to components that were not originally identified in the proposal eg: pesticide residues in Urine. These also had to be done at an international reference laboratory in Germany

(8) Intervention Study

Intervention trial was not an identified study at the inception of the research proposal and emerged during the research effort as a priority as the need to assess the efficacy of

per the final report this required sample collection and analysis of blood and urine for various components which were done by a local laboratory. The fund allocation of Rs 5,000,000 is indicated in the statement of expenditure for that however the actual expenditure has exceeded this amount due to analysis cost as well as production of placebo and procurement of enalapril etc which are all indicated in the final report

(9) Special Studies –Sociology and economic impact of CKDu and sociological studies & herbal studies

Both these studies were not indicated in the original proposal and emerged as priority studies during the research effort. The detailed reports of both studies are included in the proposal. Although the original budget allocation for these were 5,200,000 as per the statement of expenditure the actual cost was Rs 9,771,531. This was because of the large volume of work involved with the studies and also inclusion of cost for analysis. The socioeconomic study had two components- hospital based and community based and has given many recommendations for implementation which are extremely valuable for policy directions for the government of Sri Lanka. This work has also facilitated a cabinet paper through the Ministry of provincial & local governments to the ministry of social services to increase the financial assistance given to families.

(10) Preparation of final report

Although this is indicated as one activity it entailed preparing the scientific paper as well as data analysis since the inception of the project where the following also was supported:

- Drawing from sample of 800 of stage 1,2,3 (there are four stages that CKDU is categorized into according to the case definition and the severity of the disease) approximately 270 from each category from Anuradhapura district for the next study

- Developing tables for Chronic Kidney Disease of Unknown origin (CKDU) report based on previously analysed data .
- Randomizing & recruiting patients for the double blind study
- Conducting analysis of metal data in environmental and postmortem tissue samples
- Double blind study – to conduct 6 months analysis of recruited subjects in the treatment and control arms
- Conducting 12 month final statistical analysis of effects of ACEI treatment on different renal outcomes of subjects in the treatment and control arms of the double blind randomized control trial

(11) Communication Strategy for public education

A communication strategy had not been devised for CKDu and with the emergence of the research findings there were many consultations, scientific sessions, meetings both at central and district level that were supported using these funds. Advocacy documents on the interim research findings were prepared. As some of the original budget lines had exceeded their capacity it was covered from this budget line. All this was due to the emergence of new research findings and priority areas and the need for analysis of other samples than originally anticipated and where unit costs had also exceeded the original amount

Un-certified statement of income & expenditure for the period 01 November 2010 to 31 December 2012 issued by WHO regional office for South east Asia

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR SOUTH-EAST ASIA



ORGANISATION MONDIALE DE LA SANTE
BUREAU REGIONAL DE L'ASIE DU SUD-EST

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Extension :

21 January 2013

VOLUNTARY FUND FOR HEALTH PROMOTION

Contribution from National Science Foundation, Sri Lanka
Investigation & Evaluation of Chronic Kidney Disease of Uncertain Aetiology in Sri Lanka

Un-certified Statement of Income and Expenditure for the period 01 Nov 2010 to 31 Dec 2012
(Interim)
(expressed in US dollars)

Award Number: 57445

Income

Receipts	585,058
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Encumbrances/Expenditure

Expenditure

2010-11	250,948
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2012-13	<u>223,158</u>
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	474,106
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Encumbrances	<u>70,668</u>
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	544,774
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PSC@13%	<u>70,821</u>
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	<u>615,595</u>
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Deficit

	(30,537)
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Notes:1) The above figures are inclusive of PSC.

2) The encumbrances of \$70,668 will be liquidated (converted into expenditure) at a later date. Therefore, PSC on encumbrances will be adjusted accordingly upon their final conversion.

"The information provided in this report is drawn from the WHO Integrated Management System. This is an informational only report and has not been certified by the Chief Accountant. Certain period end adjustments may not be reflected in this report".

Budget & Finance Officer

SECTION 7

- i. Grantees' signatures
- ii. Comments of the Head of the Department/signature – No comments
- iii. Head of the Institution's signature

Dr F.R.Mehta
Country Representative
World Health Organisation