

Ministry of Health Sri Lanka

Clinical Practice Guidelines for Primary Care Doctors

Identification and Management of Acute Dengue Infection

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Identification and Management of Acute Dengue Infection

EPIDEMIOLOGY UNIT

MINISTRY OF HEALTH

This document includes the latest concepts on early identification and management of acute dengue infection. It is an extension to the existing National Guidelines on Clinical Management of DF/DHF in Children, Adolescents and Adults, published by the Epidemiology Unit, Ministry of Health in 2012.

These guidelines were developed based on the best available evidence at the time of writing. It will be revised periodically when new evidence becomes available.

Please forward your comments and suggestions to the following address by post or e-mail.

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FOREWORD

Dengue illness continues to be a major health problem in the South and Southeast Asian regions and Sri Lanka is no exception. The Out-Patient Departments of most hospitals and General Practice Clinics in Sri Lanka are seeing increasing number of children, adolescents and adults suspected of dengue infection. In this backdrop, growing number of patients seek hospital admission particularly late, with dengue shock/prolonged shock resulting in poor outcome. Further, the COVID-19 pandemic is placing an immense pressure on healthcare and public health systems worldwide.

This Guideline on Early Identification and Management of Acute Dengue Infection, developed by the Epidemiology Unit, Ministry of Health in collaboration with the Sri Lanka College of General Practitioners, is expected to help primary care physicians to closely follow-up fever patients in order to identify Dengue illness early and to refer/admit on time for hospitalized care. This Guidelone will help to further improve existing knowledge and bridge any gaps on this subject. I take this opportunity to thank all the experts who were involved in developing this Guideline.

This authoritative document should be used at the first contact level of health care provision in both public and private settings in Sri Lanka for the management of Dengue and Dengue Haemorrhagic Fever patients. I am sure this will help in strengthening early detection, provision of ambulatory care and timely referral of suspected severe patients for hospitalization in order to reduce complications and deaths due to dengue in Sri Lanka.

Dr. Sudath Samaraweera

Chief Epidemiologist

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1 INTRODUCTION

In the present hyper-endemic setting in Sri Lanka, dengue illness (Dengue Fever [DF] and Dengue Haemorrhagic Fever [DHF]) should be considered in the differential diagnosis of all patients presenting with acute onset of fever. Dengue shock should be considered in any person who presents with a history of acute febrile illness (with or without fever at presentation) and haemodynamic instability with poor peripheral circulation.

Traditionally, DHF was more common in children less than 15 years of age in association with repeated dengue infection (secondary infection) caused by a different virus serotype. However, currently, the incidence of DHF in adults is increasing. Unlike in DF where patients usually will have a brief febrile phase followed by the convalescent phase, in DHF, patients will have a transient plasma leakage into interstitial and serosal spaces (known as the critical phase). Increased vascular permeability (leading to plasma leakage) and abnormal haemostasis (which can cause bleeding) are the main pathophysiological hallmarks of DHF.

If not diagnosed and managed in time, plasma leakage in DHF has a tendency to progress to hypovolaemic shock (dengue shock syndrome [DSS]). Preceding warning features such as persistent vomiting, abdominal pain, lethargy, restlessness or irritability and reduced urine output are important for early detection of impending shock. In such patients appropriate interventions will prevent shock and its complications.

Primary care physicians should closely follow up fever patients to identify dengue illness early. Patients should be given proper ambulatory care with counselling for warning features. Physicians should be vigilant to identify plasma leaking early and refer on time for hospitalized care.

2 NATURAL COURSE OF DENGUE ILLNESS

Dengue virus infection may be asymptomatic or cause a spectrum of symptomatic disease such as undifferentiated febrile illness, dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS). Among symptomatic dengue patients, DF and DHF are the most significant two clinical entities encountered which are considered collectively as Dengue Illness as they are clinically indistinguishable (i.e. similar) in the initial phase.

DF and DHF are distinct from each other as DHF is characterized by a period of transient plasma leakage due to increased capillary permeability which is specifically noted in the pleural and peritoneal spaces. When the leaking is massive and not therapeutically compensated, resulting hypovolaemia in the vascular space may lead to DSS. The leaking phase, known as the 'critical period' usually lasts for 24-48 hours. DF is commoner than DHF.

While DF progresses to a convalescent phase as the temperature settles, DHF patients slip into a critical phase. Hence, the hallmark of DHF is plasma leakage which is not seen in DF. The risk of developing DHF is higher in individuals who have had dengue previously (i.e a secondary dengue infection). Haemorrhage (apparent or concealed) is more likely in DHF, though it can also be seen in DF.

Signs and Symptoms of Clinical Dengue Fever (DF)

- Acute onset of high-grade fever (Day 1 to 7) with body aches, facial flushing/ diffuse blanching erythema of the skin, back pain, myalgia, arthralgia, retroorbital pain, headache, nausea, vomiting, anorexia and skin rash are commonly seen.
- Some patients may present with atypical manifestations of respiratory symptoms; cough, coryza, rhinitis or injected pharynx and gastrointestinal

symptoms; constipation, colicky abdominal pain, diarrhoea or vomiting with or without the classical clinical presentations described above.

- Fever associated with respiratory symptoms should not exclude the possibility of Dengue illness. Even if such symptoms are suggestive of Influenza, patients should be monitored during febrile phase (with serial FBC) and treated symptomatically.
- Minor bleeding can manifest as petechial haemorrhages, mucosal bleeding or epistaxis. However, bleeding may be heavy in some patients if they had been treated recently with medications such as Aspirin, NSAIDS, steroids or longterm anti-platelet drugs.
- Occasionally, unusual haemorrhage such as gastrointestinal bleeding, hypermenorrhea and massive epistaxis may occur. Excessive GI bleeding is especially seen in those having an underlying peptic ulcer disease.

Physical examination may reveal no focus of infection except facial and skin flushing with posterior cervical lymphadenopathy, in some cases.

Currently in Sri Lanka patients may not show all classical features of dengue infection described above. However, presence of fever with at least 2 signs and symptoms mentioned above with leucopenia \pm thrombocytopenia are sufficient to consider 'probable' dengue illness (i.e. Fever +2+2).

Features of Dengue Haemorrhagic Fever (DHF)

In the first few days of DHF, patients will have signs and symptoms similar to DF. However, in DHF, (usually beyond day 2) patient will develop features of **Plasma Leakage \pm Bleeding** which are the hallmarks of DHF. Abnormal haemostasis in DHF can cause concealed or overt bleeding which may be significant in some patients.

Features of DHF includes:

- 1. Fever: acute onset high fever or recent history of acute fever
- 2. Haemorrhagic manifestations* (at least as a positive tourniquet test)
- 3. Thrombocytopenia of $<130 \times 10^{9}$ /L with a rising HCT (towards 20%)
- 4. Objective evidence of selective capillary plasma leaking into chest and abdominal cavities (visualization of fluid in the peritoneal cavity and pleural space by real-time ultra sound scan of the abdomen and chest).
- * In patients who have evidence of plasma leakage, presence of haemorrhagic manifestations in the early stages is not essential for diagnosis of DHF. However, DHF patients may develop overt or concealed bleeding during the course of the illness later.

Laboratory Findings of DF and DHF

Viraemia in a Dengue patient is short, typically occurring a day or two before the onset of fever and lasts for up to four to seven days of illness. During this period the Dengue virus, its nucleic acid and circulating viral antigen can be detected. Viral antigen detection (NS₁) has become a common early diagnostic tool, with the availability of rapid test kits in the market.

While rapid NS₁/IgM tests will provide an aetiological diagnosis, a negative result should not exclude Dengue if clinically suggestive.

NS1 Antigen and IgM/IgG Antibodies

Results depend on the tested day of fever; NS1 is usually diagnostic on first 3-4 days. Anti-dengue IgM antibody is usually detectable by day 5 of the illness or later, i.e. NS1 is positive only during the first few days of illness. **Therefore, if clinically suggestive of dengue, even if NS1 is negative, consider dengue as a possibility and manage accordingly**.

In most patients, Anti-Dengue IgM may persist up to about 60 days. In primary infection IgG is usually detectable after IgM and in a secondary infection, IgG will become positive much earlier. Therefore, IgG might be useful to differentiate primary and secondary dengue infections. If IgG is positive by day 3 it would indicate a secondary infection and may have some use in predicting DHF. However, these antibody test results could also depend on the sensitivity and specificity of the commercially available test kits.

In specialized laboratories with molecular biology facilities *RT-PCR* remains the gold standard of aetiological confirmation. The advantage of this test is its high sensitivity and specificity on acute sample and ability to identify the viral serotypes.

Full Blood Count (FBC)

- Fever (or history of fever) and other clinical features with leukopenia (WBC <5,000 cells/µl), is strongly suggestive of Dengue in endemic areas. Serial FBC may show a drop in the total WBC count with a significant reversal of lymphocyte to neutrophil ratio with atypical cells seen in the blood picture.
- Progressive decrease in WBC count is an early indication of Dengue.
- Thrombocytopenia ($<150 \times 10^9/L$)
- Haematocrit (HCT) could be normal or high

Epidemiologically, Dengue is endemic (i.e. constantly reported year round) in many parts of Sri Lanka. In such endemic areas dengue transmission occurs in clusters (i.e. several patients being reported from one locality during a particular time period). Therefore, the treating clinician should ask for a history of diagnosed cases of Dengue in the family or immediate neighbourhood during the past two weeks when a febrile patient presents to the doctor (i.e. spacio-temporal clustering). However, practitioners in non-endemic areas are likely to receive isolated patients who have acquired dengue infection from endemic areas (due to travelling), particularly during outbreak seasons.

In a febrile patient or patient with recent history of fever, thrombocytopenia (patelets<150,000/mcL) and positive IgM antibody test may suggest of current dengue infection.

3 RISK ASSESSMENT AND EARLY IDENTIFICATION OF DISEASE SEVERITY

When confronted with a fever patient suspected of having dengue infection the primary care clinician should make an early assessment to identify leaking based on duration of fever, presence or absence of warning features of plasma leakage, vital parameters including UOP (Urine Output) and values of a fresh Full Blood Count (FBC) done within 4 hours. If there is no immediate risk (plasma leakage +/- bleeding) such patients should be reviewed daily or more often. Patients with a tendency to have plasma leakage or any other complications should be referred to a hospital for specialized management.

Following risk assessment guide can be used when reviewing such patients.

Fever	Warning Signs (WS)	Vital Signs (VS) and UOP	Fresh FBC Findings	Patient's Risk Status at the time of Assessment
Short duration	Absent WS	Normal VS and Normal UOP	 WBC low (Leucopenia) Plt. >130x10⁹/L HCT 35-40% (or baseline) 	NO IMMEDIATE RISK *
fever within last ≤ 48 hours)	Positive WS	Deranged VS Reduced UOP	 WBC low (Rising trend) Plt. < 130x10⁹/L Increasing HCT → Leaking Decreasing HCT → Bleeding 	HIGH RISK **

Figure 3-1: Risk Assessment of a Dengue Patient

* "No immediate risk" patients should be followed up and assessed/monitored regularly. If moves into the high-risk status, should be referred to HDU

care.

** High-risk patients need clinical assessment and managed by a Senior Doctor.

Examples:

- Fever for 2 days with no WS and stable VS with a good UOP, fresh FBC shows WBC 4600 and PLT 160x10⁹/L, HCT 38% has no immediate risk of leaking. Hence, patient should be educated about Warning Features of leaking and given ambulatory care. Such patients should be reviewed on the following day.
- Fever for last 5 days with excessive vomiting and R/S abdominal pain for 3 hours. On examination has normal pulse and BP but not passed urine for 4 hours. Fresh FBC revealed WBC 2100, PLT count of 90x10⁹/L. This patient needs immediate referral to the nearest hospital.

Any patient suspicious of having a risk of DHF

should be immediately referred to a hospital

with a referral letter

Note:

Risk assessment tool given above is not applicable to pregnant dengue patients. Pregnant women with Dengue should be admitted to a hospital with adequate facilities early during the course of the illness, for further evaluation by a multidisciplinary team.

4 ROLE OF THE PRIMARY CARE PHYSICIAN

Following are the roles of a Primary Care Clinician:

- 1. Early identification of Dengue from other febrile illnesses (OFI)
- 2. Plan and execute ambulatory care management
- 3. How to differentiate DHF from DF
- 4. Referral of an at-risk patient (early DHF and DF with complications) to secondary care management.
- 5. Stabilize a patient in shock (i.e. DSS) before referring to the hospital.
- 6. Counselling at each stage of presentation
- 7. Notify on clinical suspicion to the area Medical Officer of Health (MOH) where patient has resided two weeks prior to the illness.

Early Identification of Dengue illness

- Patients presenting with fever from a dengue endemic area, especially during the monsoon season or during an outbreak of dengue consider dengue as the initial diagnosis.
- High fever (>40°C or >100°F) measured with a reliable thermometer with two or more accompanying features (Ref. Chapter 2) is suggestive of Dengue illness.
- A fresh FBC (preferably done within the last 4 hours) with Leucopenia (<5000) and petechial rash has a 80% positive predictive value of Dengue illness.
- RDT-NS1 test is likely to be positive during the first 3-5 days gives a diagnosis of dengue.
- When NS1 is positive and FBC already not done, do early FBC to get baseline values.

Differentiating Dengue Fever (DF) from Dengue Haemorrhagic Fever (DHF)

The major difference in DF and DHF is the presence of plasma leakage in DHF.

4.1.1 Early evidence of plasma leakage

- Usually occurs when fever is settling or has settled (**Defervescence**)
- Not gaining appetite (persistence LOA even after settling of fever)
 - > In DF appetite improves with settling of fever
- Haemodynamic changes
 - Tachycardia with low volume pulse
 - > Narrow pulse pressure
- Reduced urine output
- Full blood count changes
 - ▶ WBC (tendency to rise compared to immediate previous value)
 - > PLT (less than 100,000 cells/mm³ or a rapid fall)
 - HCT/PCV (rising towards 20% of baseline HCT. Compare the first HCT in febrile phase)
- USS evidence (if available)
 - Presence of fluid in pleural and/or peritoneal cavities confirms plasma leakage in DHF

In adults, HCT rise is an important early indication of plasma leak even in the absence of changes in vital signs. (E.g.: Absence of tachycardia and narrow pulse pressure)

Referral of an At-risk Patient to Hospital

Refer patient to secondary care hospital for specialized management with a *detailed referral letter* for admission (see details below).

Identification of "impending shock" and "shock" (late presenter)

Transient increase in capillary permeability occurs selectively into the pleural/peritoneal cavities leading to plasma leakage between 2 to 7 days in DHF. Excessive extra vascular leak, if not treated adequately, could lead to impending shock or shock. It is vital to identify such patients who need stabilization prior to referral.

The following are signs and symptoms of shock or impending shock.

- Narrowing of Pulse Pressure ≤20 mmHg (PP=Systolic BP[sBP] Diastolic BP[dBP])
- Hypotension older children and adults may present with postural hypotension /giddiness (sBP ≤80 mmHg in adults and ≤90 mmHg in children and adolescents)
- May present with clinical signs of shock
 - Rapid and weak pulse
 - Delayed capillary refilling time (>2 sec)
 - Cold clammy skin or skin mottling
 - Normal or low sBP
 - > Poor urine output
- Rising haematocrit \geq 30% and thrombocytopaenia (around 50 x 10⁹/L)

Any patient in 'impending shock' or 'shock' should be refereed to hospital: **Immediately** (*if early access to a hospital is possible*)

OR after Resuscitation and Stabilization (*if immediate access is difficult*).

Management of Patient in Shock

- Administer Normal Saline (NS) bolus over one hour (10 ml/kg/hr in children or 350-500 ml/hr for adults)
- Correct hypoglycemia
 - If CBS <70 mg/dl administer 25% Dextrose 25-40 ml IV for adults
 - > Oral sugar solution sips for children or IV 10% Dextrose
- Refer to secondary care with a referral letter.
 - A good referral letter should include;
 - ✓ Age and weight
 - ✓ locality of the patient (whether endemic or non-endemic)
 - Medication history (NSAIDs/ steroids/ long term Aspirin/ anti-platelet drugs/ antibiotics and any non-allopathic treatments)
 - ✓ Spatio-temporal clustering NS1 positive or not
 - ✓ Associated comorbidities (e.g. DM, HT)
 - ✓ co-infections (e.g. URTI, UTI)
 - ✓ Temperature (recorded by the patient)
 - ✓ Urine output and fluid intake chart over the past few hours
 - ✓ Pulse (rate and volume)/ BP / Pulse pressure
 - ✓ Peripheral perfusion (cold extremities and CRFT)
 - ✓ Lab reports including FBC & liver function tests (if available)
 - ✓ Tentative diagnosis and treatment/advice already given

5 COUNSELLING AND MANAGEMENT

Counselling:

The importance of establishing a good relationship with the patient and family members from the time of first visit cannot be over emphasized. This can be easily established by primary care doctors due to already built up good communication with the patient.

Counselling should include the following;

- 1. **Discussion about the nature of the illness**, its natural course, the possible outcomes and treatment options.
- 2. Information should be given regarding favourable outcomes of dengue, with appropriate management. However, information must also be given regarding ambulatory care and early referral to hospital when required.
- 3. **Develop an easy communication channel** (by telephone or social media) for information sharing regarding the progression of the disease (and laboratory reports).
- 4. **Maintain a patient record** (with the doctor) including temperature, vital signs (HR, BP and RR) and UOP. All investigations including FBC should be recorded sequentially. Patient should be requested to maintain a record of temperature, fluids consumption and chart UOP.
- 5. Reassure the patient and family members that dengue illness is not fatal and full recovery can be ensured if timely and appropriate management is given.
- 6. **Identify the patients' inherent fears and counsel accordingly** by providing scientific answers on misconceptions and fears.

Management at primary care level;

Management of patients at the primary care level includes the following;

- 1. Early identification of dengue illness and appropriate ambulatory care (Section 0 above)
- 2. Timely referral of probable DHF patient for specialized management (Section 0 above)
- 3. Identification and stabilization of patients presenting in shock before referral (Sections 0 & 0 above)

Advice on ambulatory care (home based)

Fever patients with a platelet count more than $130 \ge 10^9$ /L (done within last 2 hours) and clinically stable (i.e. normal vital signs and without any warning features) can be managed as outpatients.

Advices during ambulatory care:

- Suitably document relevant clinical signs and symptoms together with serial FBC reports.
- Advice on how frequent to repeat FBC
 - If platelet count is between $150-200 \ge 10^9$ /L, repeat on at least twice-a-day.
 - If platelet count is less than 150 x 10⁹/L, repeat FBC at least 3 times-a-day (*If platelets drop rapidly, consider admission to hospital*)
- Advice on warning features of plasma leakage in DHF



Note: Some patients with plasma leaking may not show any warning signs. If any of the above features are noted, refer to hospital without delay.

How to control fever?

 Fever should be controlled in children with Paracetamol ONLY (Recommended dose is 60 mg/kg/day in 3-4 divided doses which can be given as 15 mg/kg-six hourly/SOS or 20 mg/kg-eight hourly/SOS per day). In adults, Paracetamol to be given not exceeding 2 tablets 6 hourly (reduce dose for patients with lower body weight).

Paracetamol dose in children or adults should not exceed a maximum of 60 mg/kg/day.

- Use tepid sponging to bring down fever in-between Paracetamol dosing. Soak a clean towel in **moderately warm water**, squeeze the excess water away and wipe the body to reduce fever.
- Patient should rest with minimal clothing, ideally under a bed-net.
- **Do not use NSAIDs** (e.g. Ibuprofen, Diclofenac, Mefenamic acid, Celecoxib, etc.)

(Note: Fever is caused due to viraemia and therefore, antipyretics, in whatever dose, do not shorten its duration.)

• Do not use steroids (eg. Dexamethasone, Prednisolone, Methylprednisolone).

What to eat and drink?

- If the appetite is good, take frequent light and nutritious diet.
- Fluids should include not only water, but certain electrolyte solutions such as fruit juice, white rice kanji, Oral Rehydration Solution (ORS, Jeewani®, king coconut water etc.)

- Do not consume red/brown (or dark) coloured foods and beverages to avoid confusion with blood stained vomitus/stools.
- Drink adequate amounts of fluids to maintain a normal urine output.
- If body weight is between **30-50 kg**, fluid intake in milliliters should be at least **double** the body weight per hour (calculated for 4 hours).
- If the body weight is **below 30 kg** or **above 50 kg**, fluid intake should be adjusted as shown below:

Body Weight	Fluid Volume per hour
05 kg	20 ml
10 kg	40 ml
20 kg	60 ml
30 kg	70 ml
40 kg	80 ml (twice the Wt.)
50 kg	100 ml (twice the Wt.)
>50 kg	100 ml (maximum)

• Unless medically advised, dietary restrictions are not generally recommended

Nausea and Vomiting

- Domperidone (oral or rectal) can be given for nausea and vomiting.
- Look for features of dehydration admit for IV fluids if severe.
- Look for features of hematemesis (black or "coffee ground" vomitus).
- Avoid fatty foods (which can induce vomiting).

How to maintain the urine output?

• Consume at least the minimum recommended amount of fluids to maintain normal urine output.

- Fluid amount for a child for one hour is approximately equal to twice the ideal body weight (in milliliters) to a maximum of 100 ml for 50 kg or more.
- Amount of fluid intake for an average adult is 2 to 2.5 liters per day (unless there is vomiting/diarrhoea).
- Urine could be measured at least every 4 hourly to calculate the output.

Passing urine slightly more than the above expected amount is acceptable. If the urine output is less than the expected amount, patient should consume more fluids to maintain the desired urine output.

Body weight	Urine output per hour	Urine output per four hours
20 kg	20 ml	80 ml
40 kg	40 ml	160 ml
60 kg	60 ml	240 ml

- If the patient feels thirsty, taking additional fluids up to 3-4 times per day could be allowed until the thirst subsides. But if thirst continues, should be reported to the doctor as early as possible.
- Patient should record the fluid intake and the amount of urine passed with time using the following format:

Date and Time	Consumed fluids (ml)	Date and Time	Urine amount (ml)				

N.B. – Special attention should be given to Diabetics with poor glycemic control and pregnant mothers who may pass more urine even without adequate hydration.

Care at home

- Physical rest is highly recommended and patients should preferably be resting at home.
- Make sure patients are not left alone (at home). There should be somebody to look after them.
- Symptoms like repeated vomiting and/or diarrhoea can lead to dehydration. Such patients should seek immediate treatment (without waiting for the next appointment to see the doctor).
- Patients should avoid other medications especially steroids, during the fever episode. Patients who are on special medications like Warfarin, Aspirin and Clopidogrel should seek medical advice on whether to continue these drugs (as they are not recommended during Dengue fever).

6 REFERRAL FOR SPECIALIZED MANAGEMENT

Referral criteria for specialized management

Fever patients with platelet count less than 130,000/mm³ (even in normal haemodynamic status) - If the platelet count is between 150,000 to 130,000/mm³ the attending doctor should make a decision depending on his/her clinical judgment. If the platelet count (done more than 4 hours ago) is >130,000/mm³, the patient should be reviewed with a repeat count. If the repeat count shows a 'rapid drop', decide on early referral. A 'rapid drop' is considered when the platelet count shows a decline (in 2 consecutive FBC reports done over a short period of time) and the platelet count reaches near to 150,000/mm³. If fever for ≥3 days and a FBC is not done yet, the *patient should be reviewed early with a fresh FBC report* when available to decide on the next course of action.

Please refer the algorithm on Dengue Case Management Reminder for First-Contact / OPD Doctors on Page 39.

- Presence of positive warning signs If the patient is clinically unwell especially after 2nd day of illness (when the fever is settling) may show Warning Signs (WS) as given in Page 14.
- 3. If a **patient insists on admission** refer to hospital for an opinion.
- 4. **Special conditions** needing hospital referral:
 - Pregnant mothers (preferably on 1st day of fever)
 - Children less than 1 ¹/₂ years (<18 months) old
 - Elderly patients

- Patients with co-morbid conditions such as renal disease, ischaemic heart disease or any other major medical problem(s).
- Severe diarrhoea or persistent vomiting which can lead to dehydration.
- 5. **Patients with adverse social circumstances** (eg. living alone, living far from health facility without any reliable means of transportation, those showing poor compliance etc.)
- 6. All patients presenting in shock/complications should be resuscitated and referred when stable to ETU management at the hospital.

7 OUTBREAK RESPONSE PLAN FOR OPD AND GP PRACTICE

Establishing standardized OPD triage for screening of fever patients at the first-contact level during an outbreak

Fever patients seeking medical care at a medical facility should be routinely triaged at the out-patient department to decide on ambulatory care or hospital admission (**Fever Room** for short term observation).

Fever patients should not be directly sent to OPD Emergency Treatment Room (ETU) unless presenting with complications (including Shock) to prevent overcrowding of ETU facility which would probably compromise attention to more needy patients requiring close attention.

Fever Room should consist of a Triage Nursing Desk where fever patients will be registered and assessed based on duration of Fever for further assessment to be done by OPD level Medical officers:

- Patients having fever with suspected dengue will be sent to the Fever Room.
- At the Fever Room, the decision on admission or ambulatory care will be taken by an experienced Medical Officer, depending on the clinical picture (Warning Signs & Vital Signs) and Full Blood Count (done within last 2 hours).
- Admissions will get priority according to the decision of the Medical Officer in the Fever Room.
- **RDT-NS1 positivity is <u>not an indication for hospital admission</u>** on 1st day of fever.
- It is important to note that **RDT-NS1 negativity** <u>does not exclude</u> <u>Dengue infection.</u>





8 DENGUE MANAGEMENT IN THE BACKDROP OF COVID-19 OUTBREAK

The COVID-19 pandemic has spread rapidly throughout the globe, overwhelming the capacity of healthcare and public health systems of many countries worldwide. This has led to *increased mortality and morbidity of other diseases* as well, due to the diversion of limited resources towards combating COVID-19. Furthermore, control measures for vector-borne diseases such as Dengue may also be hampered due to this, placing countries at risk of outbreaks of these diseases.

Primary care clinicians should be prepared to detect these diseases without any delay. Failure to recognize Dengue will compromise the clinical management leading to impaired hydration in patients, ultimately resulting in Dengue-related deaths due to preventable complications.

On the other hand, not detecting a suspected COVID-19 patient early, in addition to delayed patient care, will facilitate community transmission of COVID-19 as the patient continues to mingle in the community, unaware of his/her disease status. Therefore, it is vital that the two diseases i.e. COVID-19 and dengue, are identified early in their disease course.

This, however requires vigilance, as both diseases share common non-specific symptoms early on. *Both conditions often present with fever of acute onset* along with other non-specific symptoms such as sore throat, headache, arthralgia and myalgia. However, *anosmia (loss of smell) and ageusia (loss of taste) may be especially seen in COVID-19 infections*. Later on, leucopenia with lymphopenia, thrombocytopenia and elevated liver enzymes may be seen in laboratory investigations.

COVID-19 with dengue as co-infection is also a possibility. These features may lead to difficulties in making an early judgment. Thus, careful consideration is needed before arriving at a final diagnosis. The OPD/ Primary care setting, as the level of first contact, plays an important role in this regard. This chapter presents an overview to differentiate between the two diseases.

Patients with fever can present to the OPD/primary care settings in several ways:

- Following a telephone consultation
- Clinically stable patients seeking treatment
- Patients presenting in shock/ complications

The following should be adhered to in all hospitals and primary care institutions dealing with first-contact clinically stable fever patients:

- Fever patients should be subjected to the COVID-19 screening tool during telephone/ direct consultation (see Figure 8-1: COVID-19 Screening Checklist).
- OPDs in all hospitals/primary care institutions should have a predetermined area (Fever Room) for the examination of fever patients. All patients presenting with fever should be given a medical face mask upon entering the facility and should be directed to the fever room (see Figure 8-2)
- The Fever Room should consist of a Triage Nursing Desk where the patients will be registered and assessed based on duration of the fever (and other symptoms) prior to further assessment by the OPD Medical Officers. Triaging should be done while maintaining a 2 meter-distance with the patient and other standard precautionary procedures for COVID-19 (such as wearing appropriate PPE) should be followed when handling these patients.

Disposition of patients fulfilling COVID-19 case definitions

- All patients suspected of COVID-19 as per the COVID-19 case definition or COVID-screening checklist (Figure 8.1) should be directed to an intermediate/isolation ward (following initial management or resuscitation if needed) and PCR testing arranged to exclude COVID-19.
- However, Dengue should not be excluded solely because a patient meets the COVID-19 case definition. RDT-NS1 test and/or Full Blood Count (FBC) should be considered on clinical suspicion in such patients.

Disposition of fever patients not suspected of COVID-19

- The focus of infection should be determined in patients who do not meet COVID-19 case definition.
- Dengue should be suspected in patients with high fever and those coming from high-risk areas (with spacio-temporal clustering). These patients could be managed in the OPD/ primary care setting and sent home (on ambulatory care), admitted due to comorbidities, admitted due to warning signs or resuscitated and stabilized at emergency treatment unit if presented in shock/complications.

If dengue is suspected, patients who are interviewed through telephone consultations should also be examined in the above manner.

Clinical examination is a vital component in the diagnosis and management of Dengue which should not be compromised at primary care/OPD level.

In an unstable patient, presenting with increased heart rate and respiratory rate with reduced oxygen saturation (<94%), Dengue Shock Syndrome (DSS) should also be considered as a differential diagnosis.

COVID-19 Screening Tool	<u>Yes /</u> <u>No</u>
Look for the presence of associated symptoms	
• Cough	
• Sore throat	
• SOB	
Travel History	
• Returning to Sri Lanka from abroad within the last 14 days	
• History of travel to or residence in a location designated as a high-risk area* within the last 14 days	
History of contact with any of the following persons:	
Confirmed COVID19 patient	
• Home or institutional quarantined patient	
• A person who had been in a quarantine center	
• A person in contact with anybody having above symptoms (COVID19 symptoms)	
• Anyone who had close contact with a foreigner or a returnee from a foreign country who arrived within the last 14 days	

Figure 8-1: COVID-19 Screening Checklist (*Locked-down or Quarantined areas)

The Fever Room

All hospitals/treatment facilities should have a predetermined room allocated for history taking and examination of fever patients.

- The room should ideally be a negative pressure room.
- Fans should be placed such that the blowing is directed to the doctor/physician before the patient, preferably with an exhaust fan to suck out air (see diagram below)
- Staff present in this room should wear appropriate PPE (i.e. surgical masks, gloves).
- Patients should be directed to this room (from the triage area) with clear signposts.
- Maintain a 2-meter distance between patients while being directed to and within the fever room.



Figure 8-2: The Fever Room

9 CASE STUDIES

Case Scenario 1

Primary Care Doctors: Early Diagnosis and First Contact Management

A previously healthy 17-year-old girl (weight 40 kg), presented to her General Practitioner with fever for 2 days along with arthralgia, myalgia, nausea and vomiting. Her younger brother was treated for Dengue Fever a week ago.

On Examination, her temperature was 102°F; hydration adequate; pulse 110/min; BP 110/70 mmHg; extremities warm; throat was inflamed but no other focus of infection.

Q1 How do you arrive at a tentative diagnosis?

- *A1* Acute febrile illness with no focus of infection but a spatio-temporal clustering suggests of dengue illness.
- Q2 What investigations would you like to carry out on her?
- A2 Full Blood Count and RDT-NS1 (if available)

Her FBC showed WBC 3,500/mm³; N 53%; L 44%; PLT 190,000/mm³; HCT 39%; Dengue RDT-NS1 Positive

Q3 What is your advice to this patient and what's your follow up plan?

- A3 Ambulatory care advice as given below;
 - *Fever management* Paracetamol 10mg/kg at 6 hourly and advice on not to take pain killers such as Ibuprofen, Mefenamic acid or steroids.
 - *Fluid intake* at least 80ml/hr (2 x Body Wt) preferably of electrolyte solutions.

- Urine output to maintain at least 120 ml/3 hrs (3 x Body Wt).
- Maintain input & output chart.
- *Diet* soft palatable diet (with less fat)
- *Rest* keep away from strenuous activities and rest at home.
- *Counselling* about Warning Signs of severe disease warranting an immediate return to the consultation for re-evaluation.
- *Follow up* recommend follow up with clinical examination and FBC.
- Notification to MOH

On follow up, patient came on Day 3 with a high temperature $(101^{0}F)$; Good hydration; Pulse 100/min.; BP 110/70 mmHg and normal peripheral perfusion.

A fresh FBC showed; WBC 2,800/mm³; N 41%; L 56%; PLT 167,000/mm³ and PCV 36%.

Q4 How do you interpret the clinical condition? What's your next plan?

- A4 Interpretation should be done based by 4 parameters
 - i. Fever (presence or absence)
 - ii. Vital signs and UOP
 - iii. Warning signs of severe disease and
 - iv. Fresh FBC

Patient was still febrile; tachycardia was proportionate to the fever with normal BP; no warning features and her WBC count has dropped further with Lymphocyte predominance; slowly dropped PLT count from 190 to 167; PCV has dropped by 3 points (possibly due to excess oral intake).

Q5 What other relevant question you like to ask this patient?

A5 Exclude any self-medication for fever (e.g. with NSAIDs)

Drop in PCV has 2 possibilities – excessive fluid intake or internal bleeding (commonly due to NSAIDs). However, internal bleeding is unlikely as the tachycardia is proportionate to fever (allowing 10 beats per every rise in 1^{0} F).

Stress on lookout for Warning Signs (of leaking seen in DHF). Plan on a follow up visit within 24 hrs with a fresh FBC.

Anticipate a plasma leakage of DHF, if fever settles during next 12-24 hrs, in the background of lymphocyte predominance in WBC report.

On the same evening, the fever settled but she started to vomit and developed giddiness when walking to the toilet. She also complained of excessive thirst and right sided abdominal pain with less UOP. She was rushed back to the GP.

Q6 How do you assess and what is your diagnosis and management plan now?

A6 Clinical assessment:

- Check the temperature and vital signs level of consciousness; cold or warm extremities; CRFT; PR & volume; BP & PP; liver tenderness; evidence of fluid in chest & abdomen cavities and input output chart.
- Clinical findings Afebrile; there was 'coffee ground' vomitus; dehydration+; PR 110/min with poor volume: BP 110/90 mmHg (with PP=20); bilateral normal air entry in lungs; cold extremities with CRFT>2s; GCS 15/15
- Investigation findings Urgent FBC WBC 2,900/mm³; N 33%; L 66%; PLT 80,000/mm³; PCV 48%; and CBS was 60 mg/dl

Based on above findings – a rapid drop in PLT crossing $100,000/mm^3$; PCV rise 20% (baseline was 39%) and WBC slight elevation compared to previous value with significant reversal of N & L ratio, these features indicate leaking phase of DHF with early features of compensated shock (as PP=20 mmHg).

- Management Give O₂ via face mask; insert wide bored IV cannula and infuse NS (bolus) 500cc over one hour (at 10 ml/kg/hr); Give Dextrose 10% 80ml via IV push (at 2ml/kg).
- *Write clear referral note with details* and inform the nearest hospital and send the patient for further management of DHF.

A 23 year old female with fever in her 2nd uncomplicated pregnancy (POA 32 weeks) presented with fever with chills, headache and abdominal pain of 1 day duration to the OPD of a Teaching Hospital. There was an ongoing dengue outbreak during this period. The doctor at OPD after examining her ordered FBC, UFR and NS1/IgM/IgG.

- *Examination findings* febrile (101⁰F); HR 100/min; BP 120/60 mmHg (PP 60); warm extremities; foetal movements + and normal FSH; there was no bleeding tendency.
- Investigations WBC 8,200/mm³; N 86%; L 6%; PLT 185,000/mm³; PCV 33.3%; RDT-NS1/IgM/IgG all were negative; UFR - Albumin+, pus cells 4-6, red cells 15-20, epithelial cells+, organisms+.

The OPD attending doctor considered a possible diagnosis of UTI as NS1 was negative and prescribed oral Co-Amoxyclav after taking urine for culture/ABST and requested the patient to come back in 2 days for further follow up.

Q1 Comment on the above scenario:

- *A1* Although RDT-NS1 was negative, Dengue as a possible differential diagnosis should be considered due to ongoing outbreak in the community.
 - Pregnant women with fever should be admitted to hospital for further investigations and management.
 - Therefore, FBC should have been requested in 24 hours even when deciding against hospital admission.

Patient retuned to the hospital OPD on Day 3 of illness complaining of reduced foetal movements with abdominal and back pain. A fresh FBC showed WBC 4.860/mm³; N 79%; L 12%; PLT 70,000/mm³; PCV 36%; CRP was 11.

She was admitted to hospital for further management on suspicion of pyelonephritis and Dengue was not considered as RDT NS1 was negative.

Q2 Comment on the above findings and management.

- *A2* Leucopenia and a drop in PLT below 100,000/mm³ with no significant elevation of CRP should alert of a possible Dengue illness requiring further investigation and follow up.
 - Dengue should be suspected early in any febrile patient with leucopenia (<5000 cells/µl), a drop in PLT count <150,000/mm³ and a rise in hematocrit (in that order) together with any petechial rash or any bleeding tendency.
 - If in doubt of aetiological diagnosis, repeating NS1 with IgM/IgG may be helpful when FBC is suggestive of dengue illness. However, NS1 may be negative in secondary dengue illness and with some serotypes and may also be time dependent. Appearance of IgG with negative IgM on day 3 is suggestive of secondary acute infection in the background of FBC changes. Also, change of IgM negative to positive in a suspected patient from viraemic to non-viraemic phase is confirmatory of dengue infection (usually occurring beyond day 5-7).
 - Since utero-placental blood flow has no auto-regulation it depends on maternal mean arterial blood pressure for its blood flow. Therefore, foetal distress may be the first indication of maternal haemodynamic decompensation in pregnancy with DHF leaking. Therefore, a febrile pregnant patient with foetal distress should alert the clinicians regarding this possibility and investigations and management be focused accordingly.
 - Patients who fall into high-risk categories (infants, obese, pregnant or elderly patients and those with co-morbidities such as DM, HT, IHD, CKD, Cirrhosis or any other) should be admitted to hospital early.

10 HEALTH EDUCATION ON DENGUE PREVENTION AND CONTROL FOR PATIENTS AND FAMILIES

Transmission of the dengue virus depends on biotic and abiotic factors. Biotic factors include the virus, vector and the host. Dengue infection is transmitted by female mosquitoes of genus *Aedes aegypti* and *Aedes albopictus*. Out of these two, *Ae. aegypti* is the major (primary) vector that causes epidemics; while *Ae. albopictus* is an important secondary vector that may cause epidemics when its density is high. Abiotic factors include temperature, humidity and rainfall.

Dengue virus is a member of the family Flaviviridae consisting of four virus serotypes, which are designated as DENV-1, DENV-2, DENV-3 and DENV-4 with extensive genetic variability within each serotype. An individual can theoretically get 4 dengue infections while the second infection from a different serotype could become a more severe infection.

The human host, of any age, if bitten by an infected female dengue mosquito has a chance of getting dengue illness. Further, the infected person's age, any previous exposure to different or infecting serotype will determine the nature of the illness. Symptoms following an infection usually start about 4-10 days (incubation period is typically 4-7 days) after a mosquito bite which transfers the virus.

To date, vector control is the mainstay of dengue prevention and control. Therefore, application of appropriate vector control interventions depend on good knowledge on vector ecology, biology, behaviour (bionomics), efficacy and effectiveness of the vector control methods.

Dengue Vectors

The lifecycle of *Aedes* mosquito has 4 distinct stages, with the egg, larva and pupa stages being aquatic and the adult stage being terrestrial. Time taken to emerge as adults from eggs is usually 7-10 days depending on the environmental factors.

Eggs: Female mosquito lays several eggs at a time on damp inner surface of wet containers just above the water level, preferably with clear water. Eggs can hatch within 2 days to become larvae. However, *Aedes* eggs can withstand even extreme dry weather conditions and retain its viability for up to six months or longer.

Larva: Developing larvae feed on organic matter contained in the water and undergo 4 developmental larvae stages lasting up to 4-5 days. The last stage of the larva is a non-feeding stage.

<u>Pupa</u>: This is the final aquatic stage before the adult mosquitoes emerge. Pupa is comma shaped and non-feeding and will develop into an adult in 1-2 days.

<u>Adult:</u> Adult mosquitoes are small to medium in size, dark in colour with white markings/bands on the body. Longevity of adult can range from 2-4 weeks depending on environmental conditions such as temperature and humidity. *Aedes* mosquitoes are different from *Anopheles* (which cause Malaria) and *Culex* mosquitoes (which cause Filariasis/Japanese Encephalitis) by the external morphological features, ornamentation and resting positions. *Aedes* mosquitoes lie parallel to the resting surface and they have black and white scales on the body and legs arranged in different patterns.

Aedes Vector Bionomics (behaviour)

Primary care doctors should be able to educate their patients regarding the breeding sites, resting and feeding habits and flight range of the *Aedes* mosquitoes responsible for transmitting the Dengue virus within the community.

Vector breeding sites: Dengue vectors are mostly container breeders and they lay eggs in a wide variety of containers, receptacles, and temporary water collections preferably holding clear (unpolluted) water. Such breeding sites are found within and outside buildings, both residential and non-residential, at ground level as well as above ground level, even in places such as overhead tanks, roof gutters and concrete slabs where small amounts of rain water can get trapped. The female *Ae. aegypti* mosquito lays her eggs in a number of containers in a single oviposition cycle ensuring maximum survival of her offspring. It produces up to 100 to 200 eggs at a time and can produce up to 5 such cycles during its lifetime.

Most common breeding sites of Ae. aegypti in Sri Lanka are:

- Discarded receptacles plastic containers, tins, clay pots, bottles, cans coconut shells, damaged ceramic items etc.
- Water storage containers uncovered cement/plastic tanks and barrels.
- Discarded automobile tyres and machinery parts.
- Building structures open concrete slabs, lift wells, unused toilets, roof gutters, shallow cemented wells.
- Appliances and ornaments refrigerator trays, flower vases, bird baths, ornamental ponds, abandoned fish tanks, cut bamboo stumps and bromeliad leaf axils.

It is noted that the predominant mosquito breeding sites may vary from area to area and during wet and dry seasons. Therefore, a good understanding about the breeding sites and any interventions applied accordingly will help to minimize the mosquito breeding and mitigate emergence of outbreaks.

<u>Adult mosquito resting, feeding and flight range:</u> *Ae. aegypti* primarily rests in dark and humid areas or secluded hanging objects inside houses or buildings - on curtains, clothes, underside of furniture and empty containers, whereas *Ae. albopictus* generally rests outdoors in vegetation, empty containers and in other hidden places close to buildings. *Ae. albopictus* is considered as a less efficient

vector for dengue transmission and therefore, if found to be the predominant vector species in a given community it is unlikely to cause major epidemics.

Female *Ae. aegypti* is highly anthropophilic (i.e. prefers feeding on humans than other animals) and it tends to feed on more than one person at once for a full blood meal (i.e. a multiple feeder). It also takes more than one blood meal to complete the gonotrophic cycle. This multiple feeding habit and gonotrophic discordant behaviour increases the human-biting rate and thereby greatly increases the efficiency in epidemic transmission.

Aedes mosquitoes are primarily daytime biters with two peak biting times i.e. one in the morning lasting for a few hours after day break (dawn) and another in the afternoon for few hours before dusk. The morning peak biting time falls between 6-11 a.m. and the afternoon peak falls between 3-6 p.m. Although the *Aedes* mosquitoes generally don't bite at night, some may feed on humans at night time in well-lit rooms.

The flight range of adult female mosquitos depends on the availability of human hosts to feed on and the abundance of egg laying sites. Generally, they fly only short distances of less than 100m horizontally to find a human host or a suitable breeding site. Sometimes, they can be found vertically up to many floors in multi storied buildings such as condominiums.

Management and control of dengue vectors

Reducing the impact of dengue infection depends on control of the mosquito vectors or in the interruption of human-mosquito contact. Activities to control transmission should target on reducing habitats favorable for development of immature stages and where applicable restricting and eliminating adult *Aedes* mosquitoes in households (as well as other settings such as schools, workplaces, hospitals, construction sites etc.). Control can be achieved mainly by eliminating

containers that are favourable for egg laying and permit the development of aquatic stages.

Elimination of breeding sites is possible by proper discarding of waste receptacles, maintaining water containers tightly closed with a lid, regularly cleaning flower vases, pet feeders, bird baths, refrigerator trays and roof gutters, and storage of discarded appliances and tyres under a cover without being exposed to rain. Eliminating the aquatic stages of the life-cycle is more effective than attacking the terrestrial adult mosquito.

However, this can be accomplished only if done on a regular and sustainable manner. Especially with the growing number of breeding sites being detected indoors rather than outside, it is difficult to control such sites in the current urban context by field health inspectors unless the community is empowered. Although chemicals are widely used as mosquito control measures for adult vectors and as larvicides, they should be used as complementary to the environmental management and as emergency measures in places such as lift wells and construction sites.

In large containers, cement tanks and open shallow wells which cannot be easily covered to be kept free from mosquitoes, usage of biological control techniques such as larvivorous fish have proven to be very effective. Doctors are good advocates to increase local community's willingness and involvement to rare and distribute native (larvivorous) fish for such sites.

Use of individual personal and household protection techniques are still weak in Sri Lanka. Covering the exposed parts of the body during day-time when mosquitoes are most active, can offer protection and should be encouraged particularly during outbreaks. For young school children and those attending daycare centers and preschools, wearing of comfortable clothes to minimize skin exposure should be encouraged. Repellents applied to exposed skin or to clothing may also provide additional benefit to keep the mosquitoes away. Repellents containing DEET or *icaridin* may be applied according to the label instructions which can give between 4-8 hour protection (depending on the active ingredients used).

Use of chemical repellents to protect infants and children less than 2 years of age is not advisable.

Primary care doctors should encourage fever patients who are suspected to be infected with dengue virus to use mosquito nets when resting especially during day time and to apply mosquito repellents to exposed skin areas as interventions to break the transmission chain. However, insecticide-treated mosquito nets will be a good alternative protection method in such a situation. Doctors should also inquire if any other family members are suffering from fever and encourage them to seek medical attention.

The *Ae. aegypti* is primarily an indoor biting mosquito, and household fixtures such as windows and doors could be screened effectively to minimize access of mosquitoes into the houses. This would be an effective longer term investment. The application of household insecticide/aerosol products (e.g. *Citronella*) may also reduce the biting activity.

ANNEXURES



Clinical Practice Dengue Guidelines for Primary Care Doctors

ж		i to be taken within an hour	do the next FBC		Dengue patients who are on home based care temporarily	f you are positive(+) for dengue NS1 antigen test you may not need	diate hospitalization.	ive NS1 test does not exclude dengue illness.	care should be always guided by a qualified doctor.	al admissious will be determined by platelet count of the latest full blood	(FBC).	والمالية والمالية والمعاملية والمعاملة ومعاملتهم والمعاملة والمعاملة والمعاملة والمعاملية والمعاملية	th home based care during early part of the illness.	al Rest	al rest is highly recommended.	g at home without exerting yourself is ideal.	control	Paracetamol only.	tot use NSAIDs such as Ibuprofen, Diciofenac,	entature actual verecondure etc. tot use steroids such as Prednísolone,	amethasoue etc.	uw your upcore suish ucuons on the duse of acetamol and fever control.	tepid sponging to bring down the fever in between the Paracetamol dosing.	k a clean towel in moderately warm water, then squeeze the excess water y and wipe the body to reduce fever.
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any doubt on how much fluids to drink please ask your doctor.	se a properly calibrated cup to measure t he fluid intake.								цу Сир сир (200ml) Glass (300 ml) t.			eouate amount of fluids are taken to produce a urtre volume per hour in	mi) equal to your body weight in kilograms to prevent dehydration.		ine measurement at least every four hourly to calculate the output.		ight Urine output per hour Urine output per four hours	20mi 80mi		40ml 160ml	60mi 240mi		ne slignuy more than the apoye expected amount is not a promem.	output is less than the expected amount, you should consume more fluids	the above urine output.		ent is feeling thirsty, taking additional fluids up to 3-4 times per day is	ntil the thirst subsides.	t continues. consult your doctor as soon as possible.
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When and how often sh	Do the FBC in 8-12 hour i	Do not delay showing the			doctor immediately.		this fever episode.	Food	If you have appetite take.	Avoid taking red or brown	This may mimic blood sta	Flatds	Fluids should include not	fruit juice, white rice kanj	Drink enough fluids to ma	instructions below to cal	If the body weight is betw	in mililiters (ml) per hou	If the weight is below 30k	below:		Body Weight	5kg	10kg	20kg	30kg	40kg	50kg	>50kg
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