WEEKLY EPIDEMIOLOGICAL REPORT

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Epidemiology and Prevention of Typhoid Fever: Disease Dynamics and Vaccination Part II

This is the second article of two in a series on "Epidemiology and Prevention of Typhoid Fever: Disease Dynamics and Vaccination"

Treatment

Effective treatment for acute typhoid fever and chronic gallbladder carriage of S. Typhi relies on antibiotics if the circulating strains are susceptible. However, the emergence of multidrug-resistant (MDR) strains of S. Typhi, resistant to traditional first-line antibiotics like ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, in the late 1980s led to widespread use of fluoroquinolones. Subsequently, strains with reduced susceptibility to fluoroquinolones emerged in the 1990s and 2000s, with some strains fully resistant to fluoroquinolones like ciprofloxacin and gatifloxacin becoming increasingly common in South Asia and spreading in sub-Saharan Africa. As fluoroquinolone resistance grew, antibiotics such as cephalosporins and azithromycin became preferred choices in affected regions, although resistance to azithromycin remains sporadic.

While extended-spectrum cephalosporins like oral cefixime and parenteral ceftriaxone were reliable until recently, reports of extended-spectrum cephalosporin-resistant strains have increased in Asia and Africa since 2010. The recent outbreak of ceftriaxone -resistant typhoid in Pakistan underscores the importance of understanding local resistance patterns to guide antibiotic selection and management of typhoid fever cases. The S. Typhi H58 clade, carrying MDR genes and fluoroquinolone resistance mutations, has contributed significantly to the spread of resistant strains, emerging on the Indian subcontinent and subsequently spreading to Southeast Asia and sub-Saharan Africa. New resistant clades have also surfaced in Nigeria and the Democratic Republic of the Congo.

Antimicrobial resistance in typhoid fever results in more patients experiencing treatment failure and complications, increased hospital admissions and longer stays, and the necessity of costlier treatment options. Ineffective antimicrobial therapy could also lead to an increase in chronic carriers. MDR S. Typhi has triggered significant outbreaks in Asia and Africa in recent years, and resistance rates can escalate rapidly, as seen in Ho Chi Minh City, Vietnam, where strains with reduced susceptibility to fluoroquinolones surged from less than 5% to 80% within months in 1998.

The escalating issue of antibiotic-resistant S. Typhi underscores the importance of introducing typhoid fever vaccination in high-risk populations. By preventing typhoid fever through vaccination and adequate hygiene, sanitation and health promotion measures, the use of antibiotics can be reduced, potentially curbing the emergence of resistant S. Typhi strains.

Prevention

Effective prevention and control of typhoid fever can be achieved through various strategies, including access to safe water and adequate sanitation, health education, hygiene practices among food handlers, and typhoid vaccination. Enhancements to water supplies, such as filtration and chlorination, have proven effective in reducing the burden of typhoid fever and have even led to its elimination in many high-income settings.

Typhoid vaccines

Repeated clinical episodes of typhoid fever are rare but have been documented, indicating that naturally acquired immunity provides only partial protection following the initial infection(s). It is believed that protection against typhoid fever involves both cell-mediated and humoral responses. After natural infection, specific antibodies are identified in both serum and the gastrointestinal tract.

At present, three types of typhoid vaccines are approved for use: typhoid conjugate vaccine (TCV), unconjugated Vi polysaccharide (ViPS) vaccine and live attenuated Ty21a vaccines. The World Health Organization (WHO) has recommended ViPS and Ty21a since 2008 for controlling typhoid in both endemic and epidemic and epidemic scenarios and these typhoid vaccines are recommended for children aged 2 years and older. Two TCVs have been prequalified by the World Health Organization since 2017, a TCV combines a polysaccharide antigen with a carrier molecule and as these TCV vaccines confer long-lasting immunity, they necessitate only a single dose and can be administered to children as young as six months old.

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Prequalification by the WHO signifies that the vaccine adheres to standards of quality, safety, and efficacy, rendering it eligible for procurement by United Nations agencies like the United Nations Children's Fund (UNICEF). In October 2017, the Strategic Advisory Group of Experts (SAGE) on immunization, an advisory body to WHO, endorsed the typhoid conjugate vaccine for routine administration to children above six months of age in countries where typhoid is endemic. The two prequalified vaccines contain Vi polysaccharide antigen linked to tetanus toxoid protein (referred to as Vi-TT conjugate vaccine to distinguish them from other TCVs with different carrier proteins). SAGE further advocated for the prioritized introduction of the typhoid conjugate vaccine in countries with the highest burden of typhoid disease or antibiotic resistance to Salmonella Typhi. The vaccine's implementation is expected to reduce the frequent use of antibiotics for presumed cases of typhoid fever, thereby helping to mitigate the rise in antibiotic resistance in Salmonella Typhi. Data from immunogenicity studies on TCV indicate that immunity may last for as long as 5 years following initial immunization, with some hints from existing data suggesting the possibility of natural boosting in endemic regions. However, there remains insufficient evidence regarding the necessity for booster vaccinations.

The Vi polysaccharide vaccine comprises OF purified Vi capsular polysaccharide from the Ty2 S. Typhi strain and the unconjugated ViPS vaccine is administered together with hepatitis A as a combined vaccine and is primarily licensed for travellers from non-endemic countries visiting typhoid endemic regions. Data for these combination vaccines demonstrate seroconversion to the component vaccine antigens similar to monovalent ViPS and hepatitis A vaccines. Ty21a is an orally administered vaccine derived from a live attenuated Ty2 strain of S. Typhi, wherein several genes have been attenuated via chemically induced mutagenesis. The resultant vaccine strain, Ty21a, lacks the Vi antigen. Currently, there is no evidence regarding the interchangeability or sequential use of different typhoid vaccines.

The Diarrhoeal Diseases Control Programme in Sri Lanka

The Diarrhoeal Diseases Control Programme was initiated in Sri Lanka in 1983 to reduce morbidity and mortality, hospital admissions, and malnutrition resulting from diarrhoeal diseases. Various activities are being implemented to enhance public water and food hygiene, thereby controlling and preventing intestinal infections, including Enteric fever. These activities include: Educating the public, particularly food handlers in common kitchens on the importance of frequent handwashing with soap and water, ensuring public water supplies are adequately treated with chlorine for drinking and food preparation, encouraging the public to use boiled or cooled water for drinking purposes, training health staff and volunteers to educate the public routinely and especially during disaster situations, on personal hygiene practices and early identification of symptoms of Typhoid fever, establishing isolation facilities in special situations such as camps for internally displaced people, designating at least one toilet facility for patients in isolation areas for enteric isolation, Proper disposal of infected children's stools into identified toilets and enforcing strict handwashing with soap and water after defecation.

Despite nationwide preventive measures, Typhoid and Paratyphoid remain endemic in certain areas of Sri Lanka while outbreaks occur due to disruptions in water supplies and sanitation systems from time to time, therefore the risk of Typhoid fever reaching epidemic proportions persists during specific disaster circumstances such as floods, droughts, landslides, tsunamis, and temporary camps housing large numbers of displaced individuals.

Vaccination for typhoid fever is not widely embraced as a preventive measure in Sri Lanka. However, certain groups or localities indicate an inability to control the disease solely through health promotion for adequate WASH facilities. Therefore, the introduction of Typhoid vaccination has been considered particularly for high-risk groups, to control cases and prevent epidemics. High-risk category of Food handlers, i.e., Individuals involved in food preparation, serving, transportation, or handling, including cooks, bakers, waiters, street vendors, and their helpers have been recommended for TCV vaccination locally. Other risk groups that have been identified by the WHO to potentially benefit from TCV are people lacking proper toilet facilities or access to clean water, close contact with typhoid patients, children experiencing frequent episodes of diarrhoea, individuals consuming water and food from unreliable sources and healthcare workers and other personnel closely interacting with typhoid patients.

The global burden of Typhoid fever remains high, alongside a rapid escalation in the prevalence and dissemination of antimicrobial-resistant strains of S. Typhi. Disease control efforts need to be enhanced, including health education, improvements in water, sanitation, and hygiene (WASH), and training of healthcare professionals in diagnosis and treatment, integrating with preferred vaccination strategies (universal, risk-based or phased) grounded in an analysis of local epidemiological data, cost-effectiveness, affordability, operational feasibility, transmission risk factors and surveillance data.

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Table 1: Selected notifiable diseases reported by Medical Officers of Health 30th – 05th Apr 2024 (14th Week)

RDHS	Dengue Fever		Dysentery		Encephalitis		En. Fever		F. Poisoning		Leptospirosis		Typhus F.		Viral Hep.		H. Rabiies		Chickenpox		Meningitis		Leishmania-		Tuberculosis		WRCD	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	132	4147	0	5	0	3	13	18	1	4	9	141	2	5	0	3	0	0	12	142	0	12	0	0	55	597	100	100
Gampaha	66	1768	2	7	0	4	1	3	1	1	13	203	0	2	0	1	0	0	7	97	4	34	0	6	34	337	87	100
Kalutara	50	1155	1	11	1	1	4	10	0	5	12	218	1	4	0	5	0	0	17	200	0	23	0	0	12	196	93	200
Kandy	47	1564	0	5	0	0	3	3	0	3	9	88	1	9	1	4	0	0	10	185	0	4	2	16	0	175	100	100
Matale	3	307	0	1	0	0	0	1	0	8	2	41	1	1	0	4	0	0	3	31	0	5	4	82	0	37	100	100
Nuwara Eliya	3	172	4	27	0	3	2	3	0	11	3	72	1	16	0	3	0	0	7	67	0	3	0	0	7	83	100	100
Galle	32	993	1	17	0	7	2	3	2	19	18	269	5	43	0	4	0	1	24	209	1	25	0	3	13	133	100	100
Hambantota	13	418	2	8	0	1	0	1	4	32	8	237	0	14	0	2	0	0	11	102	0	12	12	162	0	38	92	100
Matara	17	358	0	2	0	3	2	2	0	4	7	109	0	7	1	2	0	0	10	105	0	38	0	29	5	33	100	100
Jaffna	60	4810	2	24	0	1	0	3	0	15	0	12	8	343	0	3	0	1	4	95	0	6	0	0	10	66	100	93
Kilinochchi	3	261	0	2	0	0	1	2	0	1	2	12	0	7	0	0	0	0	1	2	0	2	0	0	0	7	100	100
Mannar	1	170	0	0	0	0	0	1	0	0	0	16	0	6	0	0	0	0	0	4	0	2	0	1	5	22	100	100
Vavuniya	1	125	0	0	0	0	0	0	0	5	2	52	0	2	0	4	0	0	1	12	0	6	0	5	0	7	100	100
Mullaitivu	3	172	0	3	0	0	0	0	0	2	1	47	0	9	0	0	0	0	0	2	0	0	0	4	0	11	100	100
Batticaloa	16	998	2	48	0	5	2	4	0	12	2	23	0	1	0	6	0	0	9	33	0	19	0	1	6	36	100	100
Ampara	7	136	0	14	0	1	0	0	0	7	1	103	0	1	0	3	0	0	2	50	0	19	0	6	4	68	67	100
Trincomalee	7	396	1	8	0	0	0	1	0	1	6	87	0	9	0	0	0	0	2	21	0	3	0	8	0	18	100	100
Kurunegala	26	1177	1	10	0	11	0	0	0	339	9	232	2	15	0	2	0	2	6	145	4	76	9	156	17	152	95	97
Puttalam	18	592	0	1	0	1	3	3	0	0	5	120	0	5	0	0	0	0	5	50	1	14	0	8	5	58	83	100
Anuradhapura	5	465	0	4	1	2	0	0	1	3	5	185	2	22	0	6	0	0	11	69	0	18	8	252	8	77	96	100
Polonnaruwa	7	178	0	8	0	0	1	1	0	2	6	115	0	1	1	2	0	0	7	57	1	12	17	153	1	27	100	100
Badulla	7	481	1	9	1	3	0	0	0	16	7	207	0	9	0	7	0	0	4	93	0	10	1	9	2	64	100	100
Monaragala	8	350	0	5	1	1	0	1	34	34	9	390	0	13	0	7	0	0	1	35	1	39	8	74	3	29	82	100
Ratnapura	49	857	5	29	0	2	2	2	0	3	43	539	0	10	2	11	0	2	6	99	2	43	0	63	0	63	95	100
Kegalle	25	803	0	3	1	3	3	3	0	2	13	196	0	8	0	5	0	0	14	218	0	19	0	12	8	94	91	100
Kalmunai	8	492	1	9	0	0	0	0	2	2	0	34	0	1	0	1	0	0	7	68	1	6	0	0	4	42	100	100
SRILANKA	**614**	**23345**	**23**	**260**	**5**	**52**	**39**	**65**	**45**	**531**	**192**	**3748**	**23**	**563**	**5**	**85**	**0**	**6**	**181**	**2191**	**15**	**450**	**61**	**1050**	**199**	**2470**	**95**	**99**

Source: Weekly Returns of Communicable Diseases (esurvillance.epid.gov.lk). T=Timeliness refers to returns received on or before 05th April, 2024 Total number of reporting units 358 Number of reporting units data provided for the current week: 356 **C****-Completeness

A = Cases reported during the current week. B = Cumulative cases for the year.

Table 2: Vaccine-Preventable Diseases & AFP

30th – 05th Apr 2024 (14th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2024	Number of cases during same week in 2023	Total number of cases to date in 2024	Total number of cases to date in 2023	Difference between the number of cases to date in 2024 & 2023
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	01	00	00	00	00	00	00	00	01	00	21	23	-8.7 %
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Mumps	00	00	00	01	00	02	01	00	02	06	02	78	63	23.8 %
Measles	00	01	01	01	00	00	00	00	00	03	00	180	00	0 %
Rubella	00	00	00	00	00	00	00	00	00	00	00	01	01	0 %
CRS**	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Tetanus	00	00	00	00	00	00	01	00	00	01	00	01	01	0 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Japanese Enceph-alitis	00	00	00	00	00	00	00	00	00	00	00	01	02	-50 %
Whooping Cough	01	00	00	00	00	00	00	00	00	00	00	02	03	33.3 %

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

NA = Not Available

Take prophylaxis medications for leptospirosis during the paddy cultivation and harvesting seasons.

It is provided free by the MOH office / Public Health Inspectors.

Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

ON STATE SERVICE

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