MOST URGENT

No.F.1-22/Advisory/FEDSD/2019
Field Epidemiology & Disease Surveillance Division
National Institute of Health, Islamabad
Phone: (92-051) 9255237 Fax: (92-051) 9255099
National Focal Point for International Health Regulations

July 2020

Subject: **Advisory for Prevention and Treatment of typhoid fever including XDR Typhoid**

Purpose: Typhoid fever is endemic in Pakistan and outbreaks of Extensively Drug Resistant *Salmonella* Typhi (XDR *S.*Typhi) have been reported since 2016 from different parts of the country, especially during summer and monsoon season. This XDR *S.*Typhi is resistant to commonly used antibiotics such as ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, fluoroquinolones and third generation cephalosporins. The XDR *S.* Typhi is sensitive only to carbapenem (Meropenem) and macrolide (azithromycin).

Keeping in view the seasonal trend of XDR Typhoid, it is important to take necessary measures to limit its transmission through preventive measures, early detection, using recommended diagnostic tools and prompt treatment. This advisory aims to alert the health authorities for timely actions for preparedness for prevention and control of typhoid fever including XDR Typhoid. Moreover, the health departments must involve other line departments such as WASA, Public Health Engineering, District and Local Administration for preparedness and response.

Case Definition:

Suspected Case: Any person with history of fever of at-least 38°C for 3 or more days with abdominal symptoms like diarrhea, constipation, abdominal tenderness and prostration.

Confirmed Case: A suspected/ probable case that is laboratory confirmed by isolation of *S.* Typhi from blood/ stool or urine.

Classification of Typhoid Fever Cases by Drug Resistance in Pakistan (WHO-2018):

Non-resistant Typhoid fever: Typhoid fever caused by *S.* Typhi and/or *Salmonella* Paratyphi A, B or C strain which are sensitive to first-line drug and third generation cephalosporins, with or without resistance to second-line drugs.

Multi-drug resistant (MDR) Typhoid fever: Typhoid fever caused by *S.* Typhi and/or *Salmonella* Paratyphi A, B or C strain which are resistant to the first-line recommended drugs for treatment, with or without resistance to second-line drugs.

Extensive Drug Resistance (XDR) Typhoid: Typhoid fever caused by *S.* Typhi strain which are resistant to all the recommended antibiotics for typhoid fever.

Mode of Transmission: Typhoid infection occurs through feco-oral route and infection spreads through contaminated food, milk, frozen fruits and water or through close contact with already infected persons. The contamination of food and water usually occurs due to poor sanitation and mixing of sewerage water with drinking water.

Incubation period depends on the inoculum size and host factors; 3 days to more than 60 days with a usual range of 8 to 14 days. Preschool children are at greater risk of developing disease and usually have milder symptoms than the adults do. Travelers to, or workers in endemic areas and care givers of the patient infected with *S.* Typhi are also at higher risk.

Diagnosis:

- S. Typhi can be isolated from blood during the first week of illness or from stool and urine after the first week of illness.
- Widal and Typhidot have ***NO diagnostic value*** due to limited sensitivity, specificity and cross reactivity and must be stopped immediately by all labs.

Treatment: Suspected patients having history compatible with case definition(s) should immediately seek medical advice from health care facilities. Sample should be collected for culture & sensitivity before starting the empirical therapy from all the suspected cases. Unnecessary use of antimicrobial agents should be discouraged to treat the patients presenting with fever. To limit the antimicrobial resistance (AMR), antibiotics should be prescribed based on the results of culture and sensitivity test. The XDR Typhoid cases information and lab culture report must be notified to the concerned district health authorities, DG Offices of the respective province and the NIH.

Since the emergence of COVID-19, it has been observed that health care professionals are frequently prescribing azithromycin for the treatment of suspected and confirmed COVID-19 infections. The increased use of azithromycin for the COVID-19 patients may develop resistance against the azithromycin through selective pressure due to overuse of azithromycin leading to resistance strains, and consequently their spread which will further limit out the treatment options in the XDR typhoid cases. This practice should therefore immediately be addressed and azithromycin must carefully be prescribed for COVID-19 cases based on local and international recommendations.

Preventive measures and Vaccination:
It is suggested that with the treatment options for typhoid becoming more limited, following preventive measures are urgently needed, including improved sanitation and vaccination campaigns:

- Use of **azithromycin** and Meropenem should be restricted and only given to XDR cases of typhoid fever based on prescription by registered medical practitioner.
- In case of other infections such as upper and lower respiratory tract infections, other available drug options should be used instead of oral azithromycin which should be spared/ reserved for lab confirmed XDR Typhoid cases and other serious medical conditions.
- Raising community awareness on the following:
    - Thorough hand washing with soap and water is highly recommended after using toilet, before and after attending patient, before handling, cooking and eating.
    - Drink treated, boiled or bottled water. Use ice, prepared from clean drinking water preferably boiled. Wash fruits and vegetable properly before eating. Eat freshly cooked, hot served and home-made food.
    - Avoid eating raw fruits or vegetables, market prepared or leftover food. Use pasteurized milk.
- Vaccination should be considered especially for those who are travelling to and from endemic areas, high risk group of people and those who are exposed to the disease. Typhoid fever vaccines do not provide 100% protection however they will reduce the severity of the illness.
- Typhoid conjugate vaccine (Typbar-TCV@) is a new conjugate vaccine with longer immunity. WHO has prequalified the first conjugate vaccine in December 2017 to prevent typhoid fever.

Laboratory Diagnosis and NIH Support:

- Only way to confirm Typhoid fever is blood or stool sample tested for the presence of *S.* Typhi
- Lab tests for Typhoid fever should be recommended to those who fulfill criteria of suspected case definition available at NIH website **(www.nih.org.pk).**
- For any further assistance in this context, the Field Epidemiology & Disease Surveillance Division (FE&DSD) (051 – 9255237 and Fax No. 051-9255575) and Virology Department of Public Health Laboratories Division (051-9255082), NIH may be contacted.

The above 'Advisory' may please be circulated widely to all concerned.

Major General
Prof. Dr. Aamer Ikram, SI(M)
Executive Director