Drug resistant Salmonella infections in Pakistan

From November 2016 to March 2018, Pakistan experienced an increase in cases of typhoid fever that was followed by emergence of a strain of Salmonella Typhi (Salmonella enterica) that acquired a plasmid resistant to multiple antibiotics including first-line antibiotics such as fluoroquinolones and third-generation cephalosporins.

Editorial note

Typhoid fever is an acute generalized infection, caused by a highly virulent and invasive enteric bacterium, Salmonella Typhi. Typhoid fever is an important public health problem in many low and middle income countries. Global estimates of typhoid fever burden range between 11 and 21 million cases and approximately 128 000 to 161 000 deaths annually. The majority of cases occur in South/South-East Asia, and sub-Saharan Africa.

Typhoid fever is endemic in Pakistan. Contributing factors to high prevalence of the disease in the country include weak water and sanitation infrastructure. Since November 2016, Pakistan had an upsurge of typhoid fever cases. The upsurge started in Hyderabad district of Sindh Province. It was followed by emergence of multi drug resistant (MDR) strain of Salmonella enterica that acquired a plasmid resistant to multiple antibiotics including first-line antibiotics (i.e. chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole), fluoroquinolones and third-generation cephalosporins. The pathogen remained sensitive to azithromycin only.

As of March 2018, a total of 858 MDR Typhoid cases were reported from 14 districts in Sindh province (see graph). Hyderabad district was the most affected with 717 cases (83.5%). Even though this was the first major upsurge of MDR Typhoid fever cases in Pakistan, it is not the first time the country has experienced an outbreak of MDR Salmonellosis. Previous documented outbreaks of MDR Salmonellosis occurred in 1989, and during 1994-95 in the country.

In response to this current surge, vaccination with Typhoid vaccine has been implemented as one of the prevention and control strategies. The provincial department of health in coordination with WHO, conducted mass immunization campaign in affected districts of Sindh Province between January and March 2018. Over 30 thousand children were vaccinated.

Even though Typhoid vaccination can contribute to reduction of use of antibiotics and delay emergence of strains resistant to effective antibiotics such as azithromycin, data on effectiveness of typhoid vaccines in controlling MDR typhoid fever are very limited and efforts to assess the value of both preventive and reactive vaccination campaigns to control this upsurge are strongly recommended.

Further more, introduction of Typhoid vaccine in countries with the highest burden of typhoid disease, and history of MDR Salmonellosis cases such as Pakistan in routine immunization programme should be considered. But this will require use of surveillance data to better understand the endemicity of the disease in the country including its burden in different age groups.

MDR typhoid cases reported from Sindh (Pakistan), November–March 2016 to March 2018

Typhoid vaccines currently recommended for use:
- an injectable typhoid conjugate vaccine (TCV), consisting of Vi polysaccharide antigen linked to tetanus toxoid protein licensed for children from 6 months of age and adults up to 45 years of age;
- an injectable unconjugated polysaccharide vaccine based on the purified Vi antigen (known as Vi-PS vaccine) for persons aged two years and above; and
- an oral live attenuated Ty21a vaccine in capsule formulation for those over six years of age.

Update on outbreaks in the Eastern Mediterranean Region

Avian influenza: 2006-2017
- Egypt (A/H5N1) [359 (122), 34%]
- Egypt (A/H9N2) [4 (0)]

Ebola virus disease (EVD): 2018
- Democratic Republic of Congo (DRC) [39 (19), 48.7%]

Lassa fever: 2018
- Nigeria [432 (116), 26.8%]

Cholera: 2017-2018
- Somalia [2 968 (17), 0.5%]
- Yemen [1 091 288 (2 275), 0.2%]
- Tanzania [1 812 (36), 2.0%]

Diphtheria: 2018
- Yemen [1 707 (90), 5.3%]
- Bangladesh [6 860 (42), 0.6%]

MERS: 2012-2018
- Saudi Arabia [1 831 (713), 38.9%]

Yellow Fever: 2017-2018
- Brazil [1,261 (409) 32.4%]