

## Call to Thwart XDR Typhoid: Beyond Futile Efforts

Sir,

Globally, 14.3 million cases of typhoid and paratyphoid infection occurred in 2017, resulting in 135.9 thousand deaths with a substantial burden (69.6%) in South Asia.<sup>1</sup> Enteric fever is endemic in low resource countries in South Asia, including Pakistan, due to limited access to safe drinking water and poor sanitation and hygiene. It is the most common bacteremic illness in children in Pakistan, with rates as high as 1000 cases per 100,000 child-years, having been reported from Karachi.<sup>2</sup>

The precise explanation of this current scenario is that the circulating strain of *salmonella* (*S.*) *typhi*; H58 haplotype is commonly resistant to first-line antibiotics used for the treatment of typhoid fever in Pakistan. *S. typhi* has shown increased resistance to chloramphenicol, ampicillin, trimethoprim-sulfamethoxazole, fluoroquinolones and ceftriaxone — extensively drug resistant (XDR) typhoid.<sup>3</sup> Studies involving the whole genomic sequence have demonstrated that the emergence of this *S. typhi* strain, which is resistant to five classes of antibiotics, is not the result of its importation from outside but the acquisition of ESBL-encoding AMR plasmid by the endemic MDR H58 clone, potentially from an *E. coli* strain or another bacterial donor.<sup>3</sup>

Being marked a sentinel event in the evolution of antibiotics resistance in *S. typhi*, there is a dire need to work on all the recommendations highlighted by WHO back in December 2018 in full letter and spirit before it pushes the healthcare professionals to a situation like pre-antibiotics era. Firstly, coming to prevention, as it is better than cure, fortunately the typhoid conjugate vaccine (TCV) is available, and that will not only save lives but also boost the fight against antimicrobial drug resistance. In contrast to the earlier typhoid vaccines, TCV can be safely administered to children less than two years of age, has long-lasting protective effect, and fewer doses are required. This makes it an ideal vaccine to be included in the country's routine immunisation programme. WHO highly recommends this vaccine to control not only the endemic and epidemic of typhoid but also its outbreaks in developing countries, like Pakistan.<sup>4</sup>

Secondly, nothing if not, the irrational use of antibiotics must be curtailed on every cost at the grassroot level. Adding further, clinicians must follow agency's surveillance programme by making sure the laboratory verification and microbiological testing of strains in patients with suspected typhoid fever, so that the strains not only get timely detection but also can be monitored for emergence of their resistance. Then sharing this data on anti-microbial resistance at both

national and international levels will make collaborative efforts possible. The dilemma has been aggravated by the COVID-19 pandemic, as the sole reliable antibiotic to XDR typhoid is azithromycin, which has now been overprescribed and/or self-medicated with, to and by COVID or suspected COVID patients.<sup>5</sup>

Furthermore, strengthening public health response is also the responsibility of healthcare workers by increasing the awareness *via* mass educational campaigns; removing the myths and concerns regarding the side effects of available vaccines, and equal emphasis on healthy water, sanitation and hygiene (WASH) practices, use of boiled water in cooking, chlorination of water storage tanks, avoiding mixing of sewage and drinking water and ensuring cleanliness among food handlers. As Pakistan struggles with the present pandemic, another health crisis can be on the horizon, if antibiotics remain available over the counter, as compared to only on prescription and clinical need.

### CONFLICT OF INTEREST:

The authors declared no conflict of interest.

### AUTHORS' CONTRIBUTION:

AJ: Wrote the initial draft and performed extensive literature review.

SH: Revised the manuscript and arranged the layout.

SH: Suggested the topic and final approval before submission.

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