

The Typhoid epidemic: Where are we heading?

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Madam, I want to draw your attention towards a grave issue plaguing the medical world. The global Typhoid burden is responsible for 12 million infections, and 128,000 to 161,000 deaths annually,¹ and hence continue to be a significant public health concern in the developing countries. The misuse of antibiotics has led us to an antibiotic resistance epidemic, whereby antibiotic resistance in Karachi is increasing by 30% each year and according to the World Health Organization (WHO) Typhoid will be resistant to multiple drugs by 2020 in the city.²

Primitively, Typhoid was a deadly disease with a high rate of morbidity and mortality, until chloramphenicol was discovered.³ This was followed by Salmonella Typhi (*S. Typhi*) developing resistance to chloramphenicol, and susceptibility to amoxicillin and trimethoprim-sulfamethoxazole (TMP-SMZ).³ In the 1980s, plasmids encoding resistance to the aforementioned antibiotics appeared in South Asia. This would have proved fatal, but fortunately for us the highly efficacious fluoroquinolones became accessible. These not only had a success rate with Typhoid fever but also treated chronic gallbladder carriers. Alas, this could not prevail for much longer, and resistant strains appeared soon after.³ In light of *S. Typhi*'s resistance to first-line anti-bacterial and fluoroquinolones, third generation cephalosporins, namely ceftriaxone became therapeutic.⁴ What is alarming is that this bug has also developed resistance to ceftriaxone, rendering the only available options to be azithromycin and meropenem.⁴ Klemm et al.⁴ described strains resistant to three first-line drugs (chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole) as well as fluoroquinolones and ceftriaxone as "extensively drug-resistant", abbreviated as XDR strains. Reports claim that since November 2016, 800 XDR cases have been stated in Sindh, Pakistan, particularly Hyderabad.⁴ This is a worrisome situation as only 4 XDR cases have been reported worldwide, contrary to the epidemic that Pakistan is harbouring. Resistant strains to azithromycin have

already been reported in India,⁵ bringing us very close to a massive fatal antibiotic resistance epidemic. Soon the only antibiotic to fall back on will be the expensive carbapenems.³ Their costs will make them inaccessible and economically unfeasible in a developing country like ours, where resources are already scarce.

Children under the age of 5 are particularly susceptible to infection by *S. Typhi*, and the greatest rate of multiple drug-resistant strains (strains resistant to first-line antimicrobials) have been discovered in Bangladesh.⁶ Vaccines that are in use consist of an antigen-based injectable vaccine given over the age of 2 years, and a live attenuated vaccine administered over the age of 5 years.¹ These vaccines do not provide long-term immunity and are also not advisable under the age of 2 years. Thus, Typhoid is easily transmittable to children in younger age groups. WHO has approved a conjugate Typhoid vaccine that will provide longer immunity, be administered in lesser doses and to children starting from the age of 6 months.¹ This vaccine will be in use from 2019. Till then, Pakistan is still susceptible to an endemic and should resort to better hygienic and infrastructural changes. Culture and sensitivity to antibiotics should lead to treatment, in order to prevent further fatalities and complications.

This brings to light a very important question. Are we heading towards an age where treatment of Typhoid will again be severely restricted or even untreatable? Perhaps this can be prevented by the strict enforcement of antibiotics prescriptions and prohibit the sale of over the counter antibiotics. Physicians should also take extra precaution in prescribing antibiotics freely, without a strict rationale. Strict measures should be taken to encourage supportive treatment for viral illnesses, as the disinhibited use of antibiotics promotes resistance. Compliance with antibiotics by the affected patients can further decrease the resistance to XDR Typhoid. Moreover, this highlights the need for preventative measures for *S. Typhi*. Awareness campaigns on hygiene and handwashing should be undertaken to restrict the spread of antibiotic-resistant strains.

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