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Letter to the Editor

War against COVID-19: looming threat of XDR typhoid battle in Pakistan



Pakistan is among low- and middle-income countries with a lack of access to potable water, defective waste disposal systems, socio-economic dysfunction and an inefficient health care infrastructure. Consequently, the country provides a perfect breeding ground for *Salmonella enterica serotype Typhi*. The global annual incidence of typhoid fever is approximately 21 million cases with 200,000 deaths per year.¹ In Pakistan, disease burden of enteric fever owing to poor sanitation and overcrowded cities is high with an annual incidence of 493.5 cases per 100,000 individuals.¹ Since 2016, extensively drug-resistant (XDR) *Salmonella typhi* cases are on the rise in two cities in southern part of Sindh¹ and sporadic outbreaks are being reported across Pakistan. This spread has raised concerns over global export of such cases especially to countries with fragile health care systems especially during this challenging period when systems are already over strained. This strain of *S. typhi* is resistant to all of recommended antibiotics; including the third generation of cephalosporins. During a period of four years from 2016 to 2020, a total of 22,571 typhoid cases were reported across Pakistan and alarmingly almost 70% of these were XDR typhoid cases.² Consequently, in 2019, Pakistan became the first country in the world to introduce and mass vaccinate its children with typhoid conjugate vaccine to contain rising typhoid cases. However, the cases of XDR enteric fever are still being reported, and as of January 1st to 10th April 2021, 505 laboratory-confirmed cases have been reported from Karachi, 150 cases from Hyderabad and 77 from other districts of Pakistan. The most affected age group for XDR enteric fever in Sindh province, the most affected province, of Pakistan is with 41% of cases in age group of 0–4 years having an estimated incidence rate of 214 cases per 100,000 persons, followed by an incidence rate of 153 cases per 100,000 individuals in the age group 5–9 years.³ The prevalence of XDR fever in Sindh is more among females than males with an attack rate of 79 cases per 100,000 individuals.³ The prospect of cross-border transmission as seen with polio is also evident in the case of XDR typhoid fever as cases have been reported globally including the USA in travellers from Pakistan. In the United States, the Centers for Disease Control and Prevention (CDC) in its Health Advisory reports that as of January 14th, 2021, has received 71 cases of XDR typhoid infection with 87% of these having a travel history to or from Pakistan in the 30 days preceding the illness. Alarmingly, nine cases from six states did not have a travel history and investigation regarding these is ongoing. The susceptibility testing of specimens from these nine patients showed a similar antibiotic resistance pattern seen in Pakistan.⁴ An important point to consider is that no XDR typhoid infection was reported in the United States before the 2016 outbreak in Pakistan.⁵ The CDC in its latest health

advisory regarding US cases with a travel history to Pakistan, advised clinicians to prescribe a carbapenem for complicated illness and azithromycin for empiric treatment.⁴ In Pakistan, azithromycin is used for XDR typhoid infection and is now being extensively used in COVID-19 cases raising concerns of antimicrobial resistance.⁶ This also opens way for the prospect of rendering ineffective the few treatment options available for XDR typhoid infection. The ongoing soaring COVID-19 cases coupled with XDR typhoid infections appears to be quite concerning given the strained situation of the health care infrastructure.

In Pakistan, the cases during the surging pandemic have shown a pattern of decline which is similar to as seen with other communicable diseases such as polio, measles and diphtheria³ which may be a consequence of three major reasons. Firstly, the decline may be due to a decrease in the surveillance activities of health authorities as Pakistan has shifted its attention towards controlling the COVID-19 pandemic. Second, the hygiene and social distancing measures practised to control COVID-19 cases may have had a preventive effect on other communicable diseases as well. Third, panic due to the pandemic is severe and unprecedented which may have inevitably incited a fear of hospitals and clinics in the masses causing them to avoid them. Consequently, few cases of XDR typhoid infection are being diagnosed. To prevent typhoid fever, vaccination remains the only viable option in Pakistan. However, keeping in view the vaccine hesitancy to polio and measles, the typhoid conjugate vaccine has also had a mixed response from the general population. Vaccine hesitancy has been a substantial challenge in Pakistan and has sprouted due to various factors including conspiracy theories tied to religious beliefs, and extensive media coverage of exaggerated falsehoods about vaccines.⁷ The government and stake-holders must step in with awareness campaigns headed by prominent religious leaders to disseminate knowledge about the safety and necessity of typhoid conjugate vaccine. The health authorities must reinstate surveillance activities in order to understand the true impact the pandemic is having on endemic communicable diseases. Moreover, it is quintessential to introduce standardised waste water plumbing, improving sanitation, in urban and rural areas, as it can decrease transmission of typhoid as well as minimise any transport of 'virus laden droplets of COVID-19' from waste reservoir.⁸ In addition, the government must ensure urgent ways to procure the required amount of typhoid conjugate vaccine as there have been reports that hundreds of children were turned down because of the shortage of vaccine. Thus, the health authorities must track down and vaccinate these children that have missed their dose. This has also been the case with rabies vaccine as its shortage has caused many deaths in Sindh.⁹ The timely intervention

of these proposed measures is important because history has shown that endemic diseases surge controllably during a pandemic.

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