

The consequences of inaction towards antibiotic Misuse; XDR typhoid cases in Pakistan

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The recent outbreak of extensively drug-resistant (XDR) typhoid cases in Pakistan has sent shockwaves throughout the medical community. The country is already grappling with a myriad of health challenges, and the emergence of XDR typhoid has added another layer of complexity to the existing healthcare crisis. Pakistan has had the worst rate of typhoid in South Asia, a problem that has only escalated since the emergence of XDR-typhoid.

According to the WHO, in 2019, about 9 million people contract typhoid annually, predominantly of the drug-resistant strain, resulting in 110,000 deaths each year (1). Over 15,000 XDR-typhoid cases have been reported in Pakistan, mainly in Sindh and Punjab, though many outbreaks remain unreported.

Salmonella typhi is the causative agent of Typhoid Fever aka Enteric Fever, - an infection that is caused by contaminated food or water, which, at its worst can kill and with it being resistant to the first and second line antibiotics, it has left us with only a limited number of treatment options available and higher death rates. Usually its symptoms include; prolonged fever, fatigue, headache, nausea, abdominal pain, and constipation or diarrhea although, some patients may even have a rash (2).

The history of typhoid, dating back to Typhoid Mary, highlighted the impact of asymptomatic carriers and the devastating effects before antibiotics like penicillin,

Chloramphenicol, and septran; reducing mortality to 20% in the late 1970s.

XDR typhoid, identified in Pakistan in 2016, refers to *Salmonella typhi* strains resistant to chloramphenicol, ampicillin, and trimethoprim/sulfamethoxazole (MDR) and additionally non-susceptible to fluoroquinolones and resistant to third-generation cephalosporins. Susceptibility testing done for Pakistani cases so far showed all isolates were resistant to ampicillin and ceftriaxone while most of them were resistant to ciprofloxacin (3).

The XDR typhoid outbreak in Pakistan can be attributed to several factors, including; poor sanitation, inadequate waste management, a lack of access to clean drinking water, having a health care system that is plagued by inadequate diagnostic facilities such as; getting "Widal and Typhi dot" tests which are useless as they do not give the desired information as a Culture and Sensitivity would, insufficient antibiotic stewardship and a lack of awareness on risks of antimicrobial resistance (AMR) among the masses (4).

So, let us discuss what can be done and how do we respond to this problem. Health facilities must be alerted, and response teams should provide treatment and awareness to contain the disease. Hygiene among food handlers, clean water access, and vaccination are crucial. There are two conjugate vaccines, prequalified by WHO-SAGE in 2017 and funded by Gavi, The vaccine alliance 2019, that have long-lasting immunity when given as a single dose to children from the age of 6 months and to adults up to 65-years of age, to save them from the ailment. With more than 30 million children vaccinated since 2019, efforts need to be extended beyond southern regions to cover Pakistan's 100+ million children especially since the infection has spread north. Common practices include completing prescribed antibiotic courses, washing hands with soap after bathroom use or animal contact, and consuming pasteurized or boiled milk and washed fruits and vegetables (5).

This all should be proof for a “wake-up call” of the global health community as it highlights the need for urgent action to address the root causes of this outbreak. It’s a pattern repeated across the world; the problem of resistant infections and Superbugs is global and borderless. If left unchecked, XDR typhoid has the potential to spread rapidly, not only within Pakistan but also to neighboring countries and beyond. The lack of effective treatment options will

lead to increased morbidity and mortality, particularly among vulnerable populations such as children, the elderly, and those with compromised immune systems. Cases have been identified in 16 other countries due to international travel from Pakistan leading to the CDC issuing a warning to all travelers to Pakistan to take precautions against the superbug. The consequences of inaction are too great to ignore.

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