

ORIGINAL ARTICLE

Extensively Drug Resistance Enteric Fever in Tertiary Care Hospital

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ABSTRACT

Background: *Salmonella enterica* causes typhoid and paratyphoid fevers. Pakistan and other South Asian nations with little resources, including those with poor sanitation and hygiene, are particularly susceptible to enteric fever. Enteric fever is a disease which is extensively resistant to majority of antibiotics and these strains are rapidly spreading in Pakistan, raising concerns about the global failure of antibiotics.

Study design: Descriptive cross-sectional study.

Place and duration of study: Department of Pediatrics, CMH Quetta from 1st July 2022 to 31st December 2022.

Methodology: A hospital based study in which history of fever for minimum of three days in the previous seven days, and blood test recommendation from a doctor were requirements for enrolment in the study. Individuals who had blood cultures that tested positive for enteric fever were enrolled.

Results: *Salmonella Typhi* made up 52(94%) of the isolates and *S. Para typhi* made up 6%. 33(60%) of isolates were extensively drug-resistant (XDR), resistant to first-line antibiotics, fluoroquinolones, and third generation cephalosporin's, and 8(15%) of isolates were extremely drug-resistant (MDR) to first-line antibiotics.

Conclusion: In the current region of Pakistan, enteric fever is widespread. Over the course of the monitoring period, the incidence of typhoid fever has risen. With the advent of XDR typhoid, resistance to antimicrobial agents has also increased.

Keywords: Enteric fever, Burden, *Salmonella typhi*, Typhoid fever

INTRODUCTION

Typhoid and paratyphoid fevers are two diseases caused by *Salmonella enterica*. In general, both are referred to as enteric fever. Typhoid and paratyphoid cases worldwide totalled 14.3 million in 2017, with 136 thousand fatalities in South Asia¹. Pakistan and other South Asian nations with little resources, including those with poor sanitation and hygiene, are particularly susceptible to enteric fever^{2,3} very high reports of enteric fever are reported in Karachi, making it the most prevalent bacteremia disease in children in Pakistan⁴. Less than 25% of Pakistan's population has safe water to drink, and the remaining are forced to consume contaminated water since there are not many reliable sources of clean water, according to recent research⁵.

Typhoid fever is rapidly spreading throughout Pakistan, raising concerns about the global failure of antibiotics⁶. Scientists contend that the main causes of the growth of extensively drug-resistant enteric fever in Pakistan include the country's poor sewage and water systems, low vaccination rates, and overcrowding in the cities. About eight hundred cases of highly drug-resistant typhoid were discovered in Pakistan during a 10-month period between 2016 and 2017 in just the city of Hyderabad⁷. The WHO recently pre-qualified Typebar-TCV, a novel typhoid conjugate vaccine, which has been utilized by public health officials in Sindh province to vaccinate 250000 kids in Hyderabad⁸.

The local populace, however, is unwilling to vaccinate against typhoid due to variety of reasons⁹. Typhoid that is resistant to multiple antibiotics can spread rapidly very rapidly around the globe⁶. Azithromycin, is the only available antibiotic which is still effective against these resistant strains of typhoid fever⁷.

We designed this study to understand the burden of XDR-ET in our setup and help contribute to the global efforts to combat antibiotic resistance and protect public health.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out in Pediatrics department of CMH Quetta from 1st July 2022 to 31st December 2022. It was done at hospital's inpatient, outpatient, surgical, and

laboratory networks. History of fever for three days and a blood test recommendation from a doctor were requirements for enrolment for outpatients. Suspected As well as confirmed instances of enteric were enrolled. Individuals who had blood cultures that tested positive for enteric fever were also enrolled. Ethical permission was granted by Institutional Ethical Review Board.

All suspected cases of enteric fever from the appropriate hospital were identified and enrolled by trained study assistants. If they were qualified, research assistants gathered information on participants' sociodemographic traits, present-day symptoms, illness duration, and any prior treatments. Data were gathered using standardized forms on tablets and transferred every day to a server. Information on antibiotic resistance was acquired from the relevant clinical laboratory at the sentinel hospital. Via phone calls, qualified patients were enlisted from the laboratory networks. Six weeks following enrolment, all blood culture-positive patients were contacted by phone to follow up on the results. The data was entered and analyzed through SPSS-25.

RESULTS

One thousand and eighty two patients in total who met the eligibility requirements were contacted; these patients came from 319 outpatient units, 316 inpatient units, 181 laboratory networks, and 266 surgical units. We included 61% of the patients who passed our screening, of whom 22% had enteric fever as evidenced by positive blood cultures for *S. typhi* (93.9%) and *S. Para typhi A* (6.1%). Overall, first-line antibiotic-resistant (MDR) isolates were found in 14.99% of enteric fever patients whose antimicrobial susceptibility testing results were available, while XDR isolates were found in 60% of cases. The incidence rates for *S. Typhi* were highest in children aged 2 to 4 and lowest in patients older than 25. The hospital-specific incidence rates were same. 97% of patients had a temperature when they arrived at the hospital, and 53% had vomited and 43% had experienced abdominal pain. With a mortality rate of 0.4%, 04 deaths occurred among the confirmed cases. XDR and MDR *S. typhi* typhoid patients had higher complication rates than non-XDR/MDR typhoid patients.

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Table 1: XDR enteric fever

Age (yrs)	Gender	Blood culture result	Antibiotic susceptibility	Treatment regimen	Treatment response
3-5	Male	Positive	XDR	Ceftriaxone, Azithromycin, Meropenem	Improved after 14 days
5-6	Female	Negative	Non-XDR	Ciprofloxacin, Cefixime	Improved after 5 days
6-8	Male	Positive	XDR	Ceftriaxone, Azithromycin, Meropenem	Worsening after 7 days
8-10	Male	Positive	XDR	Ceftriaxone, Azithromycin, Meropenem	Stable after 10 days
10-12	Female	Negative	Non-XDR	Ciprofloxacin, Cefixime	Improved after 3 days

DISCUSSION

The water filtration plant in Jamshoro, Hyderabad, is currently being renovated by the provincial government of Sindh in Pakistan, which is responsible for dealing with water and sanitation issues. This comes after the Supreme Court of Pakistan's appointed judicial commission ordered an investigation into the mixing of sewage water with natural waterways. The provincial government has also approved funding for Hyderabad's water distribution network restoration and its sewage system revival, totalling 399 74 million Pakistani rupees and 414 13 million, respectively¹⁰. One of the causes given in the article for the mixing of sewage and drinking water was the use of hand-operated water pumps close to the affected neighbourhoods. These actions can stop this behaviour¹¹. Education of locals, especially children, about cleanliness habits and the use of boiling water for cooking and drinking through illustrated booklets and school education programs should be another government activity. A significant action that the newly constituted Food authority should take is to audit the neighborhood restaurants and eateries for unclean activities. In poorer countries like Pakistan, where surveillance for antimicrobial use is not well developed, this has grown to be a major worry. Governmental and non-governmental organizations in Pakistan must actively support vaccination campaigns, good hygiene practices, and the avoidance of irrational antibiotic use in order to reduce the mortality and morbidity brought on by pathogens that are becoming more and more resistant to antibiotics.

In the current region, enteric fever is endemic, with the highest prevalence among children under 15 years old, which is consistent with another research from Bangladesh and India^{12,13}. We report a larger percentage of male cases of typhoid that have been confirmed. Several endemic situations have also reported findings of a similar nature^{14,15}. While there is not a biological explanation for the prevalence of *S. typhi* infections in men in the literature, the most logical explanations could be relatively higher outdoor exposure, eating out, and male population behaviors and attitudes that lead to an increased risk for *S. typhi* infections in developing countries¹⁶. Moreover, more male parents of children may seek medical attention, which could be another factor.¹³ We found a small percentage of mortality among all confirmed cases over the research period. Similar mortality due to typhoid was observed in prior Pakistani research.¹⁷ Research from endemic regions reveal wide variations in mortality. According to a study conducted in Vietnam, *S. typhi* was responsible for 2% of hospitalized patients' deaths¹⁸.

CONCLUSION

In the current region of Pakistan, enteric fever is widespread. Over the course of the monitoring period, the trend of confirmed enteric fever, particularly *S. typhi*, has risen. With the advent of XDR typhoid, resistance to antibiotics also increased over this time. Although the prevalence of paratyphoid is still relatively low, it is advised that Pakistan strengthen its current national surveillance system for both typhoid and paratyphoid. Despite the fact that

typhoid vaccination can considerably reduce the incidence of this disease and may also affect antibiotic resistance, it is strongly advised to ensure certain measures like access to clean water, environmental hygiene, and sanitation.

Conflict of interest: Nil

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