Original Article

Determination of the Frequency of Extensively Drug-Resistant Salmonella Typhi Isolated from Blood Cultures at the Diagnostic and Research Laboratory LUMHS Jamshoro

Um E Farwa[1], Noor Tarique[1*], Alhamd Mustafa[2], Abid Hussain Chang[1]

ABSTRACT

OBJECTIVE: To determine the frequency of XDR Salmonella Typhi in blood cultures in the Diagnostic and Research Laboratory, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro.

METHODOLOGY: This represented a retrospective cross-sectional study (Jan 1 - June 30, 2025). All positive Salmonella Typhi blood culture samples were included; however, the first isolation of each patient was taken. Demographic characteristics, culture findings and antibiotic susceptibility profiles were extracted from laboratory records. The Kirby-Bauer disk diffusion test was applied as the method of antibiotic susceptibility test according to CLSI guidelines. Descriptive statistics were used to estimate XDR frequency and to examine associations with age and sex.

RESULTS: Among 444 confirmed cases of typhoid, there were 226 (50.9%): XDR, 59 (13.3%): MDR, and 159(35.8%): nonresistant. Men accounted for 61.3 per cent of cases, with a male-to-female ratio of 1.6:1. XDR infections were most prevalent in children aged 0-4 years. Male patients were slightly more at risk of XDR Typhi, with an odds ratio of 1.16 (95% CI: 1.11-1.21) and a relative risk of 1.08, or 8% higher than in females.

CONCLUSION: A high proportion of XDR Salmonella Typhi cases was found, particularly among young male children below five years. These findings are alarming and justify local, pediatric-specific interventions, particularly in resource-deprived locales.

KEYWORDS: XDR Salmonella Typhi, typhoid fever, antibiotic resistance, blood culture, Pakistan, public health.

INTRODUCTION

Salmonella enterica serovar Typhi (S. Typhi), a Gram-negative, rod-shaped bacterium, causes typhoid fever and remains a significant public health problem of developing nations where sanitation and clean water are limited[1,2]. It is primarily transmitted through the fecal-oral route and presents itself through long-lasting fever, abdominal pain, and systemic toxicity[3]. The use of antimicrobial therapy has traditionally been instrumental in reducing morbidity and mortality[1]. However, the emergence and spread of drug resistance of the S. Typhi strains have disorganized the treatment plans[4].

The past two decades have witnessed the development of multidrug resistance (MDR) in S. Typhi due to resistance to the three conventional first-line drugs: ampicillin, chloramphenicol, and co-trimoxazole[1]. Recently, the emergence of fluoroquinolone and third-generation cephalosporin resistance has become a reality[1,5,6]. The strains essentially have clinicians with little to no treatment choices, with most often being able to select only azithromycin or carbapenems.

The XDR S. Typhi strain had its first major outbreak in 2016 in Sindh, where thousands of cases were reported in Karachi, Hyderabad, and other neighbouring areas[5,6]. Thereafter, several reports confirm that transmission continues at present, with XDR S. Typhi detected in nearly every province of Pakistan[7,8].

The limited treatment options have clinical implications of increased complications, increased hospitalizations and increased mortality[1]. From a societal healthcare perspective, the ongoing spread is an indicator of systemic problems in water, sanitation, hygiene, and antibiotic stewardship[1]. Although local studies are necessary to identify regional trends and inform clinical decisions, national surveillance remains useful for providing data[8]. Concentrated will be LUMHS Jamshoro, a major diagnostic and referral centre in Sindh province. Due to the continued presence of XDR S. Typhi in this area, this study was conducted to determine the prevalence of XDR S. Typhi among blood culture-positive typhoid patients at the Diagnostic and Research Laboratory, LUMHS Jamshoro. This research will enhance continuous monitoring and evidence-based interventions to control typhoid prevalence in Pakistan by disseminating current information on local prevalence and resistance trends.

METHODOLOGY

The Retrospective cross-sectional research was conducted at the Diagnostic and Research

[1]*Liaquat University of Medical & Health Sciences, Jamshoro*
[2]*LIMHS, Thatta*
Correspondence: *noortariq0311@gmail.com*
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Laboratory, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Pakistan. The laboratory is Sindh's regional center of inpatient and outpatient samples of the urban and rural health centers. Data analyzed all S. Typhi positive blood cultures between the duration of Jan 1 and June 30, 2025. It covers patients of all ages and genders with confirmed S. Typhi isolates.

The inclusion criteria were: positive blood cultures with S. Typhi processed at the Diagnostic and Research Laboratory at LUMHS during the study period; the initial positive isolate of a patient only; and complete microbiology and antibiotic susceptibility records.

The exclusion criteria were: records that are not available or unavailable, repeated samples of the same patient, co-infections which might invalidate susceptibility, specimens collected following embarkation on antibiotic treatment, tainted cultures or unfinished information.

All data were drawn from the lab information system and backdated. We entered age, gender, date of sample collection and full antibiotic susceptibility results in each patient. Identification of each isolate was performed using standard biochemical and serological tests, including S. Typhi.

Antimicrobial Susceptibility Testing (AST) was performed using Kirby-Bauer disk diffusion on Mueller-Hinton agar, according to CLSI 2025. Antibiotics such as ampicillin, chloramphenicol, co-trimoxazole, ciprofloxacin, ceftriaxone, azithromycin and meropenem were tested.

Extensively Drug-Resistant (XDR): This is ampicillin, chloramphenicol, cotrimoxazole, as well as fluoroquinolones and third-generation cephalosporins (e.g., ceftriaxone) resistant.

Multidrug- Resistant (MDR): Only resistant to the first three-line drugs.

Nonresistant: susceptible to all classes of antimicrobial drugs used.

We input and processed the information using Microsoft Excel and SPSS version 26. Descriptive statistics were used to compute the frequencies and percentages of XDR, MDR, and nonresistant isolates. This study also tested relationships between resistance patterns and patient demographics, namely age and gender, using cross-tabulation. Susceptibility ratios by gender were estimated using odds ratios (ORs) with 95% confidence intervals (CIs).

RESULTS

Of 444 S. typhi isolates of blood culture, 50.9 percent (226/444) were extensively drug-resistant (XDR), 13.3 percent (59/444) Multidrug-Resistant (MDR), and 35.8 percent (159/444) nonresistant as indicated in Figure 1. The percentage of XDR isolates is high, and it indicates continuous and extensive propagation of the resistant isolates in the region.

Of the 444 cases, 272 (61.3%) were male, and 172 (38.7%) were female, resulting in a ratio of 1.6:1 between men and women. Among males, there were slightly more XDR infections (143 cases) than among females (83 cases) (**Table I**). The odds ratio (1.16; 95% CI: 1.11-1.21) indicates that males were approximately 8% more likely to have an XDR infection than females.

An age-stratified analysis of samples showed that XDR S. Typhi infections were highest in children aged 0-4 years. The age bracket with the highest prevalence of XDR was the school-going age (5-14 years), followed by the age bracket with the highest prevalence of XDR. The rate of infection was lower in adults.

The temporal analysis over six months revealed variation in infection rates. It was 188 cases in February - March and 177 cases in April - May. The unspecified period also made 79 cases.

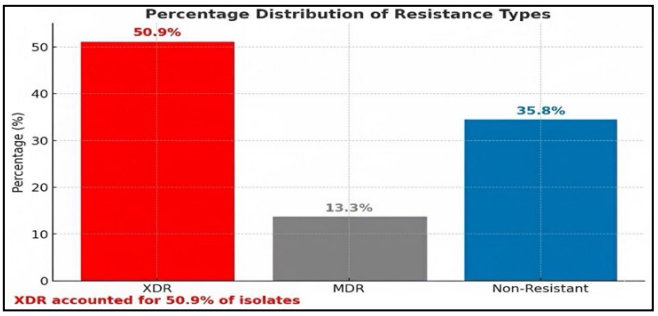

Figure 1: Proportional Distribution of Type of Resistance, **226**

Table I: Resistance Type by Gender

Resistance Type	Male Cases	Female Cases
XDR	143	83
MDR	32	27
Nonresistant	97	62
Total	272	172

Table II:
Temporal Distribution of Resistance Types

Time Period	XDR Cases	MDR Cases	Non-resistant Cases
Feb & March	132	12	44
April & May	94	8	75
Unspecified period	0	39	40

DISCUSSION

The research provides a clear understanding of the current epidemiological burden of XDR Salmonella Typhi in Sindh, Pakistan[8]. The results that more than half (50.9%) of all confirmed isolates were XDR are similar to other studies reported in the region that find high levels of resistance persistence[2]. Prior surveillance records in Sindh recorded that over 70 per cent of MDR cases happened in the past, and it has since taken the shape of XDR prevalence[9,10]. Investigations carried out in Karachi, Hyderabad, and

Sialkot have also revealed that over 50% of the S. Typhi strains are XDR, indicating the pervasiveness of the resistant strains nationwide [2,8]. The LUMHS Jamshoro findings are therefore an epiphany of the bigger crisis of the country. Several factors explain the high prevalence of XDR S. Typhi. The unregulated use of antibiotics, over-the-counter sale, and lack of compliance with the treatment and prescription results in selective pressure in favor of resistant strains. Poor sanitation and polluted water sources also continue to transmit the virus to the community. The continued prevalence of XDR of the rural and preurban Sindh region is also indicative of environmental reservoirs and ineffective surveillance facilities. Young children, aged five and under, are more susceptible to XDR infection, as they have a less developed immune system and are more exposed to contaminated food and water. The increased rate of infection among males can be related to increased exposure to the environment or dissimilarity in health-seeking behavior between males and females[11]. Adverse treatment choices include the presence of XDR S. Typhi. Fluoroquinolone or third-generation cephalosporin now forms an empirical treatment that is no longer effective in most areas in Pakistan. The only option that can be trusted is Azithromycin and carbapenems though excessive use of these will result in more resistance soon. Hence, it is important to deploy strong antibiotic stewardship initiatives. Health officials need to classify prescriptions, train clinicians and citizens on the use of relevant antibiotics, and advocacy on vaccination with the use of the WHO-qualified Typhoid Conjugate Vaccine (TCV) [12-15].

CONCLUSION

This paper establishes that the rate of XDR S. typhi among blood culture-confirmed cases is alarmingly high at LUMHS Jamshoro, Sindh (50.9 %). The results highlight a severe and unabated epidemic of poor health with limited treatment interventions. The most affected group is still the young children, especially the males below the age of five. Timely, integrated responses, such as sustained monitoring measures, antibiotic stewardship, enhanced water and sanitation infrastructure, and mass-acquired typhoid vaccination, are crucial for reducing the transmission of resistant S. Typhi strains and safeguarding vulnerable communities. Given the increasing global spread of antimicrobial-resistant S. Typhi, particularly XDR strains, continued surveillance studies are essential. Future studies are important to use multicenter and longitudinal studies involving the combination of microbiological, molecular and epidemiological data. Genome sequencing of local isolates would aid in determining transmission networks and the presence of resistance plasmids. A hasty increase in laboratory capacity and the development of data into a national-level typhoid surveillance system are necessary to detect new strains early.

Limitations

The study has limitations due to its retrospective, single-centre design, which raises concerns about its generalizability to the province as a whole. This brief six-month study may not be enough to identify seasonal fluctuation in the spread of typhoid. There is also no molecular typing, which limits understanding of the precise genetic resistance mechanisms.

Ethical permission: Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Pakistan ERC approval letter No. LUMHS/REC/-980.

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AUTHOR CONTRIBUTION

Farwa UE: Introduction, Methodology, Discussion Writing
Tarique N: Abstract, results and conclusion writing
Mustafa A: Data collection and methodology
Chang AH: Supervisor and final decision

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