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Blood Culture Isolates and Antibiogram for Salmonella at Tertiary Care Hospital

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ABSTRACT

Objective: To determine the pattern of blood culture isolates and antibiogram for salmonella at tertiary care hospital and identify frequency of multi-drug resistance and XDR.

Methodology: This descriptive, cross-sectional analysis was carried out on enteric fever/salmonella infected patients from 1-02-2020 to 31-10-2020 at Pediatrics Unit – II (Liaquat University Hospital). Children of either gender, aged 1 to 15 years, who presented with fever lasting more than 3 days, abdominal pain, headache, diarrhea, vomiting, or constipation, and who had a positive blood culture for Salmonella, were included. Data was collected into a structured questionnaire, containing enquiries pertaining to basic biodata, sociodemographic details, clinical presentation, and culture sensitivity (type of microbe and its drug sensitivity). The data obtained was analyzed using SPSS v. 21.0.

Results: Mean age of the children was 9.12 years, with males comprising 63.4%. Fever and abdominal pain were the most common clinical symptoms. In terms of antibiotic sensitivity, Cefixime and Ceftriaxone were effective in 83.9% and 85.7% of cases, respectively, while Ciprofloxacin showed 81.3% sensitivity. Both Meropenem and Azithromycin were 100% effective. Among the 14 multidrug-resistant cases, Ciprofloxacin had the highest resistance rate (11 cases), while Cefixime and Ceftriaxone were resistant in 9 and 8 cases, respectively. Meropenem and Azithromycin showed no resistance in any case.

Conclusion: Enteric fever remains a serious threat to child health, with rising multidrug resistance. While some drugs like Meropenem and Azithromycin are still 100% effective, they must be used carefully to prevent further resistance development.

Keywords: Typhoid, Salmonella Typhi, Multi Drug Resistance, Sensitivity.

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Introduction

Typhoid fever, caused by the bacterium *Salmonella enterica* serovar Typhi, remains a significant public health concern, particularly in resource-limited countries. It is prevalent across many regions of Asia, including Pakistan, where cases occur frequently.[1] Worldwide, an estimated 5.4 million people contract paratyphoid fever annually, while typhoid fever affects around 21.6 million individuals, leading to approximately 250,000 deaths.[2] Asia bears the brunt of these infections, accounting for about 80% of the global cases and deaths.[2] Without proper medical intervention, typhoid fever poses a serious health threat, with a mortality rate that could reach 30% in untreated case.[2,3] In Pakistan, enteric fever poses a significant public health challenge. In Karachi, the

estimated annual incidence rates for *S. Typhi* and *S. Paratyphi* among children are 451 per 100,000 and 76 per 100,000, respectively.[4] Enteric fever is characterized by fever, which often leads to headaches, a dry cough, and muscle pain. Many patients also experience abdominal symptoms, including abdominal pain, diarrhea or the constipation.[5,6] Children under the age of five frequently exhibit symptoms such as diarrhea, nausea, febrile seizures, and notable neurological manifestations.[5] The microbe is transmitted through the consumption of food or water contaminated with human feces. At-risk populations include those lacking access to safe drinking water, as well as individuals living in areas with poor sanitation and insufficient sewage management. Historically, the first-line treatments for enteric fever consisted of ampicillin, chloramphenicol, and trimethoprim/sulfamethoxazole. However, the emergence of antibiotic-resistant bacteria has rendered these medications ineffective.[7] The incidence of multidrug-resistant (MDR) typhoid in South Asia has been reported to range between 17% and 23%. Treatment has shifted from first-line antityphoid medications to using first- and third-generation cephalosporins, fluoroquinolones (FQs), and azithromycin as second-line agents. However, recent studies are increasingly reporting resistance to one or more of these second-line treatments.[8,9]

Correct diagnosis and quick treatment are critical for successfully managing this disease and avoiding complications. The culture of blood is the most effective method for identifying typhoid fever because it provides direct detection of the pathogenic bacterium.[4] A concerning pattern of antibiotic resistance was detected among children with enteric fever in Lahore.[7] According to a recent national study commonly used antibiotics such as Ampicillin, Ciprofloxacin, Ceftizadime, Cefotaxime and showed significant resistance rates against the most frequently identified bacterial isolates.[10] However the current understanding of the prevalence and patterns of the infectious agents responsible for illness, along with their antimicrobial sensitivities, is crucial for effectively managing bloodstream infections in hospitalized children.[10] This information is vital for guiding effective treatment strategies, as antimicrobial resistance is an evolving challenge. Communicating the results of these analyses to healthcare professionals is essential for optimizing patient care and ensuring that treatments remain effective. However the present study aims to contribute to this effort by analyzing the bacterial profile and antimicrobial sensitivity patterns associated with typhoid infections. By identifying current resistance trends, this research seeks to inform clinical decision-making and improve therapeutic outcomes.

Methodology

This descriptive cross-sectional study was conducted at the Department of Pediatrics, Liaquat University Hospital, Hyderabad, from February 1, 2020 to October 31, 2020. The sample size was determined to be 112 using the Open-Epi sample size calculator, with a prevalence of positive blood cultures at 12%, a 6% margin of error, and a 94% confidence interval. A non-probability convenience sampling technique was employed. Children of either gender, aged 1 to 15 years, who presented with fever lasting more than 3 days, abdominal pain, headache, diarrhea, vomiting, or constipation, and who had a positive blood culture for Salmonella, were included. All the malnourished children, children with comorbidities (e.g., congenital heart disease or tuberculosis), immune-compromised children, children with severe acute malnutrition (SAM) and who had already received antibiotics within the previous 48 hours were excluded. Ethical approval was obtained from the Ethical Review Committee (ERC), and the study adhered to ERC's protocols. Informed consent was obtained from all participants after explaining the study's purpose, objectives, potential benefits, and risks. Participation was voluntary, and participants could withdraw from the study at any time. Blood samples were collected on the first day of admission and sent to the microbiology lab for cultures and sensitivity testing. Data regarding the type of Salmonella, patient age, gender, symptom duration, sample collection date, and antibiotic resistance were recorded. Multidrug resistance (MDR) was defined as resistance to two or more drugs, while extensively drug-resistant (XDR) isolates were resistant to all drugs except Azithromycin and Carbapenem. The results were analyzed using SPSS version 21.0.

Results

The mean age of the sample stood at 9.12 (SD ± 2.1) years with a majority comprising of males (63.4%). Most of the patients (74.1%, n=83) resided in urban areas, while 25.9% (n=29) came from rural areas. The commonest clinical presentation was fever (100%) and abdominal pain (48.2%). Salmonella Typhi (53.6%) was present more often than Salmonella Paratyphi (46.4%). (Table I)

Table I: Gender, residence and clinical pattern of the patients. (n=112)

Variables		N	%
Gender	**Male**	71	63.40%
	Female	41	36.60%
Residence	Urban	83	74.10%
	Rural	29	25.90%
Clinical Presentation Sign/Symptom	Fever	112	100%
	Headache	68	60.7%
	Coated Tongue	23	20.5%
	Diarrhea	41	36.6%
	Constipation	59	52.7%
	Rose Spots	32	28.6%
	Anorexia	51	45.5%
	Pallor	30	26.8%
	Vomiting	64	57.1%
	Abdominal Pain	112	100%

Culture sensitivity results for 112 patients revealed varying degrees of responsiveness to different pharmacologic agents. Cefixime showed sensitivity in 83.9% (n=94) of cases, while Ceftriaxone had a slightly higher sensitivity rate at 85.7% (n=96). Ciprofloxacin demonstrated sensitivity in 81.3% (n=92) of the cases. Both Meropenem and Azithromycin showed 100% sensitivity (n=112), indicating they were effective against all the bacterial isolates tested. (Table II)

Table II: Culture Sensitivity Patterns of Pharmacologic Agents. (n=112)

Pharmacologic Agent	% of Cases Sensitive to The Agent
Cefixime	94(83.9%)
Ceftriaxone	96(85.7%)
Meronium	112(100%)
Ciprofloxacin	92(81.3%)
Azithromycin	112(100%)

Table III: Pattern of MDR. (n = 14)

Resistant Case	Cefixime (18)	Ceftriaxone (16)	Meronium (0)	Ciprofloxacin (21)	Azithromycin (0)
1	□	-	-	□	-
2	□	□	-	□	-
3	□	□	-	□	-
4	-	□	-	□	-
5	□	-	-	□	-
6	□	-	-	□	-
7	-	□	-	□	-
8	□	□	-	-	-
9	□	-	-	□	-
10	□	□	-	-	-
11	□	-	-	□	-
12	-	□	-	□	-
13	-	□	-	□	-
14	□	□	-	□	-

Out of the 14 multidrug-resistant (MDR) cases, varying resistance patterns were observed across different antibiotics. Cefixime resistance was noted in 9 cases, while Ceftriaxone resistance occurred in 8 cases. Meropenem and Azithromycin showed no resistance across all cases, maintaining their effectiveness. Ciprofloxacin resistance was the highest, observed in 11 cases. (Table III & IV)

Table IV: MDR Status according to gender and residence of children.

Variables		MDR Status		p-value
		Yes	No	
Gender	Male	11	60	0.208
		9.8%	53.6%	
	Female	3	38	
		2.7%	33.9%	
Residence	Urban	8	69	0.317
		7.1%	61.6%	
	Rural	6	29	
		5.4%	25.9%	

Discussion

Typhoid fever poses significant health risks, especially in pediatric patients. In this study, children as young as 1 year were diagnosed, with a mean age of 9.12 years (ranging from 1 to 15 years). This finding contrasts with the study by Qamar et al[11], where 60.2% of participants were 15 years old or younger, with specific age distributions indicating 21% under 5 years, 23.3% aged 5 to 10 years, and 15.9% aged 10 to 15 years. In our study, a majority of participants were boys (63.4%), while girls accounted for 36.6%. The demographic distribution showed that most patients (74.1%, n=83) lived in urban areas, compared to 25.9% (n=29) from rural regions. The findings align with those of Nusrat et al[5], who reported that male children comprised 58.5% and females 41.5% in their study; however, they noted a lower mean age among their participants. This inconsistency in mean age may stem from variations in the study populations, such as geographic location, healthcare access, and community awareness of typhoid fever, which can influence disease presentation and diagnosis in children. Additionally, Rashed et al[12] reported a diverse age distribution among their participants, with 37% aged 1-5 years, 35% aged 5-10 years, and 28% over 10 years. Their gender distribution was also similar, with 60% male and 40% female participants. In contrast, Ahmad et al[13] found that out of 62 patients (25.2%) with positive blood cultures, 54.9% were female and 45.1% were male. The discrepancy in findings regarding age and gender across the studies may reflect differing disease susceptibility or access to healthcare services, study sample size and selections criteria in various populations.

In this study the commonest clinical presentation was fever (100%) and abdominal pain (48.2%). Salmonella

Typhi (53.6%) was present more often than Salmonella Paratyphi (46.4%). Tahira. F et al[14] fever was observed in all patients (100%), followed by anorexia in 91% of cases, abdominal pain in 85%, vomiting in 63%, diarrhea in 56%, constipation in 28%, and cough in 30%. In the comparison of this study Ahmad et al[13] Out of a total of 62 cases, 58 were identified as Salmonella typhi, while 4 were classified as S. Paratyphi**.** Wani JN et al[15] also reported that the most common presenting symptom in our study was fever, which was observed in all patients (100%). This was followed by anorexia was in 97.3% cases, 30% patients had vomiting, 31.5% had diarrhea and abdominal pain was in (18.4%) of the cases. Behera JR et al[16] reported that the most frequently observed symptom was fever, which was reported in 98.21% of the patients.

Additionally, other notable symptoms included vomiting, present in 39.29% of cases, and abdominal pain, which was experienced by 21.43% of the participants. Diarrhea was reported in 26.79% of the patients, while anorexia was noted in 14.29% of cases. According to the study conducted by Alekya K et al[17] all patients experienced both fever and anorexia. Additionally, 60% of the patients reported vomiting, while 54.4% experienced diarrhea. Furthermore, approximately half of the participants had abdominal pain. These findings indicate that fever and anorexia were universal among the patients, with a significant prevalence of gastrointestinal symptoms as well.

In this study culture sensitivity results for 112 patients revealed varying degrees of responsiveness to different pharmacologic agents. Cefixime showed sensitivity in 83.9% (n=94) of cases, while Ceftriaxone had a slightly higher sensitivity rate at 85.7% (n=96). Ciprofloxacin demonstrated sensitivity in 81.3% (n=92) of the cases.

Both Meropenem and Azithromycin showed 100% sensitivity (n=112), indicating they were effective against all the bacterial isolates tested. Out of the 14 multidrug-resistant (MDR) cases, varying resistance patterns were observed across different antibiotics. Cefixime resistance was noted in 9 cases, while Ceftriaxone resistance occurred in 8 cases. Meropenem and Azithromycin showed no resistance across all cases, maintaining their effectiveness. Ciprofloxacin resistance was the highest, observed in 11 cases. Zakir M et al[18] reported that the incidence of strains of bacterial resistance to four antibiotics ciprofloxacin, Azithromycin, Imipenem, and Meropenem did not differ significantly across hospitalized patients OPD children. The OPD and pediatrics wards have the highest incidences of resistance to ampicillin and chloramphenicol. However Piperacillin /tazobactam was the most efficacious antibiotics, followed closely by co-amoxiclav.[18] Batool A et al[19] reported that the 23.5% of S. Typhi strains were classified as multidrug-resistant (MDR), while 54% were categorized as extensively drug-resistant (XDR). These strains showed sensitivity to both azithromycin and carbapenems. However, significant resistance was observed against chloramphenicol in 72% of the cases, followed by 78% ampicillin, 59% ciprofloxacin, 78% co-trimoxazole, and 56% ceftriaxone.

Sattar A et al[20] reported that the among the various species of Salmonella analyzed, 44 (80%) were identified as Salmonella typhi, while 11 (20%) were classified as Salmonella Paratyphi A. The prevalence of multidrug-resistant Salmonella was found to be 47%, with 16% exhibiting extensive drug resistance, while in their study also both Meropenem and azithromycin demonstrated a sensitivity rate of 100%, whereas ceftriaxone was effective in 84% of the cases. In another study by Shah SA et al[21] also reported that the Salmonella Typhi exhibited the highest sensitivity to Imipenem at 100% and to azithromycin at 95%. In contrast, the lowest sensitivity was observed with ciprofloxacin, which had a rate of just 3.7%. The prevalence of multidrug-resistant (MDR) cases was reported at 20%, while 47% of cases were classified as extensively drug-resistant (XDR).[21]

The spread of extensively drug-resistant S. Typhi is a serious concern, particularly with reports of cephalosporin-resistant strains emerging in parts of Asia. This poses a significant threat as it limits treatment options. Vaccination remains a key strategy to prevent enteric fever, especially in children in endemic areas.

There is a need for broader use of typhoid vaccines in immunization programs and the development of paratyphoid vaccines. This study is one of the few recent efforts to analyze resistance patterns in Salmonella Typhi, linking them to various factors. It also highlights the Meropenem and Azithromycin were highly effective. However, limitations include data from a single location over a short period and a limited range of antibiotics tested, which may affect the comprehensiveness of the findings.

Conclusion

Enteric fever remains a significant threat to child health, with increasing reports of multidrug-resistant (MDR)

cases. Fortunately, some drugs still show 100% effectiveness, but they must be used judiciously to prevent the development of resistance in Salmonella strains. As this study was limited to a single setting and limited sample size, future research should involve larger, more diverse populations and consider additional potential correlates to deepen the understanding of this issue.

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