



Antibiotic Resistance and Sensitivity Pattern in Cases of Blood Culture Proven Enteric Fever Visiting a Tertiary Care Hospital Abbottabad

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ABSTRACT

Background: Enteric fever is a common systemic infection in developing countries and mainly affect children due to poor sanitation and contaminated water. Increasing misuse and overuse of antibiotics has led to rising antimicrobial resistance which is creating difficulty in proper treatment and empirical therapy selection. **Objective:** To determine the antibiotic resistance and sensitivity pattern in cases of blood culture proven enteric fever in children visiting a tertiary care hospital in Abbottabad. **Study Design:** Descriptive cross sectional study. **Duration and Place of Study:** Conducted from 5 July 2024 to 5 January 2025 at Combined Military Hospital Abbottabad. **Methodology:** A total of 184 children aged 1–15 years with positive blood culture for Salmonella Typhi or Salmonella Paratyphi A were included. Blood samples were processed on standard culture media and antibiotic susceptibility testing was done by disc diffusion method according to Clinical and Laboratory Standards Institute guidelines. Data were analyzed using Statistical Package for Social Sciences version 23. **Results:** Mean age was 8.20 ± 4.22 years and mean weight was 24.30 ± 8.63 kg. Majority were males 119 (64.7%) and from rural areas 104 (56.5%). High resistance was observed to ampicillin 167 (90.8%), chloramphenicol 164 (89.1%), trimethoprim sulfamethoxazole 148 (80.4%) and ciprofloxacin 158 (85.9%). Ceftriaxone resistance was 122 (66.3%) and cefixime 131 (71.2%). Azithromycin showed sensitivity in 163 (88.6%) cases. Imipenem and meropenem showed 100% sensitivity. **Conclusion:** Antibiotic resistance in enteric fever is very high against commonly used drugs.

INTRODUCTION

Enteric fever is a systemic infection caused mainly by Salmonella Typhi and Salmonella Paratyphi.¹ It is usually found in school-going children of endemic regions with poor sanitation facilities and contaminated drinking water.² The infection is spread through the feco-oral route, with children being more susceptible due to poor sanitary habits. Once ingested with contaminated food and water, the pathogens invade the intestinal mucosa, gain access to the bloodstream, and lead to systemic infections.³ The common clinical manifestations of enteric fever in children include high-grade fever, irritability, decreased appetite, abdominal pain, vomiting, and sometimes diarrhea or constipation.⁴ The other clinical manifestations include a coated tongue, hepatomegaly, splenomegaly, and weight loss.⁴

Antibiotic therapy is considered crucial in the management of enteric fever in pediatric patients, and early initiation of therapy has been found to reduce morbidity and hospital stay.⁵ Traditionally, antibiotics such as chloramphenicol, ampicillin, and

trimethoprim/sulfamethoxazole are used in children, but resistance has developed over the years.⁶ Later, antibiotics such as fluoroquinolones, i.e., ciprofloxacin, were used in enteric fever, but their use in children is limited because of safety concerns and increasing resistance.⁷ Currently, third-generation cephalosporins, i.e., ceftriaxone (i.v.) and cefixime (oral), are used in the management of enteric fever in children.⁸ Azithromycin is also used in uncomplicated cases of enteric fever in children.⁸ Factors affecting the selection of antibiotic therapy include the child's age, severity of illness, resistance patterns, and availability of antibiotics in the community. Factors such as incomplete therapy, abuse of antibiotics, and over-the-counter availability of antibiotics are contributing to increasing resistance in the pediatric population.⁹

The implications of antibiotic resistance and the sensitivity pattern in blood culture-proven enteric fever in children are noteworthy for the proper prescription of empirical therapy.¹⁰ Multidrug-resistant strains, which are resistant to chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole, have been documented

in several studies among pediatric populations.¹¹ More recent data indicate the emergence of extensively drug-resistant strains, which are resistant to fluoroquinolones and third-generation cephalosporins.¹² Antimicrobial susceptibility testing of blood culture isolates from pediatric patients is performed for therapeutic options. The sensitivity pattern might differ in different geographical areas and hospitals.

Such a study is necessary in the region of Abbottabad, and the purpose would be to define the local pattern of antibiotic resistance and sensitivity in pediatric enteric fever patients with confirmed disease by blood culture. The trends of resistance may vary from region to region, and it is important to obtain local data to guide empirical therapy, avoid treatment failures, and prevent complications, and ultimately guide hospital policy for antibiotics to ensure the optimal management of pediatric patients.

METHODOLOGY

This cross sectional descriptive study was carried out at Combined Military Hospital Abbottabad from 5th July 2024 to 5th January 2025. Approval was taken from the Institutional Ethical Review Committee of Combined Military Hospital Abbottabad before starting the data collection. Sample size was calculated as 184 by using 8.4% sensitivity of Ampicillin,¹³ 4% margin of error and 95% confidence level on WHO sample size software. Children of age 1–15 years with clinical suspicion of enteric fever and having positive blood culture for *Salmonella Typhi* or *Salmonella Paratyphi A* were included. Patients who had negative blood culture, incomplete laboratory record, prior documented chronic systemic illness, or refusal of consent were excluded from the study. Enteric fever was considered present when patient had fever with isolation of *Salmonella Typhi* or *Salmonella Paratyphi A* from blood culture. Written informed consent was obtained from parents or guardians before enrollment in the study. After consent, detailed data collection was performed.

A detailed history of the patient was taken into consideration, including the history of fever duration, drinking water source, and history of consuming any outside food. A general and systemic examination of the patient was conducted. Five milliliters of venous blood samples were collected aseptically and sent to the laboratory for culture. Blood samples were inoculated into pediatric culture bottles and incubated. Subcultures were done on MacConkey media and blood agar media. Organisms were identified using Gram staining and biochemical tests. Antibiotic sensitivity tests were conducted using the disc diffusion method according to CLSI guidelines. Antibiotic discs used were ampicillin, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, chloramphenicol, ciprofloxacin, levofloxacin, ceftriaxone, cefixime, azithromycin, imipenem, and meropenem.

All collected data were entered and analyzed using SPSS version 23. Quantitative variables like age were presented as mean \pm standard deviation. Qualitative variables like gender, family SES, residence, history of outside food and antibiotic sensitivity pattern were presented as frequency and percentage.

RESULTS

The total number of patients included in the study were 184. The mean age of patients was 8.20 ± 4.22 years and mean weight was 24.30 ± 8.63 kg. Regarding gender distribution, 119 (64.7%) were male and 65 (35.3%) were female. According to family socioeconomic status, 81 (44.0%) belonged to poor class, 72 (39.1%) to middle class, and 31 (16.8%) to rich class. Majority of patients were from rural areas 104 (56.5%) while 80 (43.5%) were from urban areas. History of outside food consumption was present in 87 (47.3%) patients and absent in 97 (52.7%) patients (Table 1)

Table 1

Patient Demographics (n = 184)

Demographics	Mean \pm SD / n (%)	
Age (years)	8.20 \pm 4.22	
Weight (kg)	24.30 \pm 8.63	
Gender	Male n (%)	119 (64.7%)
	Female n (%)	65 (35.3%)
Family Socioeconomic Status	Poor n (%)	81 (44.0%)
	Middle n (%)	72 (39.1%)
	Rich n (%)	31 (16.8%)
Residence	Rural n (%)	104 (56.5%)
	Urban n (%)	80 (43.5%)
History of Outside Food	Yes n (%)	87 (47.3%)
	No n (%)	97 (52.7%)

Regarding antibiotic susceptibility pattern, Ampicillin was sensitive in 17 (9.2%) cases and resistant in 167 (90.8%) cases. Amoxicillin-Clavulanate showed sensitivity in 99 (53.8%) and resistance in 85 (46.2%). TMP-SMX was sensitive in 36 (19.6%) and resistant in 148 (80.4%). Chloramphenicol showed sensitivity in 20 (10.9%) and resistance in 164 (89.1%). Ciprofloxacin was sensitive in 26 (14.1%) and resistant in 158 (85.9%). Levofloxacin demonstrated sensitivity in 36 (19.6%) and resistance in 148 (80.4%). Ceftriaxone was sensitive in 62 (33.7%) and resistant in 122 (66.3%). Cefixime showed sensitivity in 53 (28.8%) and resistance in 131 (71.2%). Azithromycin was sensitive in 163 (88.6%) and resistant in 21 (11.4%). Imipenem and Meropenem both showed 184 (100.0%) sensitivity and no resistance was observed (0.0%) (Table 2)

Table 2

Antibiotic Susceptibility Pattern (n = 184)

Antibiotic susceptibility	Sensitive n (%)	Resistant n (%)
Ampicillin	17 (9.2)	167 (90.8)
Amoxicillin-Clavulanate	99 (53.8)	85 (46.2)
TMP-SMX	36 (19.6)	148 (80.4)
Chloramphenicol	20 (10.9)	164 (89.1)
Ciprofloxacin	26 (14.1)	158 (85.9)
Levofloxacin	36 (19.6)	148 (80.4)
Ceftriaxone	62 (33.7)	122 (66.3)
Cefixime	53 (28.8)	131 (71.2)
Azithromycin	163 (88.6)	21 (11.4)
Imipenem	184 (100.0)	0 (0.0)
Meropenem	184 (100.0)	0 (0.0)

DISCUSSION

The present study were conducted to evaluate the antibiotic resistance and sensitivity pattern in cases of

blood culture proven enteric fever. The findings of this study were showing alarming levels of antibiotic resistance in commonly used antibiotics which is a growing concern in developing countries where enteric fever is still endemic. In this study, majority of the patients were male 119 (64.7%) which may be because male childrens are more exposed to outside environment, contaminated food and water sources as compared to female childrens who mostly remains at home. Most of the patients were belongs to rural areas 104 (56.5%) which can be explained by poor sanitation, lack of clean drinking water and inadequate hygiene practices that are more common in rural settings and favors the transmission of *Salmonella typhi*. Regarding antibiotic susceptibility, Imipenem and Meropenem were showing 100% sensitivity which is expected because these are last resort carbapenems antibiotics and *Salmonella typhi* has not yet developed significant resistance mechanism against this class of drugs. Azithromycin also showed good sensitivity in 163 (88.6%) of patients because it has good intracellular penetration and accumulates inside macrophages where *Salmonella typhi* resides and replicates. Ampicillin were found to be most resistant antibiotic with resistance in 167 (90.8%) of cases and Chloramphenicol also showed high resistance in 164 (89.1%) patients. The very high resistance to these antibiotics could be best explained by the horizontal transmission of resistance plasmids between *Salmonella* strains that has accumulated over decades of extensive and irrational use of antibiotics. Resistance to ciprofloxacin was also seen at a very high level of 158 (85.9%), which is of concern because fluoroquinolones have been the drugs of choice for enteric fever until now. However, overuse of this class of drugs in humans and animals has led to mutations in the target enzymes of DNA gyrase and topoisomerase IV, resulting in high-level resistance to these drugs. Resistance to ceftriaxone was seen in 122 patients (66.3%), which suggests the possible emergence of extended-spectrum beta-lactamase-producing *Salmonella Typhi* strains that are able to hydrolyze the beta-lactam ring of third-generation cephalosporins a serious problem in the treatment of enteric fever.

In present study, majority were male 119 (64.7%) and females were 65 (35.3%), which is comparable to Lail *et al.*¹⁴ where males were 136 (68%) and Manzoor *et al.*¹⁵ with 99 (55%) males, also Ahmad *et al.*¹⁶ reported 84 (70%) males, showing male predominance in paediatric enteric fever. Mean age in present study was 8.20±4.22 years, similar to Manzoor *et al.*¹⁵ (9±2.11 years), Ahmad *et al.*¹⁷ (6.15±3.341 years) and Jabeen *et al.*¹⁸ (6.7±2.9 years), indicating that school age children are more affected, possibly due to poor hygiene and exposure to contaminated food *via* outside sources. High resistance to first-line drugs was observed, as ampicillin resistance was 167 (90.8%), chloramphenicol 164 (89.1%), and TMP-SMX 148 (80.4%), which is consistent with Anjum *et al.*¹⁹ reporting 96% resistance to ampicillin and 98.7% to chloramphenicol and TMP-SMX, and similar to Manzoor *et al.*¹⁵ where ampicillin resistance was 79.63% and chloramphenicol 83.33%. Javed *et al.*²⁰ also showed 83.1% resistance to ampicillin and 75.6% to chloramphenicol. This similarity may be due to irrational antibiotic use and

emergence of MDR strains in region. However, Ahmad *et al.*¹⁶ reported 100% sensitivity to chloramphenicol and cotrimoxazole, which is different from present findings, possibly due to temporal variation and re-emergence of sensitivity after restricted use *in vivo*. Cephalosporin resistance in present study was high, with ceftriaxone resistance 122 (66.3%) and cefixime resistance 131 (71.2%), which is comparable to Javed *et al.*²⁰ showing 68.3% resistance to ceftriaxone and Ahmad *et al.*¹⁷ with 69.4% resistance to cefixime. Lail *et al.*¹⁴ also documented 49% cephalosporin resistance. In contrast, Muhammad *et al.*²¹ and Afroze *et al.*²² reported 100% sensitivity to ceftriaxone, indicating geographical and temporal differences in resistance trend, and possible emergence of XDR strains in recent years.

Fluoroquinolone resistance was markedly high, as ciprofloxacin resistance was 158 (85.9%) and levofloxacin resistance 148 (80.4%), which is in agreement with Lail *et al.*¹⁴ showing 60% quinolone resistance, Anjum *et al.*¹⁹ with 82.2% ciprofloxacin resistance, and Javed *et al.*²⁰ reporting 83.3% resistance. Manzoor *et al.*¹⁵ also documented 66.67% resistance. This high resistance may be explained by widespread empirical use and stepwise chromosomal mutations leading to reduced susceptibility *in vitro*. Macrolide sensitivity remained high in present study, as azithromycin was sensitive in 163 (88.6%) with only 21 (11.4%) resistance, which is comparable to Lail *et al.*¹⁴ with 94% sensitivity, Manzoor *et al.*¹⁵ with 96.30% sensitivity, Ahmad *et al.*¹⁷ with 96.7% sensitivity, and Javed *et al.*²⁰ with 92.86% sensitivity. Slightly lower sensitivity in present study may indicate gradual increasing resistance due to more frequent use as oral alternative in XDR cases. Carbapenems showed 184 (100%) sensitivity for both imipenem and meropenem, which is consistent with Anjum *et al.*¹⁹ reporting 0% resistance to meropenem, Manzoor *et al.*¹⁵ with 100% sensitivity to meropenem, Sattar *et al.*²³ showing 100% sensitivity to meropenem, and Javed *et al.*²⁰ reporting 0% resistance to both imipenem and meropenem. Muhammad *et al.*²¹ also demonstrated 100% sensitivity of *S. typhi* to meropenem. This uniform sensitivity may be due to restricted hospital-based use and limited community exposure.

The limitations of the current study, which must be taken into consideration when interpreting the results, include the fact that the study was carried out at a single tertiary care hospital and, therefore, the results cannot be generalized to the entire population. The second limitation was that the sample size of the study was 184 patients, which was a small sample size, and the results might have been better if the sample size was large, as that would have given a true representation of the actual antibiotic resistance pattern of enteric fever. The third limitation was that the molecular characterization of the resistant isolates was not carried out, which would have helped to confirm the exact mechanism of resistance, such as the production of extended-spectrum beta-lactamases and plasmid-mediated resistance.

CONCLUSION

The present study has concluded that antibiotic resistance in enteric fever is highly elevated and of concern,

especially with respect to first-line antibiotics such as ampicillin, chloramphenicol, and ciprofloxacin, which have largely been ineffective in the treatment of enteric fever in children. Azithromycin has been found to be an effective oral antibiotic with high sensitivity, whereas carbapenems such as imipenem and meropenem have been found to be

the most effective in the treatment of enteric fever. These are to be used in severe cases of enteric fever.

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