



## “ANTIBIOTIC SENSITIVITY PATTERNS IN ENTERIC FEVER PT E POSITIVE BLOOD CULTURE”

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### ABSTRACT

**Background:** Enteric fever is one of the key health problems facing Pakistan, and the increasing antimicrobial resistance has diminished the efficacy of some of the widely used antibiotic drugs. Empirical therapy and antibiotic stewardship are required to be guided by local, culture-based antibiograms.

**Objective:** To learn the sensitivity pattern of the antibiotic Salmonella Typhi and Salmonella Paratyphi to positive blood cultures of enteric fever patients in Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera.

**Methods:** The study was a descriptive cross-sectional study in the Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera, between May, 2025 and October, 2025. Standard microbiological procedures were applied to blood cultures of clinically suspected cases of enteric fevers. Biochemical tests and serotyping were used to identify isolates as S. Typhi or S. Paratyphi. The Kirby-Bauer disk diffusion test on Mueller-Hinton agar was used to perform the antimicrobial susceptibility test, and the results were interpreted based on CLSI 2025 breakpoints of the antibiotics tested.

**Results:** Out of 200 cases which had been culture-confirmed, S. Typhi was identified in 152 (76.0%), S. Paratyphi A was identified in 36 (18.0%), and S. Paratyphi B was identified in 12 (6.0%). Ampicillin (61.9% in S. Typhi) and chloramphenicol (57.2%) were seen to be the least susceptible, and ciprofloxacin (50.0% sensitive) was the least susceptible. Now, ceftriaxone (84.2%), cefixime (86.8%), and azithromycin (90.8%) were kept at high sensitivity. Meropenem was still very effective (98.7% sensitive). The same tendencies were observed in the S. Paratyphi isolates.

**Conclusion:** The first-line agents and fluoroquinolones used in the traditional approach were not very reliable, whereas the third-generation cephalosporins and azithromycin were still effective. Regular

updates of institution-specific antibiograms and frequent culture-based recommendations are essential to maximize treatment, as well as prevent the further increase of resistance.

**Keywords:** *Enteric fever; Salmonella Typhi; Salmonella Paratyphi; Blood culture; Antibiotic susceptibility; Antimicrobial resistance; Ceftriaxone; Azithromycin; Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera, Pakistan.*

## INTRODUCTION

Enteric fever, which includes typhoid and paratyphoid fever, is a major health burden in the world, especially in developing countries where sanitation and hygiene are not optimal. *Salmonella enterica* serovars Typhi and Paratyphi cause the disease and can be transmitted by contaminated water and food, and are most commonly seen in low- and middle-income countries (Hassan et al., 2022) (1). Enteric fever has been a significant problem in Pakistan, with its high rates, and has been a significant challenge to public health because of poor quality of water and increased antimicrobial resistance. The emergence of a growing antibiotic resistance in *Salmonella* isolates has become a critical issue that has compromised the effectiveness of the traditional treatment and made it necessary to constantly monitor the dynamics of antimicrobial sensitivity (Sultana et al., 2023) (2).

The resistance of *Salmonella* to antimicrobials has developed considerably during the last several years, complicating empirical treatment. Strains of multidrug resistance (MDR) against chloramphenicol, ampicillin, and co-trimoxazole have developed, and then fluoroquinolones have become resistant to the effects of which were previously used as first-line agents. Research in Bangladesh and adjacent countries records a changing sensitivity pattern, suggesting fluctuating sensitivity to azithromycin and cephalosporins (Barman et al., 2024) (3). Constant observation by means of blood culture is also necessary, as it allows unambiguous identification and antibiotic susceptibility, directing the clinician in the reasonable use of antibiotics and preventing the appearance of resistance (Al Masum et al., 2022) (4).

Enteric fever relies on a number of clinical and laboratory factors to be positive in blood culture. Early presentation, pre-medication with antibiotics, and insufficient collection of the samples can affect the isolation rates. The positivity rates are higher in children according to the studies conducted by pediatrics because more bacteria are carried, and the exposure to antibiotics is lower (Srinivasan et al., 2021) (5). The difference in antibiotic sensitivity patterns in hospitals and regions is indicative of the difference in the practice of prescription and infection control (Khaliq et al., 2024) (6). Therefore, data that is specific to the region is essential in the creation of effective treatment guidelines and health strategies for the populace.

The trends of antibiotic susceptibility have always shown changes in the regional studies. In Nepal, isolates of *Salmonella* spp. were found to be variable to ciprofloxacin and nalidixic acid but sensitive to azithromycin and ceftriaxone (Maharjan et al., 2021) (7). The same study was evident in the Nowshera pediatric population, where *Salmonella* Typhi exhibited decreasing susceptibility to the fluoroquinolones but stayed susceptible to the third-generation cephalosporins (Anjum et al., 2021) (8). The rise of widely drug-resistant (XDR) typhoid strains that are resistant to multiple antibiotic classes has made the management difficult, particularly in densely populated urban regions.

Laboratory validation of enteric fever diagnosis should be based on blood culture, which is also the gold standard of pathogen identification. Other systems, including the Widal test, which is commonly employed, have poor specificity and cross-reactivity (Roy et al., 2021) (9). Tertiary care center studies highlight that culture positivity, which is supplemented by antimicrobial susceptibility profiling, is a crucial element to guide evidence-based treatment plans and prevent the use of antibiotics empirically (Manandhar et al., 2021) (10). Hospitals like Qazi Hussain Ahmed Medical Complex Nowshera, are also important focal points of sustained resistance surveillance, given that the burden of enteric infection is high in Pakistan.

Enteric fever has changed in the global epidemiology through the development of antibiotic resistance and a change in sensitivity pattern (Hamdulay et al., 2024) (11). The continuous application of the broad-spectrum antibiotics has led to selective pressure in favour of resistant strains. Reduced

sensitivity to cefixime and ceftriaxone has been noted in a number of South Asian studies, but azithromycin remains effective (Chakraborty et al., 2022) (12). The knowledge of the changing epidemiology of resistance can help policymakers and clinicians to develop rational resistance antibiotic stewardship programs, which are urgently needed in high-burden areas like Pakistan.

Enteric fever presents itself in a wide range of clinical manifestations, which include mild febrile illness to serious systemic infection with complications like intestinal perforation or encephalopathy. The symptoms of the disease in patients are often characterized by a high fever, malaise, hepatosplenomegaly, and pain in the abdomen (Chatterji et al., 2022) (13). Leukopenia, anemia, and high liver enzymes in the laboratory are likely to be found with a confirmatory blood culture. The most common isolate in the pediatric setting is *Salmonella Typhi*, and the resistance patterns vary according to age and previous exposure to antibiotics (Ullah et al., 2022) (14). The increasing resistance indicates the significance of region-specific antibiograms to inform empiric therapy.

In most developing countries, diagnosis is still a problem because there are not enough laboratory facilities to confirm a diagnosis in time. Enhancement of sensitivity in detection and minimization of misdiagnosis can be achieved through standardized culture protocols, increased sensitivity in sample collection, and the application of molecular diagnostic tools (Neupane et al., 2021) (15). Moreover, the delay in diagnostics can cause long-term empirical treatment, which can result in the emergence of resistance to treatment and failure of treatment (Shah et al., 2021) (16). The effectiveness of diagnostic accuracy and timely and targeted therapy can be enhanced by the introduction of modern laboratory technologies and the training of microbiology personnel.

Typhoid and enteric fever may cause systemic complications, such as septic shock and dysfunction in multiple organs, in the critical care setting (Ray et al., 2021) (17). Early diagnosis of the causative organism and the prescription of the antimicrobial agent are significant to enhancing a favorable clinical outcome. Therefore, continuous monitoring of the trends of antibiotic sensitivity in tertiary hospitals is an inalienable measure to prevent cases of therapeutic failures and prevent the proliferation of resistant strains. According to the recent literature, there is a necessity to develop standardized country-wide recommendations regarding the management of enteric fever with the inclusion of the local resistance information into the empirical algorithms of treatment (Diwaker et al., 2024) (18).

Considering these issues, the current research was carried out in Qazi Hussain Ahmed Medical Complex Nowshera, to establish the pattern of antibiotic sensitivity in patients with enteric fever with positive blood culture. The monitoring of the trend in sensitivities at institutional levels can be used continuously to inform clinicians in choosing useful empirical therapy and lay the foundation for the national update of the antibiotic policy. The proposed study also seeks to add local information to the growing amount of regional research on antimicrobial resistance in enteric fever, which would be helpful to optimize patient outcomes and prevent additional transmission of resistance.

**Objective:** To identify the trends of antibiotic sensitivity of *Salmonella Typhi* and *Paratyphi* in patients diagnosed with enteric fever in the blood cultures of Qazi Hussain Ahmed Medical Complex Nowshera.

## MATERIALS AND METHODS

**Study Design:** Descriptive cross-sectional.

**Study Settings and Duration:** Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera, between May, 2025 and October, 2025.

**Sample Size:** A total of 200 blood culture-positive patients diagnosed with *Salmonella Typhi* or *Paratyphi* were included in the study.

**Inclusion Criteria:** They included patients of any age and gender with clinical manifestations of enteric fever whose blood cultures showed *Salmonella Typhi* or *Paratyphi*.

**Exclusion Criteria:** Patients with negative blood cultures, mixed bacterial growths, and patients who had been administered antibiotics within 72 hours before sample collection were excluded.

## Methods

The blood samples were taken under aseptic conditions in the form of sterile syringes (5-10 mL of blood in adults and 3-5 mL in children) and inoculated in bottles of Brain Heart Infusion (BHI) broth. Incubation of the samples was done at 37 °C, and samples were checked daily in terms of bacterial growth. The subcultures were maintained in the MacConkey agar plate and the blood agar plate, and then the identification of *Salmonella Typhi* and paratyphi by the standard microbiological methods was done. Agglutination of the isolates with specific antisera was done to confirm the isolates. According to Clinical and Laboratory Standards Institute (CLSI) 2025, antibiotic testing was done with the Kirby-Bauer disk diffusion on Mueller-Hinton agar. The antibiotics that were tested were ampicillin, chloramphenicol, ciprofloxacin, ceftriaxone, azithromycin, cefixime, and meropenem. The data were obtained and processed to establish the resistance and sensitivity trends among the isolates. Clustering of the results was done according to CLSI reference breakpoints, and quality control was done by using *E. coli* ATCC 25922.

## Results

The study involved **200 patients** who had blood culture-confirmed enteric fever. *Salmonella Typhi* was identified as the most common of these, with *Salmonella Paratyphi A* and *Salmonella Paratyphi B* being found less often. The culture positivity rate of enteric fever across the study period was **28.6 percent** of all clinically suspected cases that were subjected to culture.

**Table 1. Distribution of Enteric Fever Isolates (n = 200)**

| Organism Identified           | Frequency (n) | Percentage (%) |
|-------------------------------|---------------|----------------|
| <i>Salmonella Typhi</i>       | 152           | 76.0           |
| <i>Salmonella Paratyphi A</i> | 36            | 18.0           |
| <i>Salmonella Paratyphi B</i> | 12            | 6.0            |
|                               | <b>200</b>    | <b>100.0</b>   |

The information provided in Table 1 demonstrates that *Salmonella Typhi* is the most common causal organism, with almost three-fourths of all cases of enteric fever. The trend is in line with epidemiological patterns in the region, indicating that *S. Typhi* still prevails in adult and pediatric populations in Pakistan.

**Table 2. Age and Gender Distribution of Enteric Fever Patients (n = 200)**

| Age Group (Years) | Male (n=118) | Female (n=82) | Total (%)    |
|-------------------|--------------|---------------|--------------|
| 1–10              | 22           | 18            | 20.0         |
| 11–20             | 34           | 24            | 29.0         |
| 21–40             | 42           | 28            | 35.0         |
| 41–60             | 15           | 9             | 12.0         |
| >60               | 5            | 3             | 4.0          |
| <b>Total</b>      | <b>118</b>   | <b>82</b>     | <b>100.0</b> |

Table 2 demonstrates that the age group with the highest prevalence of enteric fever was the one (11-40 years) with the highest risk of exposure (64%). The proportion of males to females was nearly **1.4:1**, which agreed with the results of the regions where greater exposure to the environment and occupation was obtained by males.

**Table 3. Antibiotic Sensitivity Pattern of *Salmonella Typhi* (n = 152)**

| Antibiotic Tested | Sensitive (%) | Resistant (%) |
|-------------------|---------------|---------------|
| Ampicillin        | 58 (38.1)     | 94 (61.9)     |
| Chloramphenicol   | 65 (42.8)     | 87 (57.2)     |
| Ciprofloxacin     | 76 (50.0)     | 76 (50.0)     |
| Ceftriaxone       | 128 (84.2)    | 24 (15.8)     |
| Cefixime          | 132 (86.8)    | 20 (13.2)     |
| Azithromycin      | 138 (90.8)    | 14 (9.2)      |
| Meropenem         | 150 (98.7)    | 2 (1.3)       |

Table 3 shows that **third-generation cephalosporin (ceftriaxone, cefixime)** and **azithromycin** had high sensitivity (>85%), and ampicillin and chloramphenicol had high resistance (>55%). It is also interesting that **meropenem** was virtually universally effective, implying that it can be used as a last resort in cases of multidrug resistance (MDR).

**Table 4. Antibiotic Sensitivity Pattern of *Salmonella Paratyphi* (n = 48)**

| Antibiotic Tested | Sensitive (%) | Resistant (%) |
|-------------------|---------------|---------------|
| Ampicillin        | 20 (41.7)     | 28 (58.3)     |
| Chloramphenicol   | 21 (43.8)     | 27 (56.2)     |
| Ciprofloxacin     | 22 (45.8)     | 26 (54.2)     |
| Ceftriaxone       | 40 (83.3)     | 8 (16.7)      |
| Cefixime          | 41 (85.4)     | 7 (14.6)      |
| Azithromycin      | 44 (91.7)     | 4 (8.3)       |
| Meropenem         | 47 (97.9)     | 1 (2.1)       |

Table 4 shows the same trends with *S. Paratyphi*, where older first-line drugs have the highest resistance, and azithromycin and cephalosporins show the lowest resistance. This homogenous distribution with the serotypes shows that fluoroquinolone resistance is prevalent in the serotypes of *S. Typhi* and *Paratyphi*. It is observed that there has been an alarming resistance to traditional first-line antibiotics, and azithromycin, ceftriaxone, and meropenem are very effective. The evidence highlights the importance of careful antibiotic therapy application and a renewed antibiogram on a local basis to guarantee the effective control of enteric fever and the occurrence of extensively drug-resistant (XDR) strains.

## Discussion

*Salmonella Typhi* was the most common isolate shown in the findings of Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera, with a smaller proportion by *S. Paratyphi*, which is also in line with regional culture series by hospitals where *S. Typhi* still represents a predominant percentage of blood culture-proven enteric fever. Implementation of these data has practical implications (1). Empiric therapy in an environment where resistance patterns are dynamically changing and where first-line agents are no longer reliable is guided by such data. Specific surveillance work on blood-culture isolates has reiterated many times that antibiograms should be produced locally, as the susceptibility can change rapidly when under pressure of an antibiotic and due to prescribing practices (3). Host-response markers are also beginning to be considered in the context of research on infection, although they are not diagnostic themselves. Indices of inflammation, like the platelet-to-lymphocyte ratio, are a simplistic example of how simple laboratory markers are being integrated into clinical stratification when definitive tests are not yet available.

The main potential indication of our antibiogram is that the resistance to older first-line drugs (ampicillin and chloramphenicol) is largely high, and they cannot be used in empiric therapy in our catchment population without confirmation of susceptibility. This is congruent with the adult enteric fever sensitivity details observed in similar South Asian settings, where resistance to these older agents is still found to be high despite the periodically varying resistance (4). The fact that our observation of decreased fluoroquinolone efficacy is similar to the commonly reported decrease in ciprofloxacin susceptibility in enteric fever requires clinicians to reflect on empirical decisions and dosing schemes. Notably, blood culture positivity varies based on sampling timing and prior exposure to antibiotics, which is why the isolates that we obtained and tested are probably a clinically meaningful subset, and culture-based surveillance is necessary to map resistance and stewardship.

Conversely, third-generation cephalosporins and azithromycin were active in our dataset, suggesting that they continue to be used as first-line agents in the culture-confirmed disease until susceptibility results are available. Similar patterns of susceptibility, that is, relative stability of ceftriaxone/cefixime and azithromycin activity against *Salmonella* isolates, have been reported in enteric fever-cohort studies in nearby countries, and this supports the argument that they still are one of the most reliable options in most cases (7). Pediatric literature on tertiary centers and other urban settings of the directional pattern is also characterized by the same direction, as older agents and fluoroquinolones have lower reliability, whereas cephalosporins and azithromycin are relatively effective (8). Since resistance may also be different within the same city, it is also important to view these results as institution-specific evidence, which must be renewed frequently and not regarded as lasting regulations.

The importance of diagnostic strategy has to do with the fact that it defines who are counted and how the trends of resistance is interpreted. Comparison studies between blood culture and serologic tests like the Widal test still indicate that culture is the most definitive test in etiologic confirmation and susceptibility testing, with Widal being limited in specificity and time (9). Here, our cultural positive cases would enhance the clinical effectiveness of the antibiogram since it indicates confirmed *Salmonella* infections as opposed to a mixed etiology of febrile illnesses. Enteric fever is described as a dynamic epidemiologic issue influenced by the pressure of antibiotic selection pressure, travel, population density, and gaps in water and sanitation, factors that, in concert, fuel the development or growth of resistant strains, which is the theme of recent regional and review-based literature.

The age pattern of our cohort, with high concentration in the teenage and young adult age group, is also consistent with trends seen in tertiary-care clinical spectrum surveys, in which exposure risk and healthcare-seeking behavior also play a role in increasing the burden of detected cases in these age groups (13). The reasons why our findings indicate that the institutional prescribing patterns need to be tied to local evidence include the fact that studies of other tertiary hospitals have reported that the sensitivity profile often changes with time, with some of them showing a tendency to predict that we may be about to lose the susceptibility even to commonly used cephalosporins, which is why they should be closely monitored and not based on historical assumptions (12). The almost universal vulnerability of our isolates to meropenem is encouraging but bears a limited interpretation, as carbapenems must be used as a last resort in severe disease, treatment failure, or in cases of suspected highly resistant infection to prevent further acceleration in the resistance development of the general bacterial population.

**Public health and diagnostic perspective.** The continuity of multiple antibiotic classes' resistance is favorable to better stewardship and enhanced testing potential. Present-day enteric fever diagnosis debates refer to the fact that the lack of access to high-quality culture facilities and delayed confirmation often prompts the clinician to a long course of empiric treatment, which subsequently leads to increased resistance (15). Further, the pediatric-absorbed diagnostic review highlights that clinical characteristics are not adequate to be specific, and that rational testing pathways, which prioritize culture where possible, are essential to the accurate treatment and surveillance. Therefore, our results are in favor of a combined approach, which is to ensure timely blood culture sampling prior to antibiotics, whereas the local susceptibility information guide the empiric therapy, and de-escalate the treatment option based on the results of the real susceptibility.

Lastly, the clinical impact of untreated therapy may be devastating, particularly in complex cases that need high-level therapy, whereby delay in administration of relevant antibiotics may lead to a high frequency of systemic complications (17). Due to different levels of accuracy and availability of diagnostic tools, the recent studies, focusing on diagnostic performance and selection of the tests, should be used appropriately, making the significance of laboratory-confirmed pathways especially significant wherever possible, especially in resistance-prone venues. As a whole, the evidence on Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera -specific culture-confirmed susceptibility provided by our study can be used to support updated empiric recommendations at Qazi Hussain Ahmed Medical Complex Nowshera avoid routine empiric use of ampicillin/chloramphenicol and be cautious with fluoroquinolones; prioritize third-generation cephalosporins and azithromycin where indicated clinically; and save carbapenems for situations that obviously require them to safeguard their future usefulness (18).

## Conclusion

This case study was done at Department of Medicine, Qazi Hussain Ahmed Medical Complex Nowshera, and it has been shown that *Salmonella Typhi* is still the leading cause of blood culture-confirmed enteric fever, with *S. Paratyphi* playing a smaller yet significant role. The resistance to older first-line agents (ampicillin and chloramphenicol) is high on the antibiogram, and fluoroquinolones have lower reliability, which means that such drugs are not favored in empiric therapy, and no susceptibility is known. Conversely, third-generation cephalosporins (ceftriaxone, cefixime) and azithromycin were found to maintain high sensitivity, which justifies the further use of these drugs as viable first-line agents in this context. Meropenem was the most active but needs to be saved to use in severe illness or possible highly resistant infections to maintain its functionality. Timely routine blood culture and susceptibility testing, and periodic updates on institutional antibiograms are imperative to ensure rational prescribing is done to improve antibiotic stewardship, decrease treatment failure, and disseminate resistance.

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