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# CLINICO-MICROBIOLOGICAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF SALMONELLA TYPHI ISOLATES: A CROSS-SECTIONAL STUDY IN ENTERIC FEVER PATIENTS

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## ABSTRACT

**Background:** The present study addresses enteric fever, a significant public health concern in India caused predominantly by Salmonella enterica serovar Typhi. The disease is transmitted via the fecal-oral route, often linked to poor sanitation and hygiene. Increasing antimicrobial resistance complicates treatment, necessitating ongoing surveillance to optimize therapeutic strategies. The study aims to determine the clinical and microbiological profile of enteric fever cases and to assess the antimicrobial susceptibility pattern of Salmonella Typhi isolates. **Materials and Methods:** A cross-sectional study design was employed over 2 years at Karnataka Medical College and Research Institute, Hubballi. All required Data were collected using a structured proforma capturing demographics, clinical features, laboratory findings, and antibiotic use. Blood culture was performed using the automated BacT/ALERT blood culture system and serological diagnosis was done using the Widal test. Antimicrobial susceptibility testing was conducted by the Kirby-Bauer disk diffusion method following CLSI guidelines. Inclusion criteria encompassed patients of all ages with fever ≥5 days fulfilling clinical case definitions of enteric fever, while those with other identifiable infections were excluded. **Results:** A total of 200 clinically suspected enteric fever cases were included. The median age of the cases studied was 11 years (IQR: 7.25–19.5 years), and males constituted 53% of the study population. Fever was present in all cases (100%), accompanied by anorexia (60%), headache (80%), and abdominal pain (70%). Clinical signs included coated tongue (12%), hepatosplenomegaly (14%), and relative bradycardia (17%). Blood culture positivity was observed in 30 (15%) cases. The isolates were identified using biochemical tests and serotyping, and all were confirmed as *Salmonella Typhi*. The Widal Test was positive in 45(22.5%) cases. Antimicrobial susceptibility testing of the isolates revealed 100% sensitivity to imipenem and high sensitivity to ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone (each 96.7%). Sensitivity to azithromycin and ciprofloxacin was 93.3% and 83.3% respectively. Resistance was most notable for ciprofloxacin (16.7%) and azithromycin (6.7%), with minimal resistance to other tested antibiotics. **Conclusion:** The present study highlights the clinical and microbiological characteristics of enteric fever in a tertiary care setting and underscores the persistence of Salmonella Typhi as the primary pathogen. High sensitivity to classical first-line antibiotics and imipenem contrasts with emerging resistance to ciprofloxacin and azithromycin. These findings emphasize the critical need for continuous antimicrobial resistance surveillance to guide effective empirical therapy and support antimicrobial stewardship efforts in the region.

## INTRODUCTION

**Background on Enteric Fever**

Enteric fever, caused by Salmonella enterica serovars Typhi and Paratyphi, remains highly endemic in India, posing a significant public health challenge. Despite global declines, India reports one of the highest burdens, with an estimated 4.5 million cases and nearly 9,000 deaths annually, largely concentrated in urban centers and southwestern regions.[1] Factors such as inadequate sanitation, unsafe drinking water, and increasing antimicrobial resistance contribute to sustained transmission.[2,3] The endemicity is compounded by geographic heterogeneity and evolving resistance patterns, underscoring the urgent need for improved hygiene, vaccination, and antimicrobial stewardship in India.[4]

Salmonella enterica serovar Typhi (Salmonella Typhi) is the primary causative agent of enteric fever, a serious systemic infection predominantly affecting tropical and developing regions.[5,6] This pathogen is transmitted through contaminated food and water, leading to high morbidity and mortality worldwide. Salmonella Typhi accounts for the majority of enteric fever cases, with studies reporting prevalence ranging from approximately 66% to over 85% among Salmonella isolates from clinical specimens.[6,7] Its ability to cause invasive disease, coupled with rising antimicrobial resistance including multidrug-resistant and extensively drug-resistant strains, poses significant challenges for treatment and public health interventions.[8,9] Understanding the clinical and microbiological characteristics and antimicrobial susceptibility profile of Salmonella Typhi remains crucial for effective management of enteric fever.

Enteric fever, caused primarily by Salmonella enterica serovar Typhi, is predominantly transmitted via the fecal-oral route through ingestion of food or water contaminated with feces containing the bacteria. This transmission is closely linked to inadequate hygiene and poor sanitation, common in low- and middle-income countries where safe water and proper sewage disposal are lacking. Contaminated water sources, unsafe food handling, and open defecation facilitate the spread of typhoidal Salmonella. Household hygiene practices and environmental sanitation play critical roles in interrupting transmission, with clean water supply, improved sanitation infrastructure, and handwashing identified as key preventive measures. Thus, enteric fever control requires integrated water, sanitation, and hygiene (WASH) improvements alongside vaccination strategies.[10–12]

Antibiotic therapy is crucial in managing enteric fever, a systemic infection caused by Salmonella enterica. Effective antimicrobial treatment reduces disease severity, prevents complications, and limits transmission. However, widespread antimicrobial resistance, particularly to fluoroquinolones and other first-line drugs, complicates treatment choices. Current guidelines recommend therapy guided by local susceptibility patterns, with ceftriaxone and azithromycin commonly used. Resistance to multiple drugs, including extensively drug-resistant strains, underscores the importance of antimicrobial stewardship and continuous surveillance. Optimizing antibiotic regimens and exploring combination therapies are vital to overcoming resistance and improving clinical outcomes in enteric fever management.[5,13,14]

Antibiotic resistance poses a significant challenge in managing enteric fever, complicating effective treatment and increasing morbidity. Resistance has emerged against many commonly used antibiotics, including chloramphenicol, amoxicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, ceftriaxone, and azithromycin, limiting therapeutic options. The rise of nalidixic acid-resistant strains and fluoroquinolone non-susceptibility has led to reliance on third- and fourth-generation cephalosporins and azithromycin, with some strains exhibiting multi-drug and extensively drug-resistant profiles. This escalating resistance jeopardizes treatment efficacy, necessitates continuous antimicrobial susceptibility surveillance, and compels exploration of alternative therapies and combination regimens to effectively manage enteric fever.[13,15–17]

Ongoing surveillance of antimicrobial resistance in enteric fever is imperative to inform effective treatment strategies and curb the spread of resistant Salmonella strains. Widespread resistance to commonly used antibiotics, including fluoroquinolones, ceftriaxone, and azithromycin, complicates empirical therapy and necessitates individualized treatment based on local susceptibility patterns. Surveillance programs such as the Surveillance for Enteric Fever in Asia Project (SEAP) reveal varied resistance profiles across regions, highlighting the emergence of extensively drug-resistant strains that severely limit options. Integrating continuous monitoring with tailored antimicrobial stewardship ensures optimized patient outcomes and supports public health efforts to manage and contain enteric fever effectively.[9,13,15]

**Aims and Objectives**

- To determine the clinical and microbiological profile of enteric fever cases.
- To assess the antimicrobial susceptibility pattern of Salmonella Typhi isolates.

## MATERIALS AND METHODS

**Study Design and Setting:** The present study employed a cross-sectional design to evaluate the clinical and microbiological profile and antimicrobial susceptibility pattern of enteric fever cases. It was conducted at Karnataka Medical College and Research Institute, Hubballi, over a period of 2 years. This setting provided a tertiary


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care environment suitable for recruiting patients with clinically suspected enteric fever and performing relevant laboratory investigations.

**Data Collection**

Data collection was performed using a structured proforma to systematically record patient demographics, clinical symptoms & signs, laboratory test reports and antibiotic usage.

**Inclusion and Exclusion Criteria**

Patients of all age groups presenting with fever lasting five or more days and fulfilling the clinical case definition of enteric fever were included.

Probable cases of enteric fever were identified based on continuous fever with malaise, headache, loss of appetite, gastrointestinal symptoms for more than one week, plus at least two clinical signs such as toxic appearance, coated tongue, rose spot, relative bradycardia, splenomegaly, history of contact with confirmed cases, any gastrointestinal complications, Widal titre of ≥1:160 or a four-fold rise in titre.

Confirmed cases of enteric fever were diagnosed by laboratory confirmation through isolation of Salmonella Typhi or Paratyphi by blood culture, biochemical tests and serotyping.

**Exclusion Criteria**

Patients with fever attributable to other identifiable infections such as lower respiratory tract infection, urinary tract infection, malaria, leukemia, or lymphoma were excluded to eliminate confounding factors.

**Specimen Collection and Processing:** Blood samples were collected from all clinically suspected enteric fever patients meeting the inclusion criteria under aseptic conditions.

Five to ten milliliters of blood were collected aseptically and inoculated into the paediatric and adult BacT/Alert blood culture bottles and incubated under the automated BacT/ALERT blood culture system to detect bacterial growth. Positive blood culture bottles were subcultured onto Chocolate agar and MacConkey agar immediately after being flagged positive**.** Isolates were identified by Colony morphology, Gram staining, biochemical tests and subsequently confirmed by serotyping to ensure accurate species determination. Antimicrobial susceptibility testing of the isolated Salmonella species was conducted by the Kirby-Bauer disk diffusion method in accordance with CLSI standards, using a routine antibiotic panel to assess antibiotic resistance patterns.

For serology 2 to 3 mL of peripheral blood was collected and inoculated separately into 4.0 mL BD Vacutainer plain tube. Widal test was performed to detect anti-O, anti-H, anti-AH and anti-BH antibodies in patient serum with antigen suspension.

## RESULTS

The study included 200 probable enteric fever cases. Clinical signs and symptoms of all these cases were analyzed. Blood samples collected from all these cases were tested for antibody detection by Widal test and identification of causative organism by blood culture using automated BacT/ALERT Blood Culture system.

**Clinical Profile of Enteric Fever Cases:**

Among the 200 probable enteric fever cases studied 106 (53%) were males and 94 (47%) were females (Figure 1) with a median age of 11 years with an IQR of 7.25-19.5.

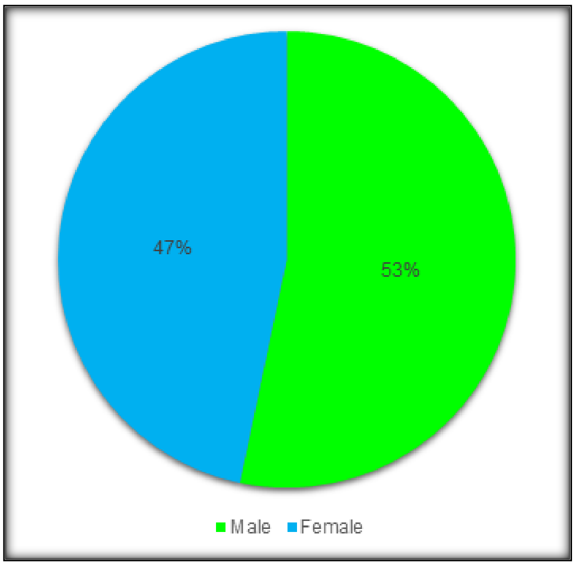


**Figure 1: Gender distribution of enteric fever cases**

The most common presenting symptom was fever, observed in all 200 patients (100%). Fever was typically prolonged with a step-ladder pattern. Anorexia was reported in 120 (60%) patients followed by headache in 160 (80%) patients and abdominal pain in 140 (70%) patients. Gastrointestinal symptoms such as nausea/vomiting 110 (55%) patients, diarrhea in 80 (40%) patients, and constipation in 66 (33%) patients were noted. On clinical examination, coated tongue was the most common sign observed in 24 (12%) patients, followed by hepatosplenomegaly 28 (14%), relative bradycardia 34 (17%) and rose spots 11 (5.5%). [Table 1]

**Table 1: Distribution of enteric fever symptom / sign**

| Enteric fever Symptom / sign | Total No of cases ( 200) | Percentage (%) |
| --- | --- | --- |
| Fever | 200 | 100 |
| Headache | 160 | 80 |
| Abdominal pain | 140 | 70 |
| Anorexia | 120 | 60 |
| Nausea/Vomiting | 110 | 55 |
| Diarrhea | 80 | 40 |
| Constipation | 66 | 33 |

| | | |
|---|---|---|
| Coated tongue<br>Hepatosplenomegaly<br>Relative bradycardia<br>Rose spots | 24<br>28<br>34<br>11 | 12<br>14<br>17<br>5.5 |

**Microbiological Profile of Enteric Fever Cases**

Among the 200 blood samples of probable enteric fever tested by automated BacT/ALERT blood culture system Thirty blood culture samples showed significant growth, while 170 showed no growth, resulting in a positivity rate of 15%. Widal test showed significant titres in 45 cases and insignificant titre in 155 cases, resulting in a slightly higher significant titre rate of 22.5%. [Table 2]

**Table 2: Blood samples tested using BacT/ALERT Blood Culture system and Widal test**

| Test Performed | Total no of blood Samples tested | Positive | Negative | Positive percentage |
|---|---|---|---|---|
| BacT/ALERT Blood Culture system | 200 | 30 | 170 | 15% |
| Widal Test | 200 | 45 | 155 | 22.5% |

30 Salmonella species isolated by automated BacT/ALERT Blood Culture system were further processed by biochemical tests and serotyping and all the isolates were identified as Salmonella Typhi and no Salmonella Paratyphi isolates were identified. [Table 3]

**Table 3: Salmonella species isolated among Study Population**

| **Organism** | Number of isolates | Percentage among total study population (n=200) |
|---|---|---|
| Salmonella Typhi isolated | 30 | 15 |
| Salmonella Paratyphi | 0 | 0 |

**Antimicrobial Susceptibility Pattern**

Antimicrobial susceptibility testing of 30 Salmonella Typhi isolates was performed for commonly used antibiotics. All isolates (100%) were sensitive to imipenem. High sensitivity rates were also observed for ampicillin (96.7%), chloramphenicol (96.7%), cotrimoxazole (96.7%), and ceftriaxone (96.7%). Sensitivity to azithromycin and ciprofloxacin was observed in 93.3% and 83.3% of isolates, respectively. Resistance was most commonly observed with ciprofloxacin (16.7%), followed by azithromycin (6.7%). Minimal resistance (3.3%) was noted for ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone, while no resistance to imipenem was detected. [Table 4, Figure 2]

**Table 4: Antimicrobial susceptibility pattern of Salmonella Typhi**

| Antibiotic | Sensitive | | Resistant | |
|---|---|---|---|---|
| | Total No of S. Typhi | Percentage of S. Typhi | Total No of S. Typhi | Percentage of S. Typhi |
| Imipenem | 30 | 100 | 0 | 0 |
| Ampicillin | 29 | 96.7 | 1 | 3.3 |
| Chloramphenicol | 29 | 96.7 | 1 | 3.3 |
| Cotrimoxazole | 29 | 96.7 | 1 | 3.3 |
| Ceftriaxone | 29 | 96.7 | 1 | 3.3 |
| Azithromycin | 28 | 93.3 | 2 | 6.7 |
| Ciprofloxacin | 25 | 83.3 | 5 | 16.7 |

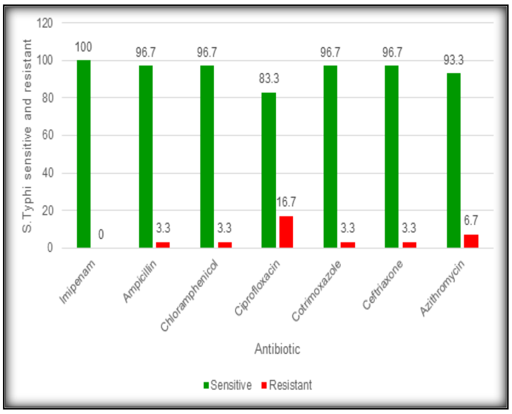


**Figure 2: Antibiotic susceptibility pattern of Salmonella Typhi isolates**

## DISCUSSION

In the present study, a total of 200 probable enteric fever cases were evaluated, revealing a median age of 11 years (IQR 7.25–19.5) and a nearly balanced gender distribution with males constituting 53% (106/200) patients, while females constituted 47% (94/200)patients) and a male female ratio of 1.13:1. These demographic findings align closely with several similar epidemiological studies. For instance, in the study conducted by the Surveillance for Enteric Fever in Asia Project in Pakistan, among hospitalized Salmonella Typhi cases, 52% (280/537) were aged 5-15 years, indicating a predominance of pediatric cases, and males were similarly more


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affected, though detailed gender percentages were not specified.[18] Likewise, the retrospective surveillance in Dhaka, Bangladesh, reported a median age of 14 years among typhoid cases with males having a higher incidence, reflected by a male-to-female ratio of approximately 1.36 (57% males).[19] These findings are consistent with our study's observation of a young median age and slight male predominance, reinforcing the vulnerability of children and early adolescents to enteric fever in endemic regions.

In contrast, the study from Patan Hospital, Kathmandu, Nepal, reported a slightly higher median age of 16 years for S. Typhi cases, with a significant male predominance particularly among those aged 15–25 years.[20] This slight age elevation compared to our median age of 11 years might be attributed to regional differences in population dynamics or exposure risks but still underscores the predominance of enteric fever among young individuals and young adults. Similarly, in the Fiji case-control study, the median age of typhoid fever cases was notably higher at 29 years, and the male proportion was 49%, showing less male predominance but an older affected population.[21] This divergence likely reflects differing epidemiological profiles due to demographic or environmental factors influencing disease transmission in Fiji compared to South Asian settings.

Moreover, a comprehensive global analysis of enteric fever incidence found that the burden remains highest among children under 15 years old, which aligns with our present study's focus on a younger cohort.[22] The slight male predominance noted in many regional studies and in our findings echoes known gender-related differences in exposure or susceptibility, with males often more involved in outdoor activities or at increased risk due to behavioral factors.

On the other hand, there are some dissimilarities worth noting. The Nigerian study on malaria and typhoid co-infection reported the highest typhoid prevalence among adults over 25 years old, with a distinct age-gradient showing a decrease in prevalence with younger age groups, differing from your observation where children and adolescents predominate.[23] Also, the male-to-female ratio in that study was more balanced (8.8% females vs. 7.1% males co-infected), in contrast to the slight male predominance we observed. Such discrepancies may reflect geographic variation, co-morbid infection patterns, and socio-environmental factors influencing disease epidemiology.

In the present study, fever was a universal presenting symptom, observed in 100% of enteric fever patients, characterized by a prolonged, step-ladder pattern. This finding resonates with multiple studies underscoring fever as the hallmark clinical feature of enteric fever. For example, the systematic review by Im et al. reported fever in over 90% of patients irrespective of age, highlighting its central role in disease presentation.[24] Similarly, a comprehensive global review of clinical profiles of enteric fever by Britto et al. found high-grade fever as a predominant symptom in nearly all hospitalized children, alongside other frequent features like coated tongue and abdominal distress symptoms.[25] The near-universal presence of fever in our cohort thus supports these established clinical patterns.

Additional symptoms observed in our study included anorexia (60%), headache (80%), and abdominal pain (70%). Gastrointestinal manifestations such as nausea/vomiting (55%), diarrhea (40%), and constipation (33%) were also prominent. These findings are consistent with prior epidemiological and clinical investigations. For instance, the clinical outbreak study in Malawi-Mozambique reported abdominal pain and headache as common symptoms alongside fever, with some patients exhibiting neurologic complications but generally sharing a similar symptom spectrum.[26,27] The systematic review by Britto et al. also emphasized that gastrointestinal symptoms such as nausea/vomiting and diarrhea are frequently reported, with variable prevalence depending on age and region, supporting our symptom distribution.[25]

Conversely, certain dissimilarities emerge when comparing with other reports. The study from Pemba, Zanzibar, highlighted a less specific clinical presentation where typhoid fever's symptomatology failed to significantly distinguish from other invasive bacterial diseases, noting fever duration rather than particular symptoms differentiated cases.[28] This contrasts with our findings wherein gastrointestinal symptoms were relatively common. Additionally, the Nepal peri-urban and rural study by Adhikari et al. described a high clinical diagnosis rate of enteric fever based primarily on fever, but only 4.1% had culture confirmation, suggesting clinical features can be misleading due to overlap with other febrile illnesses.[29] This underlines the challenge in relying solely on clinical characteristics for diagnosis in endemic areas.

Furthermore, the neurological manifestations reported during the Malawi-Mozambique outbreak, including ataxia and parkinsonism in a subset (13%) of patients, highlight atypical complications not observed in our cohort.[26,27] While these rare but severe signs suggest a spectrum of enteric fever presentation, the absence of such features in the present study aligns with the predominance of classical symptoms like fever and gastrointestinal complaints.

In the present study, clinical signs including coated tongue (12%), hepatosplenomegaly (14%), relative bradycardia (17%), and rose spots (5.5%) were observed among patients with enteric fever, all of whom were confirmed to have Salmonella Typhi infection by blood culture. These findings are consistent with the classical clinical profile of enteric fever described in multiple similar investigations. For example Britto et al. in their systematic review reported coated tongue in a majority of hospitalized children, with hepatosplenomegaly commonly observed in over half of cases, and relative bradycardia frequently acknowledged as a distinctive clinical feature.[25] The prevalence of rose spots in our cohort (5.5%) also aligns with the generally low but notable frequency reported in their review and other hospital-based studies, reinforcing its diagnostic relevance though it remains a less common sign.

Regarding microbiological findings, our present study demonstrated a 15% identification of Salmonella Typhi in blood culture isolates, underscoring the specificity of the pathogen in our patient population. This is in contrast with the prevalence of S. Typhi reported in the Aga Khan University hospitals' retrospective review by Im et al. Where 69% of positive blood cultures among enteric fever cases yielded S. Typhi.[18] The uniform confirmation by blood culture in our study strengthens the reliability of the clinical and microbiological correlations observed.

The antimicrobial susceptibility profile in our study revealed 100% sensitivity to imipenem and high susceptibility rates to ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone (each 96.7%), with somewhat lower sensitivities for azithromycin (93.3%) and ciprofloxacin (83.3%). These findings are reflective of evolving antimicrobial resistance trends documented in similar settings. The SEAP study in Pakistan reported over 90% fluoroquinolone resistance, including ciprofloxacin, contrasting with our relatively higher ciprofloxacin sensitivity.[18] This difference may indicate a regional variation or recent improvements in antimicrobial stewardship. Additionally, our observed high susceptibility to traditional first-line agents such as ampicillin, chloramphenicol, and cotrimoxazole contrasts with reports of multidrug resistance in 52% of S. Typhi isolates in Pakistan, highlighting heterogeneity in resistance patterns across geographic regions.[18] The 100% effectiveness of imipenem in our cohort corresponds with the broad-spectrum activity expected of carbapenems, though widespread use may be limited due to cost and accessibility.

However, some dissimilarities with other clinical studies are apparent. For instance, the research from Patan Hospital, Kathmandu, noted a broader clinical spectrum but did not report precise frequencies of clinical signs such as coated tongue or rose spots, and documented a significant male predominance in younger age groups infected with S. Typhi and S. Paratyphi.[20] The focus there was more on demographic patterns and antimicrobial resistance patterns rather than detailed clinical signs. In addition, the Nepal study by Adhikari et al. highlighted a very low culture-confirmed diagnosis rate (4.1%), emphasizing challenges in clinical diagnosis due to overlapping symptoms with other febrile illnesses, which contrasts with our 15% culture confirmation and defined clinical features.[29,33] Widal test in our study detected 22.5% significant titres of anti O, H, antibodies in patient serum suggestive of S. Typhi infection. These findings were comparable with study conducted by Eissa A. Saeed et al.[33]

Furthermore, the Malawi-Mozambique outbreak report by Chiodini et al.described neurologic manifestations in addition to classical enteric fever signs, which were not observed in our cohort, underscoring the variability in clinical presentation depending on the outbreak context and regional factors.[26] The unique neurologic complications highlight atypical disease expression not mirrored in our findings but important for differential diagnosis.

In the present study, antimicrobial resistance was most pronounced for ciprofloxacin, with 16.7% of isolates demonstrating resistance, followed by azithromycin resistance at 6.7%. Minimal resistance (3.3%) was noted for ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone, while no resistance was detected against imipenem. These findings correspond with broader concerns highlighted in the literature about rising resistance to key antimicrobials in enteric fever management. The editorial by,[30] emphasizes the critical importance of localized antimicrobial resistance monitoring because resistance trends can vary significantly by region, influencing treatment efficacy and clinical outcomes. Particularly, fluoroquinolone resistance, including ciprofloxacin, has been increasingly documented as a global challenge, directly impacting treatment success and calling for vigilant surveillance systems.

The observed 16.7% ciprofloxacin resistance aligns with recognized increasing resistance patterns; however, it may be comparatively lower than reports from some South Asian settings where fluoroquinolone resistance rates exceed 90% in Salmonella Typhi isolates, as discussed in the Surveillance for Enteric Fever in Asia Project (SEAP) studies.[31] This suggests that while ciprofloxacin resistance is of definite concern in our cohort, regional differences in antimicrobial pressure and prescribing practices may influence resistance prevalence. Resistance to azithromycin, at 6.7% in our findings, also warrants careful attention, especially given recent reports indicating rising azithromycin resistance in enteric fever patients, which jeopardizes oral treatment options for uncomplicated cases.[32]

Conversely, the minimal resistance observed for traditional first-line antibiotics such as ampicillin, chloramphenicol, and cotrimoxazole (each 3.3%) supports the possibility of re-introducing these agents in treatment regimens under careful stewardship, consistent with observations from some studies where multidrug resistance has declined following reduced usage.[30] The complete susceptibility to imipenem further confirms the continued reliability of carbapenems as effective agents for severe or complicated enteric fever, although their use is often limited due to cost and intravenous administration requirements.

In summary, the antimicrobial susceptibility profile documented in the present study reflects a concerning but perhaps not yet widespread resistance to ciprofloxacin and azithromycin in our setting, while retaining substantial sensitivity to classical agents and imipenem. This underscores the necessity of continuous, contextualized antimicrobial resistance monitoring to guide empirical therapy and optimize patient outcomes in enteric fever management, aligning with international calls for adaptive treatment policies informed by local resistance data.[30,32]

The present study has several limitations that should be acknowledged. First, the study was conducted at a single tertiary care center, potentially introducing selection bias toward more severe or complicated cases of enteric fever, which may not represent community-level disease patterns. Second, the study relied primarily on blood culture and Widal test for diagnosis; while blood culture is the gold standard; its sensitivity can be affected by prior antibiotic use, possibly leading to underestimation of true case numbers. Third, molecular methods for pathogen identification and resistance gene detection were not employed, limiting insights into genetic mechanisms of antimicrobial resistance. Additionally, longitudinal follow-up of patients to assess clinical outcomes and treatment efficacy was not included, restricting the ability to correlate susceptibility patterns with patient prognosis. Finally, the study did not evaluate environmental or socio-economic factors that may influence disease transmission and resistance trends. Future research with larger, multi-center cohorts incorporating molecular diagnostics and comprehensive clinical follow-up is warranted to enhance understanding of enteric fever epidemiology and resistance dynamics in this region.

The present study recommends continuous surveillance of antimicrobial susceptibility patterns in enteric fever to inform effective empirical treatment strategies. Given the observed resistance to ciprofloxacin and azithromycin, clinicians should exercise caution in their use and consider alternative antibiotics with higher sensitivity rates, such as ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone. Public health policies must prioritize antimicrobial stewardship and promote rational antibiotic use to curb resistance development. Additionally, expanding research to include molecular resistance mechanisms and broader geographic sampling will enhance understanding and guide optimized therapeutic interventions for enteric fever management.

## CONCLUSION

In the present study key findings include a median patient age of 11 years with a slight male predominance (53%), universal presentation of fever, and predominant symptoms such as anorexia, headache, and abdominal pain. Fifteen percent of cases were confirmed as Salmonella Typhi by automated BacT/ALERT Blood Culture system. Widal test showed significant titre in 22.5% of Cases. Antimicrobial susceptibility testing revealed high sensitivity to imipenem (100%) and classical first-line antibiotics including ampicillin, chloramphenicol, cotrimoxazole, and ceftriaxone (each 96.7%), with moderate sensitivity to azithromycin (93.3%) and ciprofloxacin (83.3%). Resistance was most notable for ciprofloxacin (16.7%) and azithromycin (6.7%), underscoring emerging challenges in empirical therapy. These findings highlight the critical need for ongoing surveillance and continuous monitoring of antimicrobial resistance patterns to guide effective treatment strategies and curb the spread of resistant Salmonella strains in the region. Sustained efforts in antimicrobial stewardship and periodic updates of local susceptibility data are essential to optimize clinical outcomes in enteric fever management.

## REFERENCES


1. Cao Y, Karthikeyan AS, Ramanujam K, Raju R, Krishna S, Kumar D, et al. Geographic Pattern of Typhoid Fever in India: A Model-Based Estimate of Cohort and Surveillance Data. The Journal of infectious diseases. 2021 Nov 23;224(Suppl 224e 5):S475–S483.
2. Manesh A, Meltzer E, Jin C, Britto C, Deodhar D, Radha S, et al. Typhoid and paratyphoid fever: a clinical seminar. Journal of travel medicine. 2021 Feb 6;28(3).
3. Collaborators G. Estimating the subnational prevalence of antimicrobial resistant Salmonella enterica serovars Typhi and Paratyphi A infections in 75 endemic countries, 1990–2019: a modelling study. The Lancet Global Health. 2024 Feb 14;12(3):e406–e418.
4. Divyashree S, Nabarro LEB, Veeraraghavan B, Rupali P. Enteric fever in India: current scenario and future directions. Tropical Med Int Health. 2016 Sep 8;21(10):1255–1262.
5. Khanal PR, Satyal D, Bhetwal A, Maharjan A, Shakya S, Tandukar S, et al. Renaissance of Conventional First-Line Antibiotics in Salmonella enterica Clinical Isolates: Assessment of MICs for Therapeutic Antimicrobials in Enteric Fever Cases from Nepal. BioMed Research International. 2017 Jan 1;2017(2):1–6.
6. Bhetwal A, Maharjan A, Khanal PR, Parajuli NP. Enteric Fever Caused by Salmonella enterica Serovars with Reduced Susceptibility of Fluoroquinolones at a Community Based Teaching Hospital of Nepal. International Journal of Microbiology. 2017 Jan 1;2017(2):1–6.
7. Veeraraghavan B, Pragasam AK, Ray P, Kapil A, Nagaraj S, Perumal SPB, et al. Evaluation of Antimicrobial Susceptibility Profile in Salmonella Typhi and Salmonella Paratyphi A: Presenting the Current Scenario in India and Strategy for Future Management. The Journal of Infectious Diseases. 2021 Nov 23;224(Suppl 5):S502–S516.
8. Hussain A, Satti L, Hanif F, Zehra NM, Nadeem S, Bangash TM, et al. Typhoidal Salmonella strains in Pakistan: an impending threat of extensively drug-resistant Salmonella Typhi. Eur J Clin Microbiol Infect Dis. 2019 Aug 3;38(11):2145–2149.
9. Qamar FN, Yousafzai MT, Dehraj IF, Shakoor S, Irfan S, Hotwani A, et al. Antimicrobial Resistance in Typhoidal Salmonella: Surveillance for Enteric Fever in Asia Project, 2016–2019. Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America. 2020 Dec 1;71(Suppl 3):S276–S284.
10. Andrews JR, Yu AT, Saha S, Shakya J, Aiemjoy K, Horng L, et al. Environmental Surveillance as a Tool for Identifying

High-risk Settings for Typhoid Transmission. Clinical Infectious Diseases. 2020 July 29;71(Suppl 2):S71–S78.
11. Syed KA, Saluja T, Cho H, Hsiao A, Shaikh H, Wartel TA, et al. Review on the Recent Advances on Typhoid Vaccine Development and Challenges Ahead. Clinical Infectious Diseases. 2020 July 29;71(Suppl 2):S141–S150.
12. Brockett S, Wolfe MK, Hamot A, Appiah GD, Mintz ED, Lantagne D. Associations among Water, Sanitation, and Hygiene, and Food Exposures and Typhoid Fever in Case-Control Studies: A Systematic Review and Meta-Analysis. The American Journal of Tropical Medicine and Hygiene. 2020 Sep 2;103(3):1020–1031.
13. Parry CM, Qamar FN, Rijal S, Mccann N, Baker S, Basnyat B. What Should We Be Recommending for the Treatment of Enteric Fever? Open Forum Infectious Diseases. 2023 June 2;10(Suppl 1):S26–S31.
14. Chowdhury AR, Mukherjee D, Chatterjee R, Chakravortty D. Defying the odds: Determinants of the antimicrobial response of Salmonella Typhi and their interplay. Molecular Microbiology. 2023 Dec 10;121(2):213–229.
15. Capoor M, Nair D. Quinolone and cephalosporin resistance in enteric fever. J Global Infect Dis. 2010 Jan 1;2(3):258.
16. Jain S, Chugh TD. Antimicrobial resistance among blood culture isolates of Salmonella enterica in New Delhi. J Infect Dev Ctries. 2013 Nov 15;7(11):788–795.
17. Katiyar A, Sharma P, Dahiya S, Singh H, Kapil A, Kaur P. Genomic profiling of antimicrobial resistance genes in clinical isolates of Salmonella Typhi from patients infected with Typhoid fever in India. Sci Rep. 2020 May 19;10(1):8299.
18. Qamar FN, Yousafzai MT, Sultana S, Baig A, Shakoor S, Hirani F, et al. A Retrospective Study of Laboratory-Based Enteric Fever Surveillance, Pakistan, 2012–2014. The Journal of Infectious Diseases. 2018 July 27;218(Suppl 4):S201–S205.
19. Dewan AM, Corner R, Hashizume M, Ongee ET. Typhoid Fever and its association with environmental factors in the Dhaka Metropolitan Area of Bangladesh: a spatial and time-series approach. PLoSNegl Trop Dis. 2013 Jan 24;7(1):e1998.
20. Karkey A, Arjyal A, Anders KL, Boni MF, Dongol S, Koirala S, et al. The Burden and Characteristics of Enteric Fever at a Healthcare Facility in a Densely Populated Area of Kathmandu. PLoS ONE. 2010 Nov 15;5(11):e13988.
21. Prasad N, Jenkins AP, Naucukidi L, Rosa V, Sahu-Khan A, Kama M, et al. Epidemiology and risk factors for typhoid fever in Central Division, Fiji, 2014-2017: A case-control study. PLoSNegl Trop Dis. 2018 June 8;12(6):e0006571.
22. Wang H, Zhang P, Zhao Q, Ma W. Global burden, trends and inequalities for typhoid and paratyphoid fever among children younger than 15years over the past 30years. Journal of travel medicine. 2024 Oct 25;31(8).
23. Olowolafe TA, Agosile OF, Akinpelu AO, Aderinto N, Wada OZ, Olawade DB. Malaria and typhoid fever co-infection: a retrospective analysis of University Hospital records in Nigeria. Malar J. 2024 July 24;23(1):220.
24. Kumar P, Kumar R. Enteric Fever. Indian J Pediatr. 2016 Oct 29;84(3):227–230.
25. Azmatullah A, Qamar FN, Thaver D, Zaidi AK, Bhutta ZA. Systematic review of the global epidemiology, clinical and laboratory profile of enteric fever. Journal of Global Health. 2015 Dec 1;5(2):020407.
26. Sejvar J, Lutterloh E, Naiene J, Likaka A, Manda R, Nygren B, et al. Neurologic Manifestations Associated with an Outbreak of Typhoid Fever, Malawi - Mozambique, 2009: An Epidemiologic Investigation. PLoS ONE. 2012 Dec 3;7(12):e46099.
27. Lutterloh E, Likaka A, Sejvar J, Manda R, Naiene J, Monroe SS, et al. Multidrug-Resistant Typhoid Fever With Neurologic Findings on the Malawi-Mozambique Border. Clinical Infectious Diseases. 2012 Feb 22;54(8):1100–1106.
28. Thriemer K, Ley BB, Ame SS, Deen JL, Pak GD, Chang NY, et al. Clinical and Epidemiological Features of Typhoid Fever in Pemba, Zanzibar: Assessment of the Performance of the WHO Case Definitions. PLoS ONE. 2012 Dec 20;7(12):e51823.
29. Andrews JR, Vaidya K, Bern C, Tamrakar D, Wen S, Madhup S, et al. High Rates of Enteric Fever Diagnosis and Lower Burden of Culture-Confirmed Disease in Peri-urban and Rural Nepal. The Journal of Infectious Diseases. 2017 July 28;218(Suppl 4):S214–S221.
30. Bolia R. Editorial: The Value of Monitoring Local Antimicrobial Resistance Patterns in Enteric Fever. Journal of Gastrointestinal Infections. 2023 July 1;13(02):061–062.
31. Garrett D. The surveillance for enteric fever in Asia project (SEAP): Estimating the community burden of enteric fever. International Journal of Infectious Diseases. 2016 Apr 1;45:64.
32. Alexander V, George JT, Paul JS. Increasing azithromycin resistance in patients with enteric fever: Cause for concern. Trop Doct. 2024 Apr 22;54(3):294.
33. Eissa A.Saeed ,Suman Singh and Sunil Trivedi .Study of various laboratory methods for an early diagnosis of enteric fever. Asian Jr. of Microbiol. Biotech. Env. Sc. Vol. 21, No. (4) : 2019 : 980-986.