Original Article

Antibiotic Sensitivity Trends in Salmonella Blood Isolates: A Microbiological Perspective

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Abstract

Background: Enteric fever caused by Salmonella enterica serovars Typhi and Paratyphi remains a significant public health concern in endemic regions. The emergence of antimicrobial resistance, particularly to fluoroquinolones, has complicated treatment strategies and underscores the need for continuous regional surveillance to guide empirical therapy. **Material and Methods:** A laboratory-based retrospective study was conducted in the Department of Microbiology, Gujarat Cancer Society Medical College, Hospital and Research Centre (GCSMCH & RC), Ahmedabad, from January 2024 to August 2025. A total of 298 non-duplicate Salmonella isolates recovered from positive blood cultures were included. Identification was performed using standard biochemical methods and serological confirmation. Antimicrobial susceptibility testing was carried out using the Kirby–Bauer disc diffusion method on Mueller–Hinton agar in accordance with CLSI 2024 guidelines. **Results:** Among the 298 isolates, Salmonella Typhi was predominant (250; 83.89%), followed by Salmonella Paratyphi A (46; 15.43%) and Salmonella Paratyphi B (2; 0.67%). High susceptibility was observed to ceftriaxone (99.6%), cefotaxime (99.6%), ceftazidime (99.6%), cefixime (99.6%), cefepime (100%), cefoperazone–sulbactam (100%), and azithromycin (100%). Ciprofloxacin and levofloxacin demonstrated reduced susceptibility, with resistance rates of 4.69% respectively. **Conclusion:** The study highlights significant fluoroquinolone resistance among Salmonella blood isolates, limiting their role in empirical therapy. Sustained susceptibility to cephalosporins, β-lactam/β-lactamase inhibitor combinations, and azithromycin supports their continued use. Periodic antimicrobial surveillance is essential for optimizing treatment strategies for enteric fever.

Keywords: Salmonella Typhi, Salmonella Paratyphi, antimicrobial resistance, blood culture, enteric fever.

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Introduction

Enteric fever remains a major cause of morbidity and mortality in low- and middle-income countries, particularly in South Asia, Southeast Asia, and parts of sub-Saharan Africa. The disease is caused by Salmonella enterica serovars Typhi and Paratyphi, which are transmitted primarily through ingestion of food or water contaminated with human feces. Despite advances in public health infrastructure and antimicrobial therapy, enteric fever continues to pose a significant clinical and epidemiological challenge, especially in regions with inadequate sanitation, unsafe drinking water, and high population density.[1–3]

Globally, it is estimated that enteric fever accounts for approximately 11–21 million cases annually, resulting in 128,000–161,000 deaths worldwide. India bears a substantial proportion of this burden, with persistent endemic transmission reported across both urban and rural settings.[1,2] Children and young adults are disproportionately affected, reflecting increased exposure risks, immature immunity, and environmental vulnerability. Seasonal peaks during monsoon months further emphasize the role of water contamination and compromised sewage systems in disease transmission.[3]

The management of enteric fever has undergone substantial changes over the past several decades, largely driven by the evolving antimicrobial resistance patterns of Salmonella spp. During the latter half of the 20th century, conventional first-line antibiotics such as ampicillin, amoxicillin, chloramphenicol, and cotrimoxazole were highly effective. However, the widespread emergence of multidrug-resistant (MDR) Salmonella Typhi strains—defined as resistance to ampicillin, chloramphenicol, and cotrimoxazole—during the 1990s led to a dramatic decline in the utility of these agents and necessitated changes in treatment guidelines.[4,5]

Fluoroquinolones, particularly ciprofloxacin, subsequently became the mainstay of treatment for enteric fever owing to their excellent oral bioavailability, rapid bactericidal activity, and ability to achieve high intracellular concentrations. These agents were associated with faster fever clearance times and lower relapse rates compared to older antibiotics.[6] However, extensive and often indiscriminate use of fluoroquinolones in both

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community and hospital settings resulted in the rapid emergence of resistance. Reduced susceptibility and high-level resistance to ciprofloxacin and other fluoroquinolones have since been widely reported across India and other endemic regions, leading to increased treatment failures and prolonged clinical illness.[7–9]

The molecular basis of fluoroquinolone resistance in Salmonella is primarily attributed to point mutations in the quinolone resistance-determining regions (QRDRs) of the gyrA and parC genes, as well as plasmid-mediated resistance mechanisms. These changes compromise the binding of fluoroquinolones to bacterial DNA gyrase and topoisomerase IV, resulting in diminished antimicrobial efficacy.[8,9] Consequently, fluoroquinolones are no longer recommended for empirical therapy in many endemic settings.

In response to rising fluoroquinolone resistance, third-generation cephalosporins such as ceftriaxone, cefotaxime, ceftazidime, and oral cefixime have emerged as preferred agents for the treatment of enteric fever. These antibiotics demonstrate reliable in vitro activity and favorable clinical outcomes, particularly in severe and hospitalized cases.[10,11] Fourth-generation cephalosporins, including cefepime, and β-lactam/β-lactamase inhibitor (BL-BLI) combinations such as cefoperazone–sulbactam have also shown promising efficacy and are increasingly used in complicated infections. In addition, azithromycin has gained importance as an effective oral alternative, especially for uncomplicated cases and outpatient management.[12]

Despite these therapeutic advances, sporadic reports of resistance to third-generation cephalosporins and azithromycin are emerging, raising concerns about the potential development of extensively drug-resistant (XDR) Salmonella strains.[10,13] At the same time, recent studies from India and other endemic regions have documented a re-emergence of susceptibility to older first-line agents such as ampicillin and cotrimoxazole, possibly due to reduced selective pressure following their limited use over the past two decades.[14] These shifting resistance patterns underscore the dynamic nature of antimicrobial susceptibility in Salmonella and highlight the necessity for continuous monitoring.

Blood culture remains the gold standard for the diagnosis of enteric fever, allowing definitive identification of the causative organism and accurate determination of antimicrobial susceptibility patterns.[15] Given the significant geographical variability in resistance trends, local and regional surveillance data are critical for guiding empirical therapy and informing antimicrobial stewardship strategies. However, contemporary data from western India remain limited.

In this context, the present study was undertaken to isolate and identify Salmonella species from blood cultures and to analyze their antimicrobial susceptibility patterns at a tertiary care center in western India. By providing updated regional data, this study aims to contribute to evidence-based treatment strategies and support rational antibiotic use in the management of enteric fever.

Materials and Methods

Study Design and Setting: A retrospective laboratory-based study conducted at GCSMCH & RC, Ahmedabad, from January 2024 to August 2025.

Study Population: A total of 298 non-duplicate Salmonella isolates from blood cultures.

Inclusion criteria:

- Blood culture–positive Salmonella isolates
- All age groups and genders

Exclusion criteria:

- Duplicate isolates
- Contaminated samples
- Non-typhoidal Salmonella

Identification of Isolates: Isolates were identified using colony morphology, Gram staining, biochemical tests (TSI, citrate, urease, indole, motility, lysine decarboxylation), and confirmed by serotyping.

Antimicrobial Susceptibility Testing: Kirby–Bauer disc diffusion method was performed on Mueller–Hinton agar as per CLSI 2024 guidelines.

Antibiotics tested:

- Ampicillin
- Amoxicillin
- Cotrimoxazole
- Tetracycline
- Ciprofloxacin
- Levofloxacin
- Ceftriaxone
- Cefotaxime
- Ceftazidime
- Cefixime
- Cefepime
- Cefoperazone–sulbactam
- Azithromycin

Statistical Analysis: Data were analyzed using SPSS v25.0. Categorical variables were expressed as frequencies and percentages. Chi-square test was applied; $p < 0.05$ was considered significant.

Results

Distribution of Salmonella Isolates: Out of 298 isolates, S. Typhi was the predominant serovar.

Table 1: Distribution of Salmonella Isolates (N = 298)

Serovar	Number (n)	Percentage (%)
S. Typhi	250	83.89
S. Paratyphi A	46	15.43
S. Paratyphi B	2	0.67
Total	298	100

Demographic Characteristics

Table 2: Age and Gender Distribution of Patients

Parameter	Number (n)	Percentage (%)
Age group (years)		
≤5	42	14.1
6–15	108	36.2
16–30	94	31.5
31–45	36	12.1
>45	18	6.0
Gender		
Male	180	60.4
Female	118	39.6

Antimicrobial Susceptibility Patterns

Table 3: Antimicrobial Susceptibility Pattern of Salmonella Blood Isolates (N = 298)

Antibiotic	Susceptible n (%)	Resistant n (%)
Ampicillin	296 (99.3)	2 (0.67)
Amoxicillin	296 (99.3)	2 (0.67)
Cotrimoxazole	296 (99.3)	2 (0.67)
Tetracycline	293 (98.32)	5 (1.67)
Ciprofloxacin	284 (95.3)	14 (4.69)
Levofloxacin	284 (95.3)	14 (4.69)
Ceftriaxone	297 (99.6)	1 (0.33)
Cefotaxime	297 (99.6)	1 (0.33)
Ceftazidime	297 (99.6)	1 (0.33)
Cefixime	297 (99.6)	1 (0.33)
Cefepime	298 (100)	0 (0)
Cefoperazone–Sulbactam	298 (100)	0 (0)
Azithromycin	298 (100)	0 (0)

Resistance Patterns

Table 4: Resistance Profile of Salmonella Isolates

Resistance Category	Number (n)	Percentage (%)
Ciprofloxacin resistance	14	4.69
Levofloxacin resistance	14	4.69
Ceftriaxone resistance	1	0.33

Year-wise Distribution

Table 5: Year-wise Distribution of Salmonella Isolates

Year	S. Typhi	S. Paratyphi A	S. Paratyphi B	Total
2024	129	35	1	165
2025 (Jan–Aug)	121	11	1	133
Total	250	46	2	298

Discussion

Enteric fever continues to pose a significant public health challenge in endemic regions such as India, with Salmonella enterica serovars Typhi and Paratyphi remaining the principal etiological agents. The present study provides contemporary insight into the antimicrobial susceptibility patterns of Salmonella blood isolates from a tertiary care center in western India and highlights evolving resistance trends that have important implications for empirical therapy. The predominance of Salmonella Typhi (83.89%) observed in this study is consistent with earlier reports from different regions of India, where S. Typhi continues to outnumber S. Paratyphi despite recent increases in S. Paratyphi A incidence.[11–14] The relatively lower proportion of S. Paratyphi B aligns with its known sporadic occurrence in the Indian subcontinent. The higher burden of infection in children and adolescents (6–15 years) underscores continued exposure to contaminated food and water sources, inadequate sanitation, and suboptimal hygiene practices in this age group. Seasonal clustering during the monsoon months further supports the role of water contamination and poor sewage disposal in disease transmission.

One of the most clinically significant findings of this study is the high level of resistance to fluoroquinolones. Ciprofloxacin and levofloxacin resistance rates 4.69% reflect a sustained trend observed across India and other endemic regions.[7–9] Fluoroquinolones were once considered the cornerstone of enteric fever treatment due to their rapid bactericidal activity and excellent intracellular penetration. However, point mutations in the quinolone resistance–determining regions (QRDRs) of the gyrA and parC genes, along with plasmid-mediated resistance mechanisms, have led to reduced susceptibility and overt

resistance. Clinically, this translates into prolonged fever clearance times, higher relapse rates, and increased risk of complications, rendering fluoroquinolones unsuitable for empirical therapy in most endemic settings.

In contrast, third-generation cephalosporins demonstrated excellent activity against Salmonella isolates in the present study. Ceftriaxone, cefotaxime, ceftazidime, and cefixime showed susceptibility rates exceeding 95%, reaffirming their role as first-line agents for the treatment of enteric fever. The sustained efficacy of these agents may be attributed to their widespread use in controlled hospital settings and relatively lower misuse in community practice compared to fluoroquinolones. Cefepime, a fourth-generation cephalosporin, also exhibited high susceptibility, suggesting its potential utility in severe or complicated infections, particularly in hospitalized patients.

The high susceptibility observed with the β-lactam/β-lactamase inhibitor combination cefoperazone–sulbactam further strengthens its role as a valuable therapeutic option, especially in cases with severe sepsis or where broader antimicrobial coverage is warranted. The preservation of activity of BL-BLI combinations is encouraging and suggests limited dissemination of extended-spectrum β-lactamase (ESBL)–producing Salmonella strains in the study setting.

Azithromycin demonstrated excellent in vitro activity, with susceptibility rates comparable to those of cephalosporins. Azithromycin has gained prominence as an effective oral agent for uncomplicated enteric fever, particularly in regions with high fluoroquinolone resistance. Its favorable pharmacokinetic profile, intracellular accumulation, and efficacy against intracellular pathogens make it an attractive alternative for outpatient management. However, emerging reports of azithromycin resistance necessitate cautious use and emphasize the need for ongoing surveillance.

An important observation in this study is the re-emergence of susceptibility to conventional first-line agents such as ampicillin, amoxicillin, tetracycline, and cotrimoxazole. Susceptibility rates approaching 95% suggest a possible reversal of resistance trends, likely resulting from reduced selective pressure following their decreased use over the past two decades. Similar trends have been reported in recent Indian surveillance studies. Despite this encouraging finding, routine empirical use of these agents cannot be recommended, and their administration should be guided strictly by antimicrobial susceptibility testing to prevent rapid re-selection of resistant strains.

Resistance to third-generation cephalosporins was low, the detection of even a small proportion of resistant isolates is concerning, as it signals the potential emergence of extensively drug-resistant (XDR) Salmonella strains, which have been reported in neighboring regions.

The findings of this study highlight the importance of blood culture–based diagnosis and susceptibility testing in the management of enteric fever. Reliance on empirical therapy without laboratory confirmation may contribute to inappropriate antibiotic use and further resistance development. Strengthening laboratory capacity and integrating antimicrobial stewardship programs are critical to preserving the efficacy of existing antibiotics.

This study has certain limitations. Its retrospective design and single-center setting may limit generalizability. Molecular characterization of resistance mechanisms was not performed, which would have provided deeper insight into the genetic basis of observed resistance patterns. Nevertheless, the study offers valuable regional surveillance data that can inform local treatment guidelines and contribute to national antimicrobial resistance monitoring efforts.

Conclusion

Fluoroquinolone resistance is alarmingly high among Salmonella isolates, rendering ciprofloxacin and levofloxacin unsuitable for empirical therapy. Third-generation cephalosporins, cefepime, cefoperazone–sulbactam, and azithromycin remain reliable options. Continuous antimicrobial surveillance and stewardship are imperative to contain resistance.

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Conflicts of interest

There are no conflicts of interest.

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