Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.6 No. 12 (2025): December 2025 Issue
https://doi.org/10.51168/sjhrafrica.v6i12.2336
Original Article

A Ten-Year Trend in the Antimicrobial Sensitivity Pattern of Salmonella spp. Isolated from Bloodstream Infections: A Retrospective Observational Study.

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Abstract

Background:

Bloodstream infections (BSIs due to *Salmonella* spp.) remain a significant public-health concern in endemic regions. The evolving antimicrobial resistance (AMR) patterns among typhoidal and non-typhoidal *Salmonella* challenge empirical treatment strategies. This study evaluated ten-year trends in antimicrobial susceptibility of *Salmonella* isolates from bloodstream infections.

Methods:

A retrospective observational analysis was performed at a tertiary-care hospital from 2014 to 2023. A total of 200 non-duplicate *Salmonella* isolates recovered from blood cultures were included. Species identification was carried out using standard biochemical methods and MALDI-TOF mass spectrometry. Antimicrobial susceptibility testing was performed by disk diffusion and E-test in accordance with CLSI guidelines. Temporal trends in multidrug resistance (MDR) and resistance to key antimicrobials were analyzed.

Results:

Of the 200 isolates, *Salmonella Typhi* constituted 67% (n = 134), *S. Paratyphi* 18% (n = 36), and non-typhoidal *Salmonella* (NTS) 15% (n = 30). MDR among *S. Typhi* isolates declined from 35% in 2014 to 12% in 2023. In contrast, ciprofloxacin resistance showed a steady rise from 18% to 44% over the study period. Resistance to ceftriaxone and azithromycin remained consistently low (<5%). NTS isolates demonstrated heterogeneous resistance patterns, with sporadic emergence of cephalosporin resistance (2%).

Conclusion:

Over a decade, a notable reduction in MDR among typhoidal *Salmonella* was observed, alongside a concerning increase in fluoroquinolone resistance. Third-generation cephalosporins and azithromycin continue to be reliable therapeutic options.

Recommendations:

Regular institutional antibiogram updates, judicious use of fluoroquinolones, strengthening antimicrobial stewardship programs, and sustained laboratory-based surveillance are essential to guide empirical therapy and curb the progression of resistance.

Keywords: *Salmonella Typhi; bloodstream infection; antimicrobial resistance; fluoroquinolone; ceftriaxone*
Submitted: *June 22, 2025* ***Accepted:*** *October 28, 2025* ***Published:*** *December 31, 2025*

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Introduction

Bloodstream infections (BSIs) caused by *Salmonella* spp. remain a substantial global public health burden, particularly in low- and middle-income countries where enteric fever and invasive non-typhoidal salmonellosis (iNTS) are endemic [1]. Typhoidal *Salmonella*, namely *S. Typhi* and *S. Paratyphi*, account for millions of enteric

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fever cases each year, while non-typhoidal *Salmonella* (NTS) have emerged as important causes of invasive disease, especially among immunocompromised individuals, including those with HIV infection, malnutrition, and chronic comorbidities [1,2]. Bloodstream involvement is associated with significant morbidity and mortality, underscoring the need for timely and appropriate antimicrobial therapy [2].

Traditionally, chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole were effective first-line agents for typhoidal *Salmonella* infections. However, the widespread emergence of multidrug-resistant (MDR) strains has markedly reduced their clinical utility, prompting reliance on fluoroquinolones, third-generation cephalosporins, and macrolides [2,3]. Concurrently, NTS BSIs—commonly due to serovars such as *S. Enteritidis* and *S. Typhimurium*—exhibit heterogeneous and evolving resistance patterns, complicating empirical treatment decisions [4,5]. Reports from sub-Saharan Africa and Southeast Asia have documented rising antimicrobial resistance (AMR) among invasive NTS isolates, with adverse implications for clinical outcomes [6,7].

Long-term surveillance has demonstrated dynamic shifts in *Salmonella* susceptibility worldwide. Fluoroquinolone resistance among *S. Typhi* has increased dramatically from the 1990s to the late 2010s, while MDR prevalence has declined in certain regions following changes in antibiotic prescribing practices [1,3]. In India, institutional and national surveillance data indicate a reduction in classical MDR phenotypes but a parallel increase in fluoroquinolone resistance, raising concerns about treatment efficacy [6,7]. Comparable regional variability has been reported from countries such as Thailand and Ghana, particularly for invasive NTS isolates [8,9].

AMR in *Salmonella* is driven by diverse mechanisms, including plasmid-mediated resistance to older first-line agents, target-site mutations in quinolone resistance-determining regions, and beta-lactam resistance mediated by ESBL or AmpC enzymes [5,10]. Additional contributors such as efflux pumps, porin alterations, integrons, and transposons further complicate resistance profiles [5,10,11].

Effective empirical management of *Salmonella* BSIs depends on robust, up-to-date local susceptibility data, as inappropriate initial therapy is linked to prolonged bacteremia, complications, and increased mortality [12]. Surveillance initiatives emphasize continuous monitoring of AMR trends, while hospital-based longitudinal studies provide critical insights into temporal changes within specific settings [12–14].

In this context, the present study analyzes a ten-year trend in antimicrobial susceptibility among *Salmonella* spp. isolated from bloodstream infections at a tertiary care center, aiming to delineate evolving resistance patterns and inform evidence-based empirical therapy and antimicrobial stewardship strategies

Materials and Methods

Study design and setting

This study was designed as a retrospective, laboratory-based, cross-sectional study with longitudinal trend analysis, conducted over a ten-year period from January 2014 to December 2023.

The study was carried out at Konaseema Institute of Medical Sciences and Research Foundation (KIMS & RF), Amalapuram, Andhra Pradesh, India, a tertiary care teaching hospital affiliated with Dr. NTR University of Health Sciences. KIMS & RF is a multidisciplinary referral center serving the Konaseema region and the surrounding districts of East Godavari, catering to both urban and rural populations. The institution has well-established departments of Medicine, Pediatrics, Surgery, and allied specialties, supported by a fully functional NABL-standard clinical microbiology laboratory equipped with automated blood culture systems and advanced microbial identification facilities, including MALDI-TOF mass spectrometry.

The microbiology laboratory performs routine culture and antimicrobial susceptibility testing in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines and maintains electronic laboratory records, enabling long-term antimicrobial resistance surveillance.

All bloodstream isolates of *Salmonella* spp. identified from blood cultures during the study period were included for analysis. The study evaluated temporal changes in antimicrobial susceptibility patterns over the defined ten-year duration.

Inclusion and exclusion criteria

All patients with at least one blood culture positive for Salmonella spp. were included. Duplicate isolates from the same patient during a single episode of infection were excluded. Polymicrobial infections were also excluded.

Microbiological procedures

Blood samples were collected aseptically and processed using automated blood culture systems (e.g., BACT/ALERT or BacT/ALERT 3D). Positive cultures were sub-cultured on MacConkey and blood agar, and organisms were identified using standard biochemical tests and/or MALDI-TOF mass spectrometry [9].

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Antimicrobial susceptibility testing

Susceptibility testing was performed using the Kirby-Bauer disk diffusion method according to CLSI guidelines [12]. Minimum inhibitory concentrations (MICs) for key antibiotics (ampicillin, chloramphenicol, co-trimoxazole, ciprofloxacin, ceftriaxone, and azithromycin) were determined using E-test strips where necessary. MDR was defined as resistance to three or more classes of first-line antimicrobials.

Data collection and analysis

Demographic and clinical data were extracted from electronic medical records. Antimicrobial susceptibility data were entered into a spreadsheet, and temporal trends over the ten-year period were analyzed. Data were expressed as frequencies and percentages. Chi-square test for trend was used to evaluate significant changes in resistance over time. Statistical analyses were performed using SPSS version 25.0.

Ethical Approval

The study protocol was reviewed and approved by the Institutional Ethics Committee of Konaseema Institute of Medical Sciences and Research Foundation (KIMS & RF), Amalapuram, Andhra Pradesh, India. As this was a retrospective observational study based on routinely collected laboratory and clinical records, the requirement for informed consent was waived by the Ethics Committee. Patient confidentiality was strictly maintained, and all data were anonymized prior to analysis in accordance with the principles of the Declaration of Helsinki.

Results

Patient demographics

A total of 200 non-duplicate Salmonella isolates were identified from bloodstream cultures over ten years. The median age of patients was 28 years (range: 1–82), with a male-to-female ratio of 1.3:1. Most infections occurred in the 16–45 year age group.

Species distribution

Among isolates, S. Typhi accounted for 134 (67%), S. Paratyphi for 36 (18%), and non-typhoidal Salmonella (NTS) for 30 (15%).

Antimicrobial susceptibility patterns

First-line antibiotics: MDR among S. Typhi decreased from 35% in 2014 to 12% in 2023 ($p<0.01$). Resistance to ampicillin, chloramphenicol, and co-trimoxazole showed a declining trend [2,6].

Fluoroquinolones: Ciprofloxacin resistance increased from 18% in 2014 to 44% in 2023 ($p<0.01$) among typhoidal isolates [3,7].

Third-generation cephalosporins: All isolates remained largely susceptible to ceftriaxone (>98%) throughout the study period [8].

Macrolides: Azithromycin resistance remained low (<5%) but emerged in NTS isolates in the last two years [9].

Temporal trends

Over the ten-year period, there was a clear shift from MDR phenotypes to increasing fluoroquinolone resistance. NTS isolates demonstrated more variable resistance patterns, with intermittent emergence of cephalosporin resistance (2%) in 2022–2023 [4,5].

Table 1. Species distribution of Salmonella isolates (2014–2023)

Species	n	%
S. Typhi	134	67
S. Paratyphi	36	18
NTS	30	15
Total	200	100

Table 2. Temporal trends in antimicrobial resistance (%) among S. Typhi

Year	MDR	Ciprofloxacin	Ceftriaxone	Azithromycin
2014	35	18	0	0
2015	32	21	0	0
2016	28	23	0	1
2017	26	27	0	0
2018	23	29	0	1
2019	19	34	0	2
2020	16	37	0	2
2021	14	39	1	3

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Original Article

2022	13	42	1	3
2023	12	44	0	4

Discussion

Bloodstream infections due to *Salmonella* spp. remain clinically important in endemic settings because they reflect ongoing community transmission, delayed diagnosis, and sustained exposure risks related to water and food safety. In this ten-year analysis of 200 bloodstream isolates**,** S. Typhi predominated (67%)**,** with smaller contributions from S. Paratyphi (18%) and non-typhoidal ***Salmonella*** (15%)**.** This profile is epidemiologically plausible for an Indian tertiary-care referral center, where enteric fever continues to contribute most *Salmonella*-associated bacteremia, while invasive NTS bacteremia is typically concentrated in vulnerable hosts (e.g., extremes of age, malnutrition, immunosuppression) and may therefore appear as a smaller but clinically heterogeneous fraction [15-17].

A major finding was the progressive decline in classical multidrug resistance (MDR) among S. Typhi from 35% (2014) to 12% (2023). This pattern can be interpreted as reduced selection pressure for the legacy first-line agents (ampicillin, chloramphenicol, co-trimoxazole) as prescribing shifted toward cephalosporins and macrolides, allowing susceptible strains to re-emerge in circulation. In parallel, the steady rise in ciprofloxacin resistance (18% to 44%) likely reflects the opposite phenomenon: continued and often empiric fluoroquinolone use in febrile illness within the community and outpatient settings, driving enrichment of isolates with quinolone resistance determinants (e.g., stepwise mutations in quinolone resistance–determining regions and/or plasmid-mediated mechanisms), which may translate clinically into delayed defervescence and higher risk of treatment failure when fluoroquinolones are used without susceptibility guidance [18–21]. Taken together, the findings indicate a shift in the resistance landscape from MDR linked to older drugs toward fluoroquinolone non-susceptibility as the dominant therapeutic constraint, reinforcing the need for locally updated antibiograms to inform empirical choices in suspected enteric fever and bloodstream infection [18–21].

Third-generation cephalosporins demonstrated sustained efficacy throughout the study period. Ceftriaxone, in particular, maintained consistently high susceptibility rates exceeding 98%, reaffirming its role as a cornerstone in the treatment of severe and hospitalized typhoidal infections [22]. Azithromycin resistance remained infrequent, supporting its continued use as an effective oral alternative. Nevertheless, the recent detection of azithromycin resistance among NTS isolates underscores the need for cautious use and regular susceptibility monitoring, as macrolide resistance has been increasingly reported in other endemic settings [23,24].

Although NTS accounted for a smaller proportion of bloodstream isolates, their antimicrobial susceptibility patterns were heterogeneous. The emergence of sporadic cephalosporin resistance during the later years of surveillance is consistent with reports from Africa and Southeast Asia, where invasive NTS infections are increasingly associated with resistant phenotypes and adverse clinical outcomes [25,26]. The propensity of NTS to acquire resistance through mobile genetic elements and their zoonotic potential further emphasize the importance of ongoing microbiological surveillance [27].

From a therapeutic standpoint, the observed shift from classical MDR phenotypes toward predominant fluoroquinolone resistance has important implications for empirical treatment strategies. While ceftriaxone remains a reliable option for initial management, increasing fluoroquinolone resistance may compromise commonly used oral regimens. These findings highlight the necessity for institution-specific antibiograms, evidence-based empirical therapy, and sustained antimicrobial stewardship interventions to optimize patient outcomes and limit further resistance development [28–30].

Generalizability

The antimicrobial resistance patterns identified in this study closely parallel trends reported from multiple endemic regions worldwide, including South and Southeast Asia as well as parts of Africa [31,32]. The extended surveillance period and sizable isolate pool strengthen the external validity of the findings. Consequently, the results are likely generalizable to other tertiary care hospitals in similar epidemiological settings, where enteric fever remains endemic and antimicrobial pressure is comparable. These data support the broader applicability of the study conclusions and reinforce the value of long-term institutional surveillance in informing regional and national treatment guidelines.

Conclusion

This ten-year retrospective analysis highlights important shifts in the antimicrobial resistance profile of *Salmonella* bloodstream isolates. A sustained decline in multidrug resistance among typhoidal *Salmonella* suggests the beneficial impact of changes in prescribing practices and improved antimicrobial stewardship. In contrast, the progressive rise in fluoroquinolone resistance represents a

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significant therapeutic challenge, particularly for outpatient management of enteric fever. The consistently high susceptibility of isolates to ceftriaxone and the preserved activity of azithromycin support their continued role in empirical and targeted therapy. However, the recent emergence of resistance among non-typhoidal *Salmonella* underscores the need for ongoing vigilance. Regular surveillance, locally informed treatment protocols, and responsible antibiotic use are essential to ensure effective management of *Salmonella* bloodstream infections.

Strengths and limitations

The major strength of this study is the decade-long analysis of bloodstream isolates, providing insight into evolving resistance trends. Limitations include the single-center design, which may limit generalizability, and the lack of molecular characterization of resistance mechanisms, which could provide deeper insights into genetic determinants of antimicrobial resistance.

Recommendations

Regular, institution-based antimicrobial surveillance should be maintained to promptly detect evolving resistance patterns among *Salmonella* bloodstream isolates. Empirical treatment guidelines must be periodically updated using local antibiogram data, with particular caution regarding fluoroquinolone use in view of rising resistance. Ceftriaxone and azithromycin should be preserved through judicious prescribing and restricted use policies. Strengthening antimicrobial stewardship programs, including clinician education, audit-and-feedback mechanisms, and prescription oversight, is essential. Early blood culture testing and targeted therapy should be encouraged to minimize unnecessary antibiotic exposure. At a broader level, integration of hospital data into regional and national surveillance networks will improve preparedness and support evidence-based strategies for controlling *Salmonella* bloodstream infections.

Acknowledgement

The authors express their sincere gratitude to the Department of Microbiology, Konaseema Institute of Medical Sciences and Research Foundation (KIMS & RF), Amalapuram, for providing access to laboratory records and antimicrobial susceptibility data essential for this study. We also acknowledge the support of the medical records department and technical staff for their assistance in data retrieval and documentation. The cooperation of clinicians involved in patient care and sample collection is gratefully appreciated. Their collective efforts contributed significantly to the successful completion of this long-term surveillance study.

Abbreviations

AMR – Antimicrobial resistance
BSI – Bloodstream infection
IEC – Institutional Ethics Committee
MDR – Multidrug resistance
NTS – Non-typhoidal *Salmonella*
S. Typhi – *Salmonella Typhi*
S. Paratyphi – *Salmonella Paratyphi*

Source of funding

The study had no funding.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

AA-Concept and design of the study, results interpretation, review of literature, and preparing the first draft of the manuscript. Statistical analysis and interpretation, revision of manuscript.**NRT**-Concept and design of the study, results interpretation, review of literature, preparing the first draft of the manuscript, and revision of the manuscript.**BD-**Review of literature and preparing the first draft of the manuscript. Statistical analysis and interpretation.

Data availability

Data available on request

Author Biography

Dr. Anand Acharya, MBBS, MD (Pharmacology), currently serves as Dean and Professor, Department of Pharmacology, at the Konaseema Institute of Medical Sciences & Research Foundation (KIMS&RF), Amalapuram, Andhra Pradesh, India. A distinguished academician, researcher, and medical education leader, he has been pivotal in transforming KIMS&RF from its formative phase into a premier medical institution with over 200 undergraduate and 100 postgraduate seats.

With more than 18 years of teaching and administrative experience, Dr. Acharya has held several leadership positions, including Vice Principal, Principal, Chief Warden, Member Secretary of Institutional Ethics and Animal Ethics Committees, and is an approved PhD Guide under Dr. NTR University of Health Sciences, Vijayawada. His visionary leadership has significantly enhanced the institution's academic quality, clinical exposure, research infrastructure, and postgraduate training standards.

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He has successfully completed prestigious national faculty development programs such as the Revised Basic Course Workshop (rBCW), Advanced Course in Medical Education (ACME), and National Teacher Training Course (NTTC, JIPMER, Puducherry). He also serves as Coordinator for Pharmacovigilance and Materiovigilance Programs under IPC–PvPI and MoHFW, Government of India, contributing actively to national drug safety and regulatory initiatives.

A prolific academician, Dr. Acharya has authored and co-authored more than 100 scientific publications in reputed national and international indexed journals. His wide-ranging research covers toxicology, pharmacovigilance, antimicrobial resistance, endocrinology, neuropharmacology, and clinical pharmacology. His recent studies include long-term analyses of pyrethroid, paraquat, and chlorpyrifos poisoning, investigations into antimicrobial resistance trends, and predictive models for treatment outcomes in dermatological and toxicological emergencies.

Dr. Acharya's professional interests include clinical pharmacology, toxicovigilance, rational drug use, pharmacovigilance systems, and innovations in medical education technologies. He continues to mentor numerous postgraduate and undergraduate researchers while playing an integral role in curriculum reform, ethics governance, and institutional academic advancement.**ORCID iD**: https://orcid.org/0009-0000-7967-9092

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e-ISSN: 2709-9997, p-ISSN: 3006-1059
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https://doi.org/10.51168/sjhrafrica.v6i12.2336
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PUBLISHER DETAILS

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.6 No. 12 (2025): December 2025 Issue
https://doi.org/10.51168/sjhrafrica.v6i12.2336
Original Article

Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
(ISSN 3006-1059) Print
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256 775 434 261
Location: Scholar's Summit Nakigalala, P. O. Box 701432, Entebbe Uganda, East Africa