









ORIGINAL RESEARCH ARTICLE

Antibiotic Susceptibility Pattern of *Salmonella Enterica* Serovar Typhi Isolated from Suspected Typhoid Fever Cases in General Hospital Minna

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ABSTRACT

Background: *Salmonella enterica* subspecies *enterica* serovar Typhi, especially resistant strains, remains a major cause of typhoid fever, causing significant morbidity, mortality, and economic loss in poor, developing countries. This study investigated the antibiotic susceptibility patterns of *S. Typhi* isolated from stool samples of suspected typhoid fever patients at the General Hospital, Minna. **Methods:** Stool samples were collected from three hundred (300) suspected typhoid fever patients, and cultured for the detection of *S. Typhi* using standard microbiological techniques. The isolates were identified using relevant biochemical tests, and antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method. The susceptibility results were interpreted according to the CLSI standard, and isolates with a Multiple Antibiotic Resistant Index (MARI) > 0.7 were identified using molecular techniques. Similarly, ESBL production was investigated using the double-disk synergy test (DDST). **Result:** Overall, 17 (5.6%) stool samples were culture-positive for *Salmonella* Typhi. The isolates showed variable resistance to the antibiotics examined: ciprofloxacin (76.5%), cefotaxime (64.7%), ceftriaxone (58.8%), azithromycin (58.8%), levofloxacin (52.9%), and the least resistance (23.5%) to pefloxacin. Overall, 82.4% of the *S. Typhi* isolates were resistant to multiple antibiotics, with a multiple-antibiotic resistance index ranging from 0.3 to 0.9. Both isolates with ≥ 0.7 MARI were identified as *Salmonella enterica* with $\geq 99\%$ per identity. Further results analysis revealed that none of the *Salmonella* Typhi produce ESBL phenotypically. These results underscore the endemicity of Typhoid fever in the study area and the need for a laboratory-guided diagnosis prior to antibiotic prescription to address the increasing resistance to potent, cheap antibiotics.

ARTICLE HISTORY

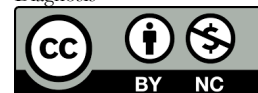
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INTRODUCTION

Salmonellosis remains a significant foodborne and zoonotic disease in Nigeria, with several studies reporting its presence in ready-to-eat foods and poultry production systems. For instance, *Salmonella* species have been isolated from roasted meat (*suya*) in Ilorin, Kwara State, with reported multidrug resistance among the isolates (Oludairo *et al.*, 2022). Similarly, studies conducted in Minna, Niger State, documented the prevalence of antibiotic-resistant *Salmonella enterica* in ready-to-eat meat and contact surfaces, indicating poor hygiene practices and public health risks (Ekli *et al.*, 2025). In southwestern Nigeria, molecular detection of *Salmonella* in poultry farms further confirmed the circulation of resistant strains within animal production systems, posing a risk of transmission to humans through the food chain

(Adekunle *et al.*, 2025). These findings show that salmonellosis continues to pose a major public health challenge in Nigeria, particularly due to the increasing prevalence of antimicrobial resistance.

Salmonella is a of Gram-negative, facultatively anaerobic rod-shape bacteria belonging to the family Enterobacteriaceae and is transmitted through the faecal-oral route via ingestion of contaminated food or water (Ferrari *et al.*, 2019; Stanaway *et al.*, 2019; WHO, 2023). Typhoidal serovars, such as *S. Typhi* and *S. Paratyphi* A, B, and C, are highly adapted to humans and cause systemic infections (typhoid and paratyphoid fever), which can lead to severe complications if untreated. Globally, the burden of *Salmonella* infections is disproportionately high in poor

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developing countries (LMICs), where factors such as poor sanitation and hygiene, poor food safety, and limited access to good healthcare exacerbate transmission (Tadesse *et al.*, 2019; Marchello *et al.*, 2022). Similarly, according to (WHO, 2023), typhoid fever remains endemic in regions with poor water infrastructure, contributing to an estimated 11–21 million cases and 128,000–161,000 deaths annually (WHO, 2023).

A critical challenge in managing salmonellosis is the rising prevalence of antimicrobial resistance (AMR), which complicates treatment. Irrational antimicrobial use is a significant worldwide health threat, particularly in poor developing countries with inadequate antibiotic regulation (Deb *et al.*, 2023). The recent, emerging resistance to fluoroquinolones (e.g., ciprofloxacin) and third-generation cephalosporins (e.g., ceftriaxone) has been reported, leaving few therapeutic options for the management of severe infections (NARMS, 2024). Multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Salmonella* strains further threaten global health security, as highlighted by the World Health Organization’s (WHO) classification of fluoroquinolone-resistant *Salmonella* as a "high-priority pathogen" for research and intervention (WHO, 2023).

Several studies in Nigeria have documented the emergence of multidrug-resistant *Salmonella* Typhi strains associated with typhoid fever. For instance, isolates exhibiting resistance to fluoroquinolones such as ciprofloxacin, macrolides including azithromycin, and β -lactam antibiotics have been reported (Adikwu *et al.*, 2021). Similarly, a study conducted among patients attending military hospitals in Minna, Niger State, identified *S. Typhi* isolates showing significant resistance to commonly used antimicrobial agents (Adabara *et al.*, 2012). In addition, another investigation involving patients with pelvic inflammatory disease in Niger State reported multidrug-resistant *S. Typhi* isolates resistant to antibiotics such as ofloxacin, nalidixic acid, amoxicillin/clavulanate, cephalexin, pefloxacin, and streptomycin (Oyedum *et al.*, 2023). Despite these findings, most of the previous studies in the region have largely focused on general antimicrobial resistance patterns without investigating extended-spectrum β -lactamase (ESBL)-producing *Salmonella* strains, which contribute significantly to resistance to β -lactam antibiotics. Moreover, there is limited recent data on the antibiotic susceptibility patterns of *Salmonella* Typhi isolates from patients with suspected typhoid fever in healthcare facilities within Minna. This lack of updated local surveillance data may hinder effective empirical clinical practices, including antimicrobial stewardship, common in most developing countries, like Nigeria. Therefore, the present study investigates the antibiotic susceptibility patterns of *Salmonella* Typhi isolated from suspected typhoid fever cases and phenotypically screens for the presence of ESBL among isolates obtained from patients attending General Hospital, Minna. The findings from this study are expected to provide updated local

susceptibility and ESBL production data among *Salmonella* Typhi in the study area, thereby contributing to improved treatment strategies and proactive control measures.

MATERIALS AND METHODS

Study Area

This study was conducted at the Clinical Microbiology Laboratory of the General Hospital, Minna, a referral Hospital that serves the majority of the inhabitants of Minna Metropolis. Approval to conduct the study (Approval No.: HMB/GHM/136/VOL.III/706) was obtained from the Research Ethics and Publication Committee (REPC) of the Hospital, and informed consent was obtained from individual participants.

Sample Collection and Isolation of Isolates

Exactly 300 Stool samples were collected over a period of four months (July to October, 2025) from participants suspected to have typhoid fever, irrespective of age or gender, in sterile, disposable containers. Prior to stool collection, patients were properly guided on how to take samples without contamination.

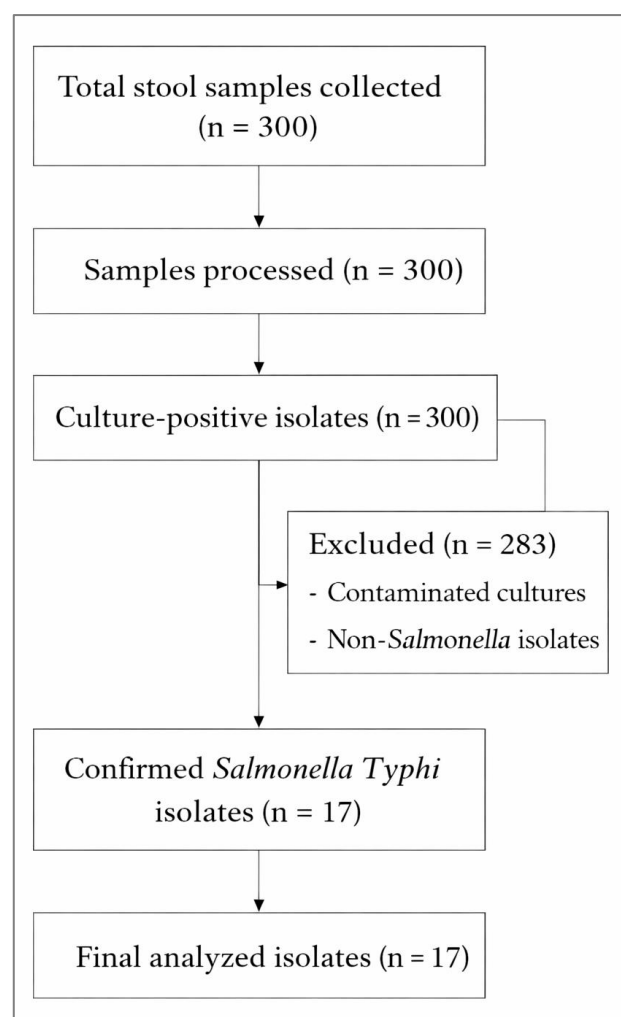


Figure 1: Participant/sample flow diagram showing stool collection, culture-positive isolates, and final analyzed isolates.

Samples were inoculated in selenite F broth (Difco) using a calibrated wire loop and incubated for 24 h, after which

pure cultures were obtained by sub-culturing on Salmonella-Shigella Agar (SSA) (Oxoid) and incubating at 37°C for 24 h. Subsequently, agar slants of the pure culture were prepared for further analysis. The sampling process is summarized in Figure 1.

Characterization and Identification of Isolate

Gram's staining and biochemical tests, including the oxidase test, triple sugar ion Agar. (TSI), catalase, indole, motility, methyl red (MR), urease, citrate, glucose, lactose, and sucrose tests (Terna et al., 2021) were performed on probable Salmonella sp. colonies. Molecular identification using gel Electrophoresis, PCR, and sequencing was used to confirmed the identity of *S. Typhi* isolates showing greater than or equal to 7 MDRI.

Briefly, bacteria DNA was isolated using the Zymo Research extraction kit. The 16S rRNA region of bacterial DNA was amplified by PCR using the 27F (5' AGAGTTTGTATCMTGGCTCAG3') and 1525R (5' AAGGAGGTGATCCAGCC3') primers following the standard protocol. The integrity of the PCR amplicons was assessed by electrophoresis; thereafter, they were separated using Sanger sequencing at Iqaba Biontech, Ibadan, Nigeria. The obtained sequence data were analyzed using MEGAX Software (version 12) and then compared against those in the NCBI database using the BLAST algorithm to identify the closest related species.

Antibiotic Susceptibility Test

Antimicrobial susceptibility testing (AST) was performed using the modified Kirby-Bauer disc diffusion method to determine the resistance profile of each isolate, according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2020). Pure colonies from 18 h old cultures were suspended in sterile normal saline adjusted to match the 0.5 McFarland standard (1.5×10^8 CFU/ml). The bacterial suspension was uniformly spread onto a sterile Mueller-Hinton agar (MHA, Oxoid Ltd., UK) plate. The test antibiotic disc which includes levofloxacin (20 µg), cefotaxime (10 µg), sparfloxacin (10 µg), ciprofloxacin (30 µg), amoxicillin (30 µg), Augmentin (10 µg), gentamycin (30 µg), pefloxacin (30 µg), ofloxacin (10 µg) and azithromycin (12 µg), ceftriaxone (30 µg), and ceftazidime (30 µg) was placed gently on the agar surface using sterile forceps. Plates were incubated at 37°C for 24 hours, after which zones of inhibition were measured in (mm) and interpreted as susceptible, intermediate, or resistant according to CLSI standards (Weinstein et al., 2020). Multidrug resistance patterns and multiple antibiotic resistance indices were calculated based on percentage resistance, while the double-disk synergy test was used to screen for the presence of extended beta-lactamase enzymes, as described by Magiorakos et al. (2012).

Double-disk synergy test (DDST)

The double-disk synergy test (DDST) was performed to detect ESBL production, as described by Das et al. (2023). Briefly, a test bacteria inoculum (0.5 McFarland standard) was swabbed onto a Mueller-Hinton agar plate, and a

susceptibility disc containing amoxicillin-clavulanate (30 µg, Bioanalyte, Turkey) was placed at the center of the lawn. Discs containing ceftazidime, ceftriaxone, and cefuroxime were then placed 15 mm (center to center) from the amoxicillin-clavulanate disc, followed by incubation at 37°C for 16–24 hours. The zone of inhibition around the disks was observed. A positive result was indicated by an enhanced zone of inhibition around the inhibitor disk, creating a "synergy arrowhead" or a straight zone that widens toward the disk. If no enhancement was seen, the test is negative for synergy, and the bacterium is likely not susceptible to the combination of drugs (Das et al., 2023)

Data Analysis

Data arising from this study were entered into an Excel sheet and proofread by an independent researcher. All categorical data variables, including sociodemographic data, sources of drinking water, and typhoid treatment history was summarised using frequencies and percentage. Cross-tabulation was used to examine the relationship between the independent and dependent variables in SPSS version 26.0. at $p = 0.05$.

RESULTS

Out of the 300 stool samples from 300 patients, 17 were culture-positive for Salmonella Typhi, yielding a prevalence of 5.6% (Figure 2).

Distribution of culture-positive Salmonella Typhi according to demographic categories

Differences in demographics and prevalence of Salmonella Typhi were observed among the 300 sampled patients, 59.00% of the patients were married, female (52.00%), above 18 years of age (69.9%), and literate (86.00%). Patients were mostly unemployed (51.33%) and residents in urban areas (52.33%). The major source of drinking water of patients was bore hole (45%), and 66% had a history of previous treatment for typhoid fever. A higher prevalence of Salmonella Typhi infection was observed in females (7.1%) compared to males (4.2%) and in adults (6.7%) compared to children (3.3%). Prevalence was higher in singles (6.7%) than in married patients (4.6%), and in non-literate patients (14.3%) than in literate patients (4.3%). persons with no previous typhoid treatment history (5.5%) and persons who had well water as their primary source of drinking water (11.57%).

From Table 1, out of the seventeen (5.6%) positive stool samples, 17 (5.6%) were identified as Salmonella Typhi using biochemical analysis. Table 1 also presents the association between demographic characteristics and culture-confirmed Salmonella prevalence among study participants. Chi-square analysis showed no statistically significant association ($p > 0.05$) between Salmonella isolation and gender ($\chi^2 = 1.166$, $p = 0.2803$), age group ($\chi^2 = 1.372$, $p = 0.2414$), marital status ($\chi^2 = 0.5828$, $p = 0.4452$), and typhoid treatment history ($\chi^2 = 0.01345$, $p = 0.9077$). Although a higher proportion of females (7.1%) was positive than males (4.2%), and adults (6.7%) had higher positivity than children (3.3%), these differences

were not statistically significant. Similarly, participants who had never been treated for typhoid (5.8%) had a

slightly higher prevalence than those previously treated (5.5%), but this difference was not significant.

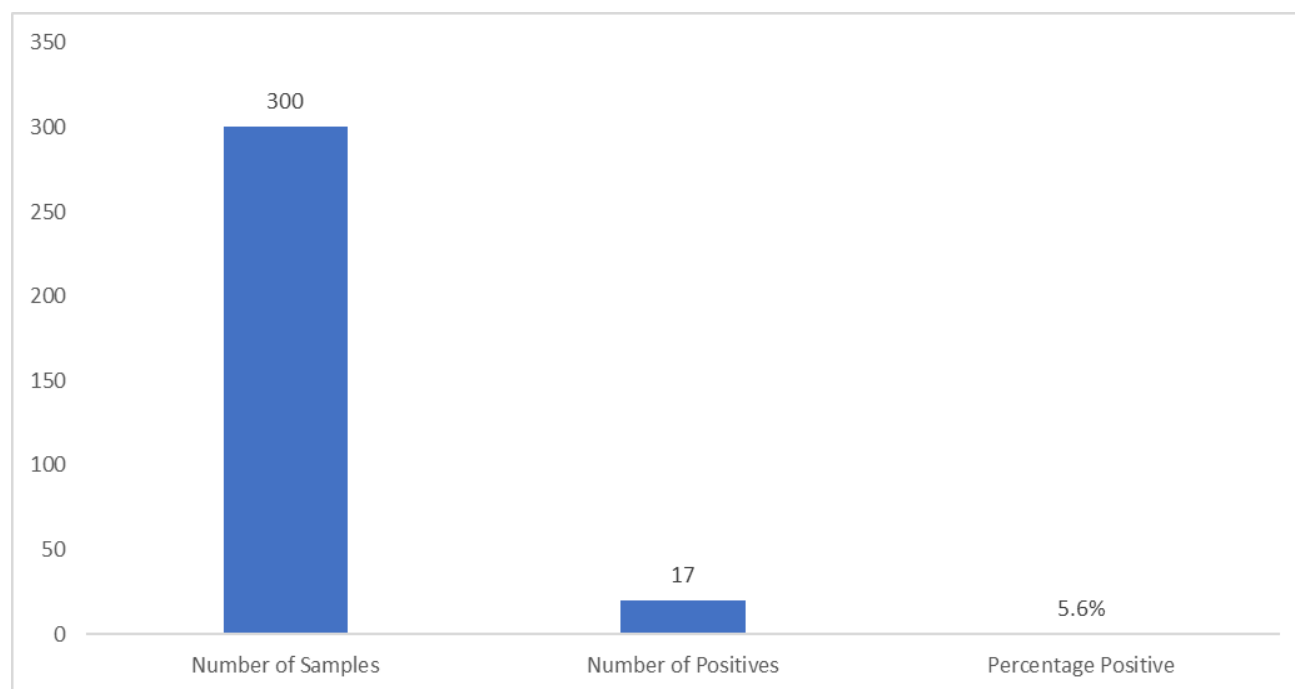


Figure 2: Distribution of culture-positive *Salmonella* Typhi among 300 patients' stool samples

Table 1: Association Between Demographic Characteristics and Prevalence of *Salmonella* Among Study Participants

Demographic characteristic	No of sample	No of Positive (%)	χ^2	<i>p-value</i>
Gender				
Male	144	6 (4.2)	1.166	0.2803
Female	156	11 (7.1)		
Age (years)				
Children (Below 18)	91	3 (3.3)	1.372	0.2414
Adults (Above 18)	209	14 (6.7)		
Marital Status				
Single	149	10 (6.7)	0.5828	0.4452
Married	150	7 (4.6)		
Divorced	0	0 (0.0)		
Widowed	1	0 (0.0)		
Educational Status				
Non-Literate	42	6 (14.3)	6.787	0.0092
Literate	258	11 (4.3)		
Occupation				
Civil Service	86	6 (6.9)	8.697	0.0336
Private Service	58	4 (6.8)		
Retiree	2	1 (50.0)		
Unemployed	154	6 (3.9)		
Residence				
Urban	157	4 (2.5)	54.14	<0.0001
Semi-urban	125	5 (4.0)		
Rural	18	8 (44.4)		
Typhoid Treatment History				
Treated Before	198	11 (5.5)	0.01345	0.9077
Never Treated Before	102	6 (5.8)		
Sources of Drinking Water				
Bore hole	135	5 (3.7)	5.995	0.0499
Well	95	11 (11.57)		
Bottled water	5	0 (0.0)		
Sachet water	63	4 (6.34)		
River	0	0 (0.0)		

P value less than 0.05 ($p < 0.05$) indicates a significant association between variables.

Table 2. Resistance pattern of *Salmonella* isolates.

IC	Antibiotic-resistant pattern	MARI	No of Antibiotics classes Resistant to	No of Antibiotics Resistant to	Resistance Category
ST1	PEF, AU, CF, TRX, CTZ	0.4	2	5	Non MDR
ST2	TRX, CTZ	0.1	1	2	Non MDR
ST3	CN, AM, TRX, CTZ	0.3	2	4	Non MDR
ST4	AZ, OFX, AU, CPX, CN, LEV, CF, AM, SP, TRX, CTZ	0.9	4	11	MDR
ST5	AU, CPX, LEV, CF, AM, SP, TRX, CTZ	0.6	2	8	Non MDR
ST6	AZ, AU, CPX, LEV, CF, SP, TRX, CTZ	0.6	3	8	MDR
ST7	AZ, AU, CPX, LEV, AM, SP, CTZ	0.5	3	7	MDR
ST8	AZ, OFX, AU, CPX, LEV, CF, AM, TRX, CTZ	0.7	3	9	MDR
ST10	AU, CPX, CN, CF, AM, TRX, CTZ	0.5	3	7	MDR
ST11	PEF, AU, CPX, CN, CF, AM, SP, TRX, CTZ	0.7	3	9	MDR
ST12	AZ, OFX, PEF, AU, CPX, CF, AM, TRX, CTZ	0.7	3	9	MDR
ST13	AZ, AU, CPX, LEV, AM, SP, TRX, CTZ	0.6	3	8	MDR
ST15	AZ, OFX, AU, CPX, LEV, CF, AM, TRX, CTZ	0.7	3	9	MDR
ST16	AZ, AU, CPX, LEV, AM, SP, TRX, CTZ	0.6	3	8	MDR
ST17	OFX, AU, CPX, CN, CF, AM, TRX, CTZ	0.6	3	8	MDR
ST18	AZ, OFX, AU, CPX, LEV, CF, AM, TRX, CTZ	0.7	3	9	MDR
ST20	AZ, PEF, AM, TRX, CTZ	0.4	3	5	MDR

KEY: IC = Isolate code; ST=*Salmonella typhi*; AZ= Azithromycin; OFX= ofloxacin; PEF= Pefloxacin; CN= Gentamycin; AU= Augmentin; AM= Amoxicillin; CPX= Ciprofloxacin; SP=Sparfloxacin; CF= Cefotaxime; LEV= Levofloxacin; TRX: Ceftriaxone; CTZ: Cefazidime; MARI: Multiple antibiotic resistance index; MDR: Multi-drug resistant; --: No resistance

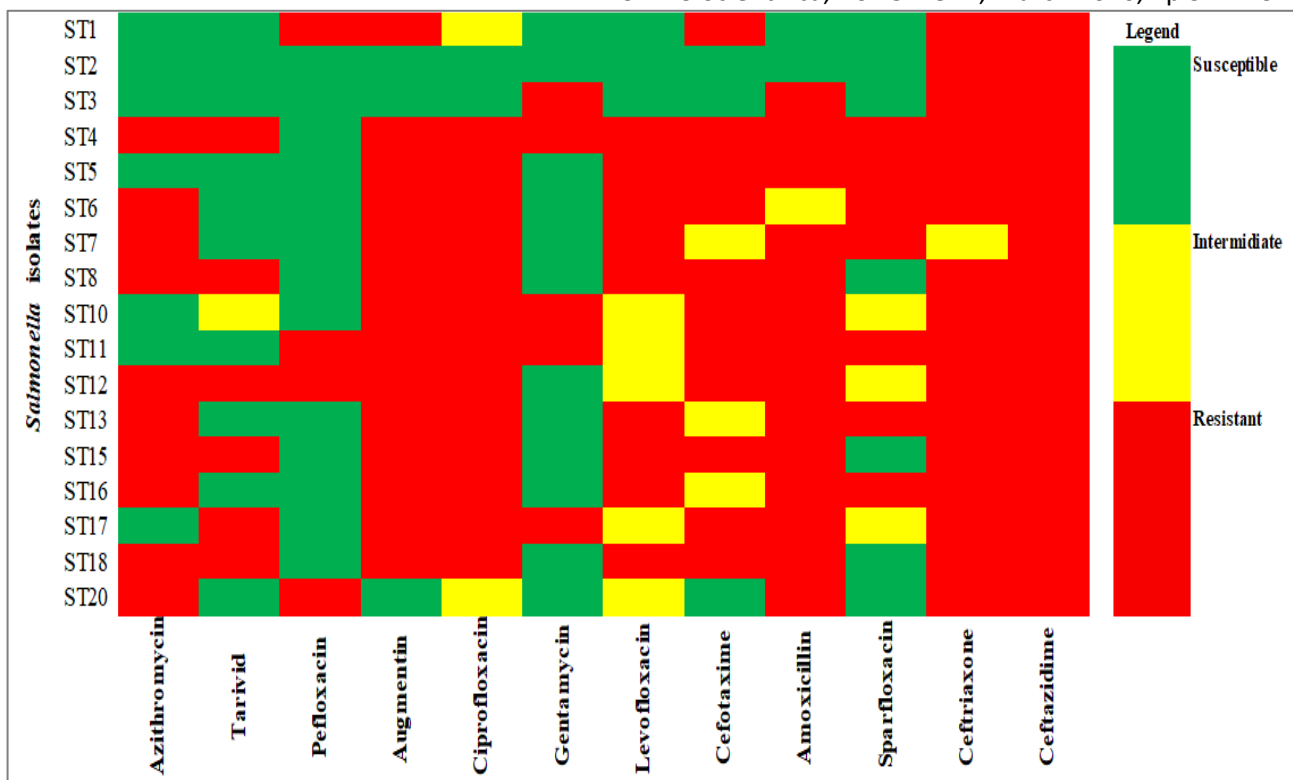


Figure 3: Heat map showing the antimicrobial susceptibility profile of suspected *Salmonella* isolates

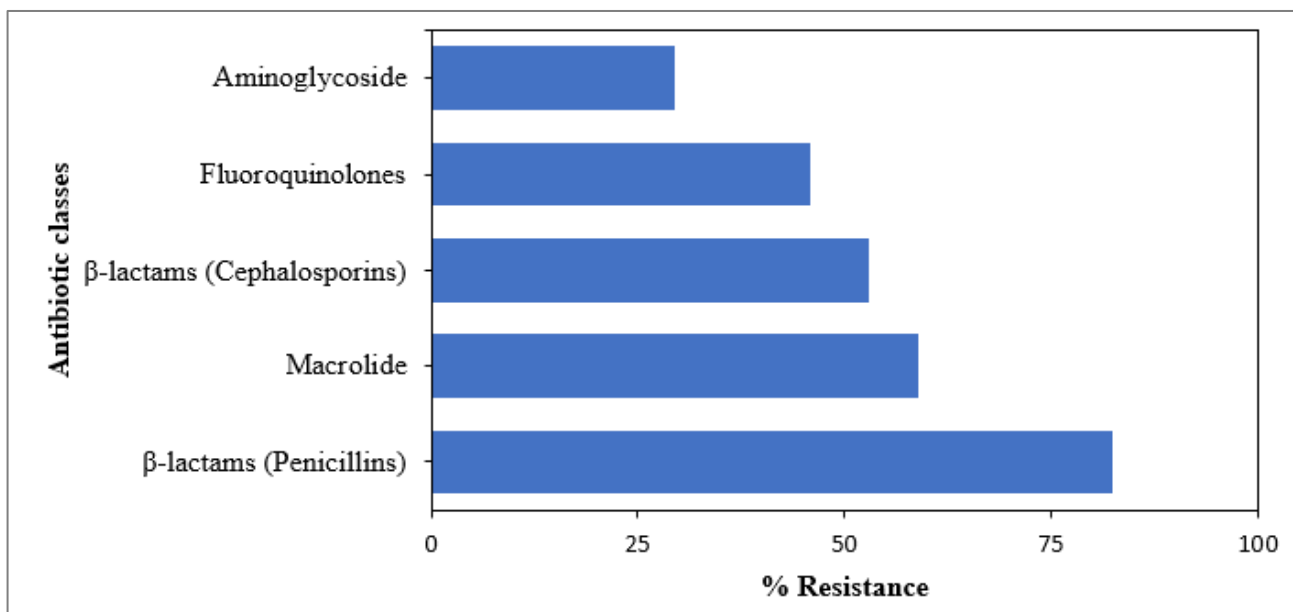


Figure 4: Percentage resistance of *Salmonella* Typhi isolates according antibiotic classes.

Statistically significant associations ($p < 0.05$) were observed between *Salmonella* positivity and educational status ($\chi^2 = 6.787, p = 0.0092$), occupation ($\chi^2 = 8.697, p = 0.0336$), residence ($\chi^2 = 54.14, p < 0.0001$), and source of drinking water ($\chi^2 = 5.995, p = 0.0499$). Non-literate participants had a significantly higher prevalence (14.3%) compared to literate participants (4.3%). Regarding occupation, retirees had the highest prevalence (50.0%), followed by civil servants (6.9%) and private workers (6.8%), while the unemployed had the lowest prevalence (3.9%). Participants residing in rural areas had a markedly higher prevalence (44.4%) compared to those in semi-urban (4.0%) and urban areas (2.5%). Furthermore, individuals who consumed water from wells had a higher

prevalence (11.57%) than those who used boreholes (3.7%) or sachet water (6.34%).

Antimicrobial susceptibility profile of suspected *Salmonella* isolates

The antibiotic susceptibility test revealed that the isolates were unevenly resistant to the antibiotics commonly prescribed for the treatment of typhoid fever in the study area with the highest resistance against drugs such as Ceftriaxone (58.8%), cefotaxime (64.7%), Azithromycin (58.8%), levofloxacin (52.9%), ciprofloxacin (76.5%) and the least resistance against ofloxacin (35.3%), gentamycin (29.4%), Ceftazidime (35.3%) and pefloxacin (23.5%) (Figure 3).

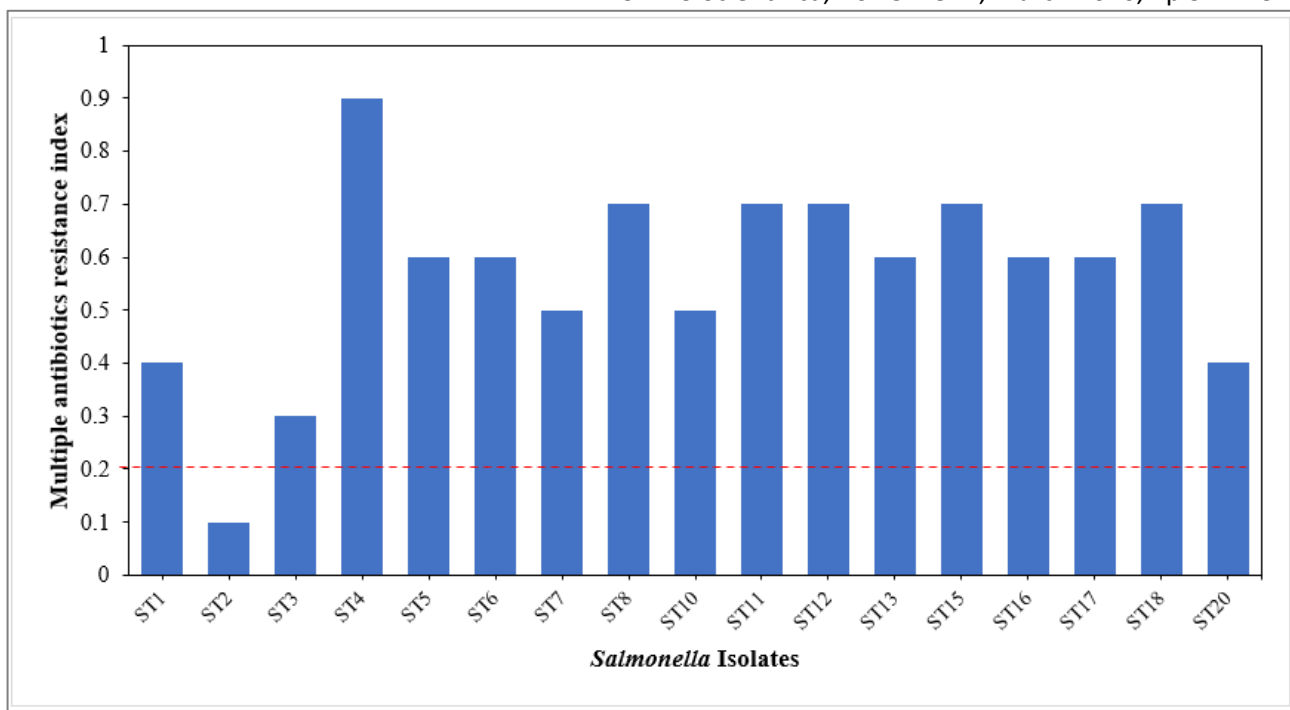


Figure 5: Multiple Antibiotic Resistance Index (MARI) distribution among Isolated *Salmonella Typhi*

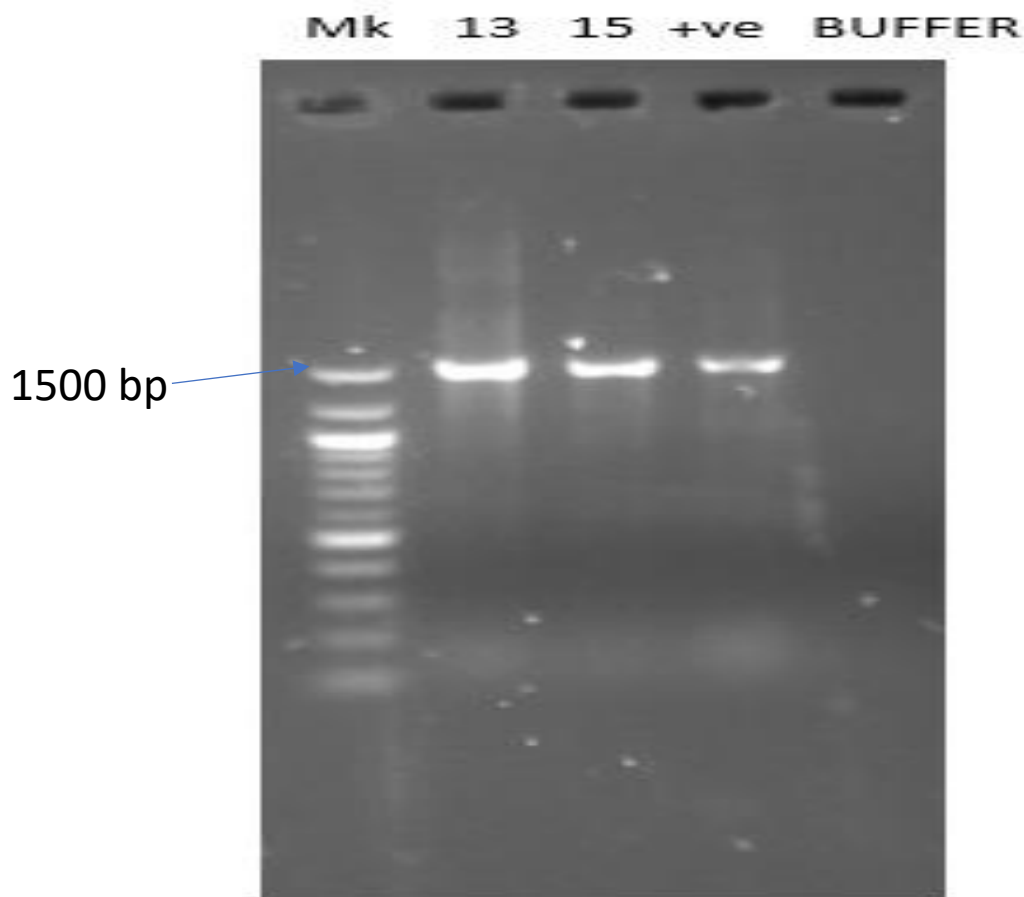


Figure 6: Electrodrogram of amplified 16S rRNA genes from *Salmonella* isolates DNA; Key: MK: 10kp DNA ladder; + ve: positive control; 13 & 15 (*Salmonella* isolates DNA)

Percentage resistance of *Salmonella Typhi* isolates across antibiotic classes

Figure 4 shows the percentage of resistant *Salmonella Typhi* by antibiotic class. Exactly 82.4% of the isolates were

resistant to beta-lactams; however, only 52.9% were resistant to cephalosporins. Similarly, 58.8% were resistant to macrolides, 45.9% to fluoroquinolones, and the least, 29.4%, were resistant to aminoglycosides.

Table 3. Summary of 16S rRNA gene sequences from *Salmonella* isolates with ≥ 0.7 MARI

Sample ID	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Identity	Accession
	<i>Salmonella enterica</i>	1391	9713	100%	0	99.74%	
	<i>Salmonella enterica</i>	1369	9558	99%	0	99.47%	

Multiple Antibiotic Resistance Index

The multiple antibiotic resistance index is not just a primary indicator of an organism's resistance profile, but also provides insight into the level of antibiotic pressure to which an organism may have been exposed. The determination of the antibiotic resistance index for each isolate showed multiple antibiotic resistance indices (MARI) ranging from 0.1 to 0.9, as shown in Table 2 and Figure 5).

The horizontal line at MARI = 0.2 indicates the threshold above which isolates are considered to originate from high-risk sources with frequent antibiotic exposure.

Double Disk Synergy Test (DDST)

Result analysis revealed that none of the *Salmonella* isolates harbors an extended-spectrum beta-lactamase enzyme, as none of the culture plates demonstrated the characteristic shape associated with a positive DDST result (Plate 1).



Plate 1: Diagram of a negative double disk synergy test result.

Molecular Identification of the organisms.

Figure 6 shows the electrogram of the PCR amplicon of the 2 *Salmonella* Isolates with ≥ 0.7 MARI index. The amplicon size is consistent with the 1500 bp of the 16S rRNA gene in bacteria. Based on the molecular analysis, all selected isolate DNA sequences were identified as *Salmonella enterica* with $\geq 99\%$ identity (Figure 6; Table 3).

DISCUSSION AND CONCLUSION

The study found that 17 of 300 stool samples (5.6%) collected from patients suspected of typhoid fever were positive for *Salmonella* Typhi. This prevalence indicates that typhoid fever remains endemic in the study area, though at a moderate level. The result is comparable with recent studies conducted in Nigeria and other developing countries. For instance, Terna *et al.* (2021) reported a prevalence of 5.7% among patients attending selected healthcare facilities in Lafia, Nigeria, while Abdulrahman *et al.* (2022) documented a prevalence of 6.1% in a similar hospital-based study in northern Nigeria. Variations in prevalence reported across studies may be attributed to differences in sample size, study duration, diagnostic methods, prior antibiotic use, and environmental sanitation conditions. Stool culture, although specific, may underestimate prevalence due to self-medication with antibiotics before hospital presentation, which is common in many low- and middle-income countries (Mogasale *et al.*, 2014; Akinyemi *et al.*, 2018). These observations once again underscore the importance of a definitive diagnosis and laboratory-guided antibiotic prescription in the management of typhoid fever cases in health facilities. Untreated typhoid fever cases pose a significant risk to patients because of the possible complications, but a misused antibiotic is far more dangerous because of far reaching effect on the usefulness of antibiotics and the promotion of antibiotic resistance.

The current study revealed a slightly higher prevalence of *S. Typhi* among females (7.05%) than males (6.25%). Similar trends have been reported by Okoro *et al.* (2022), who found that higher female prevalence was associated with greater exposure to contaminated food and water through domestic activities such as food preparation and caregiving. Adults aged 18 years and above had a higher prevalence (7.65%) than children (4.39%).

A similar study shows that adults in endemic regions are more frequently exposed due to occupational activities, increased mobility, and consumption of food outside the home. Educational status played a significant role, as non-literate participants showed a markedly higher prevalence (19.04%) compared to literate individuals (4.65%). Stanaway *et al.* (2020). A Studies by Ali *et al.* (2022) demonstrated that low educational attainment is associated with poor hygiene practices and limited awareness of disease transmission routes Similarly, a higher prevalence among individuals using well water (11.57%) corroborate findings by Boakye Okyere *et al.* (2025), who reported that untreated water sources significantly increased the risk of typhoid fever due to fecal contamination. Rural residents also demonstrated higher infection rates, emphasizing the role of inadequate sanitation infrastructure.

The antibiotic susceptibility profile showed high resistance to commonly used antibiotics, particularly amoxicillin (85%), Augmentin (85%), ciprofloxacin (80%), cefotaxime (70%), and levofloxacin (60%), sparfloxacin (45%), ceftriaxone (95%), ceftazidime (100%), cefotaxime (70%). These findings reflect the growing challenge of antimicrobial resistance in *S. Typhi* and are have similar reports from sub-Saharan Africa and South Asia. Studies by Kariuki et al. (2021) and Browne et al. (2020) show increasing resistance to fluoroquinolones and beta-lactam antibiotics, attributing this trend to widespread antibiotic misuse and incomplete treatment. Lower resistance levels observed for pefloxacin (25%), ofloxacin (40%), and gentamycin (40%) suggest that these antibiotics may still retain some effectiveness. However, WHO (2023) emphasizes that local susceptibility data should guide treatment decisions to prevent further resistance development.

The Multiple Antibiotic Resistance Index (MARI) analysis shows that 80% of the isolates were multidrug-resistant (MDR), with MARI values ranging from 0.1 to 0.9. MARI values greater than 0.2 indicate isolates originating from high-risk environments with frequent antibiotic exposure. These findings are consistent with those of Afolayan et al. (2022) and Eze et al. (2023), who reported MDR prevalence ranging from 65% to 85% among *Salmonella Typhi* isolates in Nigeria. The values recorded for the multiple antibiotic resistance index (MARI) in this study for the majority of the isolates raise concern because of their implications not only for the control of *S. Typhi* but also for all other Gram-negative pathogens and public health management generally.

According to Isaiah et al. (2025), a high MAR index is a potent indicator of treatment failure, which translates into increased morbidity, long hospital stays, higher healthcare costs, and, invariably, fatalities.

Phenotypic ESBL production screening using the Double Disk Synergy Test (DDST) indicated that all isolates were ESBL-negative. This suggests that ESBL-producing *S. Typhi* strains are not yet widespread in the study area. Similar findings have been reported by Olorunshola et al. (2021), who observed low ESBL prevalence among *Salmonella* isolates. The inability of the isolates to produce ESBL in DDST screening, therefore, suggests that the observed resistance to cephalosporins may have been due to mechanisms other than beta-lactamases. However, previous studies (Jacoby, 2009) opined that a negative DDST result, despite observed resistance to cephalosporins among the enteric isolates, suggests the involvement of alternative resistance mechanisms, such as AmpC β -lactamase production, which are capable of hydrolyzing cephalosporins but are not inhibited by clavulanic acid. Similarly, Jacoby (2009) reported that reduced outer membrane permeability due to porin loss reduces the entry of β -lactam antibiotics into bacterial cells, thereby decreasing their effectiveness (Delcour, 2009). Other mechanisms, such as efflux pump overexpression, which actively expel antibiotics from the bacterial cell, thus lowering intracellular drug concentrations and reducing susceptibility to

cephalosporins, had been described by Li et al. (2015). Overall, these findings validate the findings of the present studies, where isolated *S. Typhi* were resistance to multiple cephalosporins and are non-ESBL producers

The findings of this study have demonstrated a high level of antibiotic resistance among *S. Typhi* isolates to the 12 antibiotics tested in the study area. MARI index ranges from 0.4 to 0.9, and no isolates exhibit resistance due to ESBL activity. The study therefore underscores the need for the full implementation of antibiotic stewardship and the creation of awareness of the dangers of self-medication.

RECOMMENDATIONS

Based on the findings of this study, the following recommendations are proposed:

1. Routine culture and antibiotic susceptibility testing should be performed before initiating typhoid fever treatment to reduce inappropriate antibiotic use.
2. Antimicrobial stewardship programs should be strengthened to curb the misuse and overuse of antibiotics, particularly fluoroquinolones and beta-lactams.
3. Public health authorities should improve access to safe drinking water and sanitation facilities, especially in rural and semi-urban communities.
4. Future studies should incorporate molecular methods to confirm ESBL production and identify resistance genes for better epidemiological understanding.

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