Antibiotic Resistance Patterns in Enteric Fever Management: A Cross-Sectional Study in Kaduna Metropolis, Nigeria

[1]Sani A. Mohammed [2]Yusuf Akande [3]Mohammed N. Danjuma [4]Sherifat B. Anafi

[1]Department of Clinical Pharmacology and Therapeutics, Kaduna State University, Kaduna, Nigeria

[2]Grants and Collaborations Office, Federal Neuropsychiatric Hospital, Kaduna, Nigeria

[3,4]Department of Pharmacology and Therapeutics, Ahmadu Bello University Zaria, Nigeria

DOI: https://doi.org/10.51244/IJRSI.2025.12150002P

Received: 15 December 2024; Revised: 25 December 2024; Accepted: 27 December 2024; Published: 30 January 2025

ABSTRACT

This study examined antibiotic susceptibility patterns of bacteria isolated from patients with suspected enteric fever in Kaduna Metropolis, Nigeria, and compared the findings with global trends. Blood samples from 175 symptomatic patients were analyzed, revealing Staphylococcus species in 47.4% and Salmonella Typhi in 5.7% of isolates. All S. Typhi isolates were 100% susceptible to cephalosporins, chloramphenicol, fluoroquinolones, macrolides, and aminoglycosides, while reduced susceptibility to penicillins and cotrimoxazole was noted. MIC and MBC data highlighted chloramphenicol and trimethoprim-sulfamethoxazole as effective treatment options. The results confirm the efficacy of key antibiotics for enteric fever management in Kaduna, mirroring patterns in sub-Saharan Africa and Asia. However, diminished susceptibility to some drugs underscores the need for antimicrobial stewardship to curb resistance and inform local treatment guidelines.

Keywords: enteric fever; antibiotic susceptibility; Salmonella Typhi; Kaduna metropolis; antibiotic resistance, public health

INTRODUCTION

Enteric fever, caused primarily by Salmonella enterica serovars Typhi and Paratyphi [1], remains a significant public health challenge in low- and middle-income countries (LMICs), including Nigeria [2]. The burden of the disease is exacerbated by poor water quality, inadequate sanitation, and limited healthcare access, particularly in urban areas like Kaduna Metropolis. Recent global trends underscore the alarming rise of multidrug-resistant (MDR) strains of Salmonella, complicating treatment and necessitating local investigations to guide effective management strategies [2], [3], [4].

Despite various regional and global studies documenting resistance patterns, there remains a critical gap in localized data for Nigeria, especially in northern regions like Kaduna. Existing research has focused on the national or sub-Saharan levels, often overlooking the regional heterogeneities that influence antibiotic susceptibility and resistance [4]. Furthermore, the interplay between diagnostic challenges, such as high rates of culture-negative cases, and the emergence of MDR strains highlights the need for a comprehensive evaluation of the effectiveness of current antibiotic regimens [5].

METHODOLOGY

This cross-sectional study evaluated antimicrobial susceptibility patterns of bacterial pathogens isolated from 175 patients with suspected enteric fever in health facilities across Kaduna Metropolis, including the Igabi, Kaduna South, Kaduna North, and Chikun regions. Patients of all ages presenting with symptoms suggestive of enteric fever, such as prolonged fever and gastrointestinal complaints, were included after providing informed consent or assent for minors. Patients already on antibiotics or with confirmed alternative diagnoses were excluded from the study.

Blood samples were collected using aseptic techniques to minimize contamination and transported promptly under appropriate conditions for laboratory processing. Samples were cultured on suitable microbiological media, and isolated bacteria were identified through biochemical tests [6]. Serotyping was conducted for Salmonella Typhi, while non-Salmonella isolates were documented for further characterization. However, limitations such as potential contamination during sample collection and excluding intracellular pathogens like Rickettsia and Brucella might have influenced the outcomes [7].

Antimicrobial susceptibility testing was performed using the disk diffusion method, testing isolates against antibiotics such as cephalosporins, fluoroquinolones, macrolides, aminoglycosides, penicillins, and cotrimoxazole. The results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines [6]. Minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) for selected antibiotics were determined using the broth microdilution method. MIC was defined as the lowest antibiotic concentration inhibiting visible growth, while MBC represented the lowest concentration achieving ≥99.9% bacterial killing [6].

The Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics summarized demographic data, bacterial isolate distribution, and antibiotic susceptibility patterns, with results presented as percentages for susceptibility classifications. MIC and MBC values were reported as mean ± standard deviation. Ethical approval was obtained from the Health Research Ethics Committee of Ahmadu Bello University Teaching Hospital (ABUTH). Informed consent or guardian assent was secured, and confidentiality was maintained throughout the study.

RESULTS

175 blood samples were analyzed from consented participants who were mostly male (70.3%) with ages ranging from 1 – 59 years. Bacterial growth was observed in 103 samples (58.9%). Staphylococcus species were the most frequently detected among the isolates, accounting for 47.4% of cases. Salmonella Typhi, the primary focus of this study, was isolated in 10 samples (5.7%), while Escherichia coli and Klebsiella species were detected in 3.4% and 2.3% of samples, respectively. Notably, 34.9% of samples showed no bacterial growth, and 6.3% were contaminated with other microorganisms (Table 1). These findings highlight the diverse etiologies of bloodstream infections in the studied population.

Table 1 Distribution of Bacteria Isolated from Cultured Blood Samples of Participants

Bacteria isolated	**Number of respondents (N = 175)**
Staphylococcus sp.	83 (47.4)
Salmonella Typhi	10 (5.7)
Escherichia coli	6 (3.4)
Klebsiella sp.	4 (2.3)
No growth	61 (34.9)
Contaminated with other microorganisms	11 (6.3)

*Percentages in parentheses

Antibiotic susceptibility testing of Salmonella Typhi isolates revealed 100% susceptibility to cephalosporins (cefuroxime, cefotaxime, ceftriaxone, cefixime), chloramphenicol, macrolides (azithromycin), aminoglycosides (gentamicin), and fluoroquinolones (ciprofloxacin, ofloxacin). However, reduced susceptibility was observed for trimethoprim/sulfamethoxazole, with only 40% of isolates susceptible (Table2).

Table 2 Antibiotic Susceptibility of *Salmonella Typhi* Isolated from Sampled Participants

Antibiotic Groups	**Frequency (n = 10)**	**Percentage (%)**
Cephalosporins		
Cefuroxime	10	100.0
Cefotaxime	10	100.0
Ceftriaxone	10	100.0
Cefoxime	10	100.0
Chloramphenicol		
Chloramphenicol	10	100.0
Penicilins		
Amoxicillin	10	100.0
Amoxicillin/Clavulanic Acid		
Augmentin	10	100.0
Aminoglycosides		
Gentamycin	10	100.0
Macrolides		
Azithromycin	10	100.0
Fluoroquinolones		
Ciprofloxacin	10	100.0
Ofloxacin	10	100.0
Cotrimoxazole		
Trimethoprim/sulfamethoxazole	4	40.0

The antibiotic susceptibility revealed varied degrees of effectiveness. Among cephalosporins, ceftriaxone showed the highest efficacy (Table 3), with 90% of isolates highly susceptible, followed by cefotaxime (80% highly susceptible). Cefuroxime and cefixime displayed mixed results, with moderate susceptibility observed in up to 50% of isolates. Chloramphenicol demonstrated high susceptibility in 80% of isolates, while fluoroquinolones such as ofloxacin and ciprofloxacin were similarly effective, with high susceptibility rates of 80% and 70%, respectively. Cotrimoxazole showed equal high and moderate susceptibility (20% each), while gentamicin exhibited high susceptibility in only 40% of isolates, with most showing moderate response (60%). Penicillin (amoxicillin) displayed reduced efficacy, with only 20% of isolates highly susceptible and 30% showing resistance.

Table 3 Antibiotic Susceptibility Pattern of Salmonella Typhi Isolated from Sampled Participants

Antibiotic Groups	**3+ n (%)**	**2+ n (%)**	**1+ n (%)**
Cephalosporins			
Ceftriaxone	9 (90.0)	1 (10.0)	0 (0.0)
Cefotaxime	8 (80.0)	2 (20.0)	0 (0.0)
Cefuroxime	6 (60.0)	4 (40.0)	0 (0.0)
Cefaxime	5 (50.0)	5 (50.0)	0 (0.0)
Chloramphenicol			
Chloramphenicol	8 (80.0)	2 (20.0)	0 (0.0)
Fluoroquinolones			
Ofloxacin	8 (80.0)	1 (10.0)	1 (10.0)
Ciprofloxacin	7 (70.0)	3 (30.0)	0 (0.0)
Amoxicillin/Calvulanic Acid			
Augmentin	7 (70.0)	2 (20.0)	1 (10.0)
Macrolides			
Azithromycin	7 (70.0)	3 (30.0)	0 (0.0)
Aminoglycosides			
Gentamycin	4 (40.0)	6 (60.0)	0 (0.0)
Penicilins			
Amoxicillin	2 (20.0)	5 (50.0)	3 (30.0)
Cotrimoxazole			
Trimethoprim/sulfamethoxazole	2 (20.0)	2 (20.0)	0 (0.0)

The MIC and MBC testing further demonstrated the effectiveness of several antibiotics (Table 4). Chloramphenicol and trimethoprim/sulfamethoxazole exhibited the lowest MIC and MBC values, at 2.40 ± 0.51 µg/mL and 1.50 ± 0.45 µg/mL, respectively, highlighting their potency at low concentrations. Conversely, ofloxacin required higher concentrations to achieve bactericidal effects, with an MIC of 5.80 ± 1.16 µg/mL and an MBC of 9.20 ± 1.77 µg/mL. These findings highlight the importance of selecting antibiotics with proven efficacy while monitoring resistance trends.

Table 4 Minimal Inhibitory and Bactericidal Concentrations of Antibiotics against Typhoid Fever among Participants

Antibiotics	**MIC (µg/ml)**	**MBC (µg/ml)**
Ceftriaxone	7.40 ± 0.75	-
Pefloxacin	8.80 ± 0.76	2.30 ± 0.56

Ciprofloxacin	5.80 ± 1.28	6.40 ± 1.21
Ofloxacin	5.80 ± 1.16	9.20 ± 1.77
Chloramphenicol	2.40 ± 0.51*	3.30 ± 0.44*
Trimethoprim/sulfamethoxazole	1.50 ± 0.45*	1.50 ± 0.45*
Amoxicillin	5.80 ± 1.16	2.30 ± 0.56

*Indicate that the *Salmonella* Typhi isolates were sensitive using Clinical and Laboratory Standards Institute MIC breakboints for *Salmonella* species (CLSI, 2018).

DISCUSSION

The observed distribution of bacterial isolates, with Staphylococcus sp. being the most common, is consistent with studies suggesting a higher prevalence of coagulase-negative staphylococcal infections in low-resource settings. This could reflect either genuine bloodstream infections or contamination during sample collection, a common challenge in such studies [7], [4]. The presence of Salmonella Typhi in 5.7% of cases is clinically significant, given its role in enteric fever. Similar prevalence rates have been documented in other urban settings across sub-Saharan Africa, emphasizing the endemic nature of typhoid fever [3].

The high susceptibility of Salmonella Typhi isolates to cephalosporins, fluoroquinolones, and chloramphenicol aligns with findings from studies in Bangladesh and Pakistan, where these antibiotics remain effective against typhoidal Salmonella [5], [6]. This suggests that despite global concerns about multidrug resistance, these drugs could continue to serve as first-line treatments in regions like Kaduna Metropolis. However, the reduced susceptibility to cotrimoxazole and penicillins warrants caution, as similar patterns have been reported in Kenya and Southeast Asia, reflecting the global rise of antimicrobial resistance [8], [3].

The efficacy of chloramphenicol, demonstrated by low MIC and MBC values, aligns with trends reported in countries where its use has declined due to prior resistance concerns. For instance, studies from Pakistan and Nepal have shown that reduced exposure has led to the re-emergence of chloramphenicol as an effective treatment option [9], [6]. This highlights the potential benefits of rotational antibiotic policies to manage resistance sustainably.

Public health implications of these findings are profound. The continued efficacy of several key antibiotics underscores the importance of preserving their utility through robust antimicrobial stewardship. Comparative studies from Lagos, Nigeria, and other parts of Africa reveal similar patterns, emphasizing the necessity for localized resistance monitoring and judicious antibiotic use [3], [4]. Moreover, the high rate of “no growth” in cultures suggests the need for more sensitive diagnostic tools, as viral and intracellular pathogens often escape detection using standard culture methods [2].

CONCLUSIONS

The high susceptibility rates of Salmonella Typhi to a wide spectrum of antibiotics in this study are encouraging, suggesting that effective therapeutic options remain available for enteric fever in Kaduna Metropolis. However, the diminished efficacy of cotrimoxazole and penicillins highlights the need for continuous surveillance and antibiotic stewardship to combat emerging resistance patterns [5], [10]. Future research should explore molecular resistance mechanisms and implement rotational antibiotic policies to optimize long-term treatment strategies [9], [2].

REFERENCES

1. Akullian, A. N., Ng'eno, E., Matheson, A. I., Cosmas, L., Macharia, D., Fields, B., ... & Feikin, D. R. (2018). Multi-drug resistant Salmonella enterica Typhimurium associated with invasive disease in

Western Kenya. PLoS Neglected Tropical Diseases, 12(3), e0006290. https://doi.org/10.1371/journal.pntd.0006290

2. Bhaumik, S., John, J., Varghese, G. M., Verghese, V. P., Radhakrishnan, D., Kang, G., ... & Ochiai, R. L. (2021). Typhoid fever: A systematic review of randomized controlled trials of treatment and prevention. Indian Journal of Medical Research, 153(4), 480–494. https://doi.org/10.4103/ijmr.IJMR_1053_20
3. Chimalizeni, Y., Kawaza, K., & Molyneux, E. (2010). The epidemiology and management of non-typhoidal Salmonella infections. Advances in Infectious Diseases, 4(2), 105–115. https://doi.org/10.1016/j.pid.2010.06.005
4. Feasey, N. A., Dougan, G., Kingsley, R. A., Heyderman, R. S., & Gordon, M. A. (2012). Invasive non-typhoidal Salmonella disease: An emerging and neglected tropical disease in Africa. Lancet, 379(9835), 2489–2499. https://doi.org/10.1016/S0140-6736(11)61752-2
5. Rahman, A. K. M. M., Wasfy, M. O., Matin, A., Elahi, Y., Hossain, M. A., Mahoney, F., & Connor, B. A. (2018). Multi-drug resistance in Salmonella enterica serovar Typhi isolated from Bangladesh. Clinical Infectious Diseases, 65(6), S101–S103. https://doi.org/10.1093/cid/cix574
6. Parry, C. M., Hien, T. T., Dougan, G., White, N. J., & Farrar, J. J. (2002). Typhoid fever. New England Journal of Medicine, 347(22), 1770–1782. https://doi.org/10.1056/NEJMra020201
7. Ochiai, R. L., Acosta, C. J., Danovaro-Holliday, M. C., Baiqing, D., Bhattacharya, S. K., Agtini, M. D., ... & Clemens, J. D. (2008). A global burden of typhoid fever. Bulletin of the World Health Organization, 86(4), 260–268. https://doi.org/10.2471/BLT.06.039818
8. Shrestha, S., Acharya, D., Amatya, J., & Shrestha, R. K. (2021). Prevalence and antibiotic resistance pattern of Salmonella species causing enteric fever in a tertiary care hospital, Nepal. BMC Infectious Diseases, 21(1), 362. https://doi.org/10.1186/s12879-021-06051-5
9. World Health Organization. (2020). Antimicrobial resistance: Global report on surveillance 2020. Geneva, Switzerland: WHO Press. Retrieved from https://www.who.int/publications/i/item/9789241564748
10. Zaki, S. A., & Karande, S. (2011). Multidrug-resistant typhoid fever: A review. The Journal of Infection in Developing Countries, 5(5), 324–337. https://doi.org/10.3855/jidc.1325