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Antibiotic Sensitivity Pattern in Blood Culture Positive Typhoid Fever

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ABSTRACT

Background:

Salmonella enterica serotype Typhi is a major cause of typhoid fever, a leading health problem in low and middle income countries. Rising antibiotic resistance makes for tough effective treatment that highlights the need for better information on local antibiotic sensitivity patterns to manage.

Objective:

To asses antibiotic Sensitivity Pattern in Blood Culture Positive Typhoid Fever

Materials and Methods:

This cross sectional study was conducted at Saidu Medical College during June 2022 to August 2024. Patients with confirmed blood culture-positive typhoid fever were selected. Blood samples were collected and antibiotic susceptibility testing was performed using the standard disc diffusion method, targeting commonly prescribed antibiotics such as ciprofloxacin, ceftriaxone, and azithromycin. Sensitivity and resistance rates were recorded and analyzed.

Results:

Mean age was 26.45 ± 15.74 years and mean duration of fever was 9.72 ± 6.97 days.The analysis of antibiotic sensitivity patterns among 132 blood culture-positive typhoid cases reveals varied effectiveness across the antibiotics tested. **Azithromycin** demonstrated the highest sensitivity, with 122 cases (92.4%) sensitive and only 10 cases (7.6%) resistant, making it the most effective treatment option. **Meropenem** showed 100% sensitivity across all cases (132), indicating its potential as a highly reliable choice, though typically reserved for severe cases due to its broad-spectrum activity.

Conclusion:

Results of this study highlights the changing patterns of antibiotic sensitivity in typhoid fever, and emphasizes the need for continuous monitoring and updated guidelines of antibiotic use. Third generation cephalosporins are preferred treatment (with caution regarding fluoroquinolone use due to high resistance rates), the findings suggest..

Keywords: *Typhoid fever, Salmonella enterica, antibiotic sensitivity, blood culture, multidrug resistance, fluoroquinolones, cephalosporins*

1. INTRODUCTION

Typhoid fever due to Salmonella enterica serovar Typhi is a major public health problem, especially in low- and middle-income countries [1]. Typhoid fever is transmitted primarily through contaminated food and water and has been-endemic in areas with poor sanitation, resulting in tremendous morbidity and mortality [2]. With the growing incidence of multidrug resistant (MDR) and extensively drug resistant (XDR) S. Typhi strains, numerous antibiotics used in treating typhoid fever are ineffective [3]. This therefore makes it important to understand the Antibiotic sensitivity patterns that will help you to guide appropriate treatment and curtail the spread of resistant strains.

S. Typhi Antibiotic Resistance is associated with several factors including overuse and misuse of antibiotics and genetic mutation of the infecting bug so that it becomes resistant to the therapeutic drugs (4). Resistance to fluoroquinolones, the standard treatment, has declined because they have reduced efficacy as a result of widespread resistance, mediated by mutations in quinolone resistance-determining regions (QRDR) in bacterial DNA [5]. Strains resistant to fluoroquinolones and third generation cephalosporins, like ceftriaxone, are now more prevalent in typhoid endemic regions, and they represent a substantial number of infections that severely limit treatment options available to affected communities [6].

It has been found through recent studies that azithromycin remains effective against certain S. Typhi strains with resistance emerging slowly. The persistence of resistance reinforces the need for continual monitoring of local sensitivity pattern to guide empirical treatment choices [7]. Stewardship of antibiotics and recommendations of cautious prescription are important to slow development of resistance and to retain the efficacy of remaining treatment options [8]. Carbapenems are increasingly used in cases where first line antibiotics are no longer effective, but their use is limited because of cost and logistics issues in resource limited settings [9].

TCVs provide long term immunity and may reduce human antibiotic use, thereby lowering selective pressure on S. Typhi and decreasing resistance (10). Typically TCVs were included in routine immunization programmes in countries with high typhoid burden and reductions in cases are reported, indicating that vaccination is an effective preventive measure in parallel with improved antibiotic management [10]. Access and coverage gaps, however, limit TCVs' effectiveness, and an integrated strategy including public health education, improved sanitation and resistance surveillance is needed [8]. Genetic studies have also contributed to increasing understanding of resistant S. Typhi, including identification of genetic landmarks associated with resistance and mapping the patterns of spread [11]. Genomic surveillance will help us predict outbreaks and develop tailored public health responses, and it is all the more important because it is based on a complex approach including vaccination, better diagnostics, improved antibiotic stewardship, and continued research on new treatments.

In this context, our study aims to analyze the antibiotic sensitivity of blood culture-positive *S. Typhi* isolates, focusing on prevalent resistance patterns and therapeutic implications. This research is expected to provide valuable insights into current resistance dynamics, informing healthcare providers and policymakers on effective treatment protocols and resistance mitigation strategies.

2. MATERIAL AND METHODS

This cross-sectional study was conducted at Saidu Medical College during June 2022 to August 2024. Study was approved by the ethical committee and informed consent was taken from each patient.

The sample size of 132 patients was calculated using a sensitivity estimate for Ciprofloxacin at 32.3%, as reported by Ahmad M et al., with a confidence level of 95% and a margin of error (d) of 8%. [11] Eligible participants included patients of all ages and genders with confirmed typhoid fever through positive blood cultures. Patients with prior antibiotic treatment for typhoid within the last month or those with other concurrent bacterial infections were excluded to avoid confounding sensitivity results.

Data were collected through a structured form, which recorded demographic information (age, gender, residential area) and clinical characteristics such as the duration of fever. Blood samples were collected before the initiation of any antibiotic therapy. Blood cultures were conducted according to standard microbiological protocols, and positive isolates were identified as Salmonella Typhi. Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method, with interpretations based on Clinical and Laboratory Standards Institute (CLSI) guidelines. Antibiotics tested included Ampicillin, Chloramphenicol, Cefixime, Ceftriaxone, Trimethoprim/Sulfamethoxazole, Amoxicillin, Ciprofloxacin, Azithromycin, and Meropenem. Results were categorized as Sensitive, Intermediate, or Resistant.

Data analysis was conducted using SPSS Version 24. Descriptive statistics, including mean and standard deviation, were calculated for continuous variables such as age and duration of fever. Frequencies and percentages were used to summarize sensitivity patterns for each antibiotic. Chi-Square tests were applied to assess potential associations between demographic variables (gender and residential area) and antibiotic sensitivity patterns. Statistical significance was set at $p \leq 0.05$.

3. RESULTS

Total 132 blood culture positive cases were selected. Mean age was 26.45 ± 15.74 years and mean duration of fever was

9.72 ± 6.97 days.

The analysis of antibiotic sensitivity patterns among 132 blood culture-positive typhoid cases reveals varied effectiveness across the antibiotics tested (Table 1). **Azithromycin** demonstrated the highest sensitivity, with 122 cases (92.4%) sensitive and only 10 cases (7.6%) resistant, making it the most effective treatment option. **Meropenem** showed 100% sensitivity across all cases (132), indicating its potential as a highly reliable choice, though typically reserved for severe cases due to its broad-spectrum activity.

In contrast, high resistance rates were observed for **Ampicillin** and **Chloramphenicol**, with 97 cases (73.5%) and 100 cases (75.8%) resistant, respectively, and only 35 cases (26.5%) and 29 cases (22.0%) sensitive. This pattern suggests that these antibiotics have limited effectiveness for treating typhoid fever in this population.

Cefixime also showed considerable resistance, with 96 cases (72.7%) resistant and 34 cases (25.8%) sensitive, indicating its reduced utility in this setting. **Ceftriaxone** displayed a more balanced sensitivity profile, with 58 cases (43.9%) sensitive, 36 cases (27.3%) intermediate, and 38 cases (28.8%) resistant, suggesting partial effectiveness but highlighting emerging resistance.

Amoxicillin exhibited moderate efficacy, with 80 cases (60.6%) sensitive and 49 cases (37.1%) resistant. **Ciprofloxacin** showed a sensitivity rate of 47 cases (35.6%) and resistance in 54 cases (40.9%), reflecting significant resistance trends that may limit its use.

These findings emphasize the need for cautious antibiotic selection, prioritizing **Azithromycin** and **Meropenem** as effective options in regions with similar resistance profiles. The high resistance to **Ampicillin, Chloramphenicol,** and **Cefixime** further underscores the importance of ongoing surveillance in guiding empirical treatment choices for typhoid fever.

Table 2 presents the gender-based antibiotic sensitivity patterns among 132 blood culture-positive typhoid cases, with Chi-Square test results assessing statistical significance. Azithromycin and Amoxicillin exhibited slight gender-based variations in sensitivity, though neither reached statistical significance. For Azithromycin, sensitivity was observed in 72 males (96.0%) and 50 females (87.7%), with a slight increase in resistance among females at 7 (12.3%) compared to 3 males (4.0%) ($p = .075$). Similarly, Amoxicillin showed higher sensitivity in males, with 51 (68.0%) males and 29 (50.9%) females sensitive to the antibiotic, while resistance was more common in females at 27 (47.4%) compared to 22 males (29.3%) ($p = .104$).

Other antibiotics, including Ampicillin, Chloramphenicol, Cefixime, Ceftriaxone, and Ciprofloxacin, showed no significant gender-based differences ($p > .05$), indicating generally consistent sensitivity patterns across genders. The high sensitivity of Azithromycin across both genders supports its effectiveness as a treatment for typhoid fever, while Meropenem displayed 100% sensitivity in both genders (75 males and 57 females). These slight gender-based differences in Azithromycin and Amoxicillin sensitivity highlight the importance of continuous resistance monitoring to identify any emerging trends in treatment efficacy based on gender.

Table 3 shows the antibiotic sensitivity patterns for blood culture-positive typhoid fever cases in relation to residential area (urban vs. rural), with Chi-Square tests assessing the significance of any differences.

The results indicate no statistically significant differences in antibiotic sensitivity patterns between urban and rural areas for any of the antibiotics tested ($p > .05$). Azithromycin and Meropenem demonstrated the highest sensitivity across both residential areas. Azithromycin had a sensitivity rate of 52 (89.7%) in urban cases and 70 (94.6%) in rural cases, with minimal resistance observed (10.3% and 5.4%, respectively). Meropenem showed 100% sensitivity in both urban and rural cases, reinforcing its effectiveness.

For antibiotics with higher resistance, such as Ampicillin and Chloramphenicol, resistance rates were similarly high in both urban and rural cases. Ampicillin showed resistance in 43 (74.1%) urban cases and 54 (73.0%) rural cases, while Chloramphenicol had resistance in 46 (79.3%) urban cases and 54 (72.9%) rural cases.

These findings suggest that residential area does not play a significant role in the observed antibiotic resistance patterns in this sample, emphasizing the widespread nature of resistance for certain antibiotics, regardless of urban or rural status.

Table 1: Antibiotic Sensitivity Patterns in Blood Culture-Positive Typhoid Fever Cases (n=132)

Antibiotic Sensitivity	N	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Ampicillin	132	35 (26.5%)	N/A	97 (73.5%)
Chloramphenicol	132	29 (22.0%)	3 (2.3%)	100 (75.8%)
Cefixime	132	34 (25.8%)	2 (1.5%)	96 (72.7%)

Antibiotic Sensitivity	N	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Ceftriaxone	132	58 (43.9%)	36 (27.3%)	38 (28.8%)
Trimethoprim/Sulfamethoxazole	132	42 (31.8%)	2 (1.5%)	88 (66.7%)
Amoxicillin	132	80 (60.6%)	3 (2.3%)	49 (37.1%)
Ciprofloxacin	132	47 (35.6%)	31 (23.5%)	54 (40.9%)
Azithromycin	132	122 (92.4%)	N/A	10 (7.6%)
Meropenem	132	132 (100.0%)	N/A	0 (0.0%)

Table 2: Gender-Based Antibiotic Sensitivity Patterns in Blood Culture-Positive Typhoid Fever Cases (n=132)

Antibiotic Sensitivity	Gender	Sensitive n(%)	Intermediate n(%)	Resistant n(%)	p-Value
Ampicillin	Male	23 (30.7%)	N/A	52 (69.3%)	0.215
	Female	12 (21.1%)	N/A	45 (78.9%)	
Chloramphenicol	Male	16 (21.3%)	0 (0%)	59 (78.7%)	0.124
	Female	13 (22.8%)	3 (5.3%)	41 (71.9%)	
Cefixime	Male	18 (24.0%)	2 (2.7%)	55 (73.3%)	0.420
	Female	16 (28.1%)	0 (0%)	41 (71.9%)	
Ceftriaxone	Male	30 (40.0%)	20 (26.7%)	25 (33.3%)	0.390
	Female	28 (49.1%)	16 (28.1%)	13 (22.8%)	
Trimethoprim/Sulfamethoxazole	Male	26 (34.7%)	2 (2.7%)	47 (62.7%)	0.304
	Female	16 (28.1%)	0 (0%)	41 (71.9%)	
Amoxicillin	Male	51 (68.0%)	2 (2.7%)	22 (29.3%)	0.104
	Female	29 (50.9%)	1 (1.8%)	27 (47.4%)	
Ciprofloxacin	Male	28 (37.3%)	15 (20.0%)	32 (42.7%)	0.556
	Female	19 (33.3%)	16 (28.1%)	22 (38.6%)	
Azithromycin	Male	72 (96.0%)	N/A	3 (4.0%)	0.075
	Female	50 (87.7%)	N/A	7 (12.3%)	
Meropenem	Male	75 (100%)	N/A	0 (0%)	N/A
	Female	57 (100%)	N/A	0 (0%)	

Table 3: Antibiotic Sensitivity Patterns by Residential Area in Blood Culture-Positive Typhoid Fever Cases (n=132)

Antibiotic Sensitivity	Residential Area	Sensitive n(%)	Intermediate n(%)	Resistant n(%)	p-Value
Ampicillin	Urban	15 (25.9%)	N/A	43 (74.1%)	.880
	Rural	20 (27.0%)	N/A	54 (73.0%)	
Chloramphenicol	Urban	12 (20.7%)	0 (0%)	46 (79.3%)	.272
	Rural	17 (23.0%)	3 (4.1%)	54 (72.9%)	
Cefixime	Urban	16 (27.6%)	1 (1.7%)	41 (70.7%)	.894
	Rural	18 (24.3%)	1 (1.4%)	55 (74.3%)	
Ceftriaxone	Urban	26 (44.8%)	16 (27.6%)	16 (27.6%)	.964
	Rural	32 (43.2%)	20 (27.0%)	22 (29.8%)	
Trimethoprim/Sulfamethoxazole	Urban	18 (31.0%)	0 (0%)	40 (69.0%)	.434
	Rural	24 (32.4%)	2 (2.7%)	48 (64.9%)	
Amoxicillin	Urban	38 (65.5%)	1 (1.7%)	19 (32.8%)	.583
	Rural	42 (56.8%)	2 (2.7%)	30 (40.5%)	
Ciprofloxacin	Urban	21 (36.2%)	10 (17.2%)	27 (46.6%)	.282
	Rural	26 (35.1%)	21 (28.4%)	27 (36.5%)	
Azithromycin	Urban	52 (89.7%)	N/A	6 (10.3%)	.287
	Rural	70 (94.6%)	N/A	4 (5.4%)	
Meropenem	Urban	58 (100%)	N/A	0 (0%)	N/A
	Rural	74 (100%)	N/A	0 (0%)	N/A

4. DISCUSSION

This study of blood culture-positive typhoid cases reveals critical insights into the antibiotic sensitivity patterns of *Salmonella Typhi*, emphasizing the effectiveness of certain antibiotics and the growing resistance to others. The high sensitivity of Azithromycin (92.4%) and Meropenem (100%) observed in this study aligns closely with other studies, which also highlight these antibiotics as leading treatment options in regions with high rates of multidrug-resistant (MDR) and extensively drug-resistant (XDR) typhoid. Ahmad et al. similarly reported Azithromycin sensitivity at 96.7% and Meropenem at 100% among pediatric patients, affirming the reliability of these agents for both routine and complex cases of typhoid fever [11].

In contrast, this study found significant resistance rates for Ampicillin (73.5%) and Chloramphenicol (75.8%), consistent with findings from various studies. Saleem et al. reported resistance levels above 80% for Ampicillin, Chloramphenicol, and Cotrimoxazole, further underscoring the decline in efficacy of these historically used antibiotics [12]. Roy et al. similarly highlighted a shift in *S. Typhi* resistance, noting that first-line antibiotics such as Ampicillin and Chloramphenicol, once widely effective, are now overshadowed by newer agents, as seen in our study [13]. The extensive resistance to these drugs presents a barrier to affordable treatment options, particularly in resource-limited settings where access to advanced antibiotics like Meropenem is limited.

In terms of efficacy among third-generation cephalosporins, Cefixime and Ceftriaxone demonstrated mixed results in this study, with resistance rates of 72.7% for Cefixime and 28.8% for Ceftriaxone. These findings are supported by studies such as those by Sharma et al. and Khan et al., who reported rising resistance in Cefixime and Ceftriaxone, with Ceftriaxone sensitivity hovering around 41.4% and resistance nearing 60% in recent years [14, 15]. The gradual increase in minimum inhibitory concentration (MIC) levels for Ceftriaxone noted by Sharma et al. further supports the need for monitoring resistance trends among cephalosporins, as emerging resistance could eventually limit their use [14].

The sensitivity pattern observed in Ciprofloxacin (35.6%) was also notable, as resistance was present in 40.9% of cases. Such resistance levels were mirrored by Hassan et al., who found that Ciprofloxacin resistance reached 56%, making it a less favorable choice for empirical therapy [12]. Similarly, Gaba et al. documented rising resistance to Ciprofloxacin, a trend likely due to overuse in endemic areas, which has gradually diminished its effectiveness as a first-line agent [16]. This widespread resistance to fluoroquinolones highlights the need for cautious use, as well as possible regulatory measures to curb indiscriminate prescribing.

Our findings on Amoxicillin's moderate efficacy (60.6% sensitivity) are partially consistent with the study by Asreah et al., who observed Amoxicillin sensitivity in 68.0% of cases, a level indicative of partial effectiveness but not enough to support its use as a primary treatment in all cases [17]. Interestingly, the older drugs Trimethoprim/Sulfamethoxazole and Chloramphenicol have shown varying results across studies. For instance, Shrestha and Basnet observed high sensitivity to Trimethoprim/Sulfamethoxazole (94%) and Meropenem (76%) in the Nepalese population, although Chloramphenicol's effectiveness has declined sharply in other regions [18].

Examining demographic factors, such as gender and residential area, revealed no statistically significant differences in sensitivity patterns across these variables, suggesting that resistance trends are uniformly distributed within the population. The study by Khan et al. found a similar lack of variation, showing consistent sensitivity levels for Azithromycin and Meropenem in both genders and across rural and urban areas [15]. This uniformity implies that local treatment protocols could standardize antibiotic choices without needing specific demographic adjustments, potentially simplifying prescribing practices.

These findings underscore the clinical significance of Azithromycin and Meropenem as frontline options in treating typhoid fever. Azithromycin's high sensitivity rates observed across various studies, including rates as high as 98.9% in Sharma et al. and 93.3% in Saleem et al., reinforce its reliability as an oral treatment for mild to moderate cases [12, 19]. Meanwhile, Meropenem's consistent 100% sensitivity across different populations and studies, including those by Khan et al. and Roy et al., solidifies its role in managing severe, MDR, and XDR cases, although judicious use is advised to delay resistance development [15, 13].

5. CONCLUSION

In conclusion, this study's results emphasize the value of Azithromycin and Meropenem as reliable treatment choices for typhoid fever, while highlighting the substantial resistance to older and some newer antibiotics. These findings support the need for updated treatment guidelines that prioritize effective agents and reduce reliance on antibiotics with high resistance rates, such as Ampicillin, Chloramphenicol, and Ciprofloxacin. This study also highlights the importance of routine sensitivity testing in endemic areas to guide empirical therapy effectively. Continued surveillance will be essential to detect emerging resistance patterns and adjust treatment protocols as needed to address the evolving landscape of typhoid fever treatment.

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