ORIGINAL ARTICLE

Antimicrobial Profile and Prevalence of *Salmonella Species* from Blood Culture in A Tertiary Care Hospital

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ABSTRACT

Introduction: Enteric fever is a major public health concern around the world and endemic in low- and middle-income countries like, India. Typically, it spreads through contaminated food or water. *Salmonella Typhi* proliferate and spread throughout the bloodstream seeding multiple organs in the body. Incidence data of culture confirmed Typhoid cases is approximately 377per 100000 population with an approximate case fatality rate of 1% in India. The management of cases are hampered due to emerging the drug resistance of isolates because of rampant and misuse of antibiotics. This study investigates to analyse the current pattern of antibiotic susceptibility among Salmonella isolates from cases of enteric fever seen at ESIC Medical College & Hospital, Faridabad. **Methods:** This is a retrospective, cross-sectional study. Blood cultures from patients with suspected enteric fever from Jan 2017 to Dec 2019 were included. The blood cultures were processed using the BacT/Alert automated blood culture system. **Results:** During the study period, a total of 4064 blood culture specimens were received from the patients suspected for fever. Out of a total of 2717 culture positive samples, 373 (13.73%) were found positive for the growth of *Salmonella enterica* [*Salmonella typhi 87.13% (325/373), Salmonella paratyphi A (12.86%)]*, confirming the enteric fever. **Conclusion:** Treatment with appropriate antimicrobial drugs is crucial for patients with typhoidal infections and the antimicrobial susceptibility of such isolates must be reported as soon as possible.

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Introduction

Enteric fever is a major public health concern around the world and endemic in low- and middle-income countries like, India. Typhoid fever and Paratyphoid fever, which are both life-threatening illnesses, are caused by *Salmonella Typhi* and *Salmonella Paratyphi A*, respectively.[1,2] Typically, it spreads through contaminated food or water. *Salmonella Typhi* proliferate and spread throughout the bloodstream seeding multiple organs in the body.[1] The disease's signs and symptoms are likely to appear gradually, one to three weeks after contact. Incidence data of culture confirmed Typhoid cases is approximately 377 per 100000 population with an approximate case fatality rate of 1% in India.[3] Early disease management can be aided by quick diagnosis, and precise antibiotic sensitivity testing guiding the treatment protocol.[4] Empirical therapy is usually followed when laboratory confirmation is not done in many outpatients setup. Typhoid fever morbidity and mortality have decreased dramatically in industrialised countries as a result of improved housing conditions and the use of drugs.[1] The management of cases are hampered due to emerging the drug resistance of isolates because of rampant and misuse of antibiotics.

Chloramphenicol, ampicillin, and cotrimoxazole are no longer frequently used to treat typhoid fever in endemic areas, and quinolones have taken their place as the drug of choice. This is because Multi-Drug Resistant (MDR) strains have emerged.[5] Nalidixic acid-resistant bacteria linked to decreased sensitivity to fluoroquinolones in patients treated with quinolones have been observed more frequently over the past few years. Alternative possibilities for effective medication and management of enteric fever cases are becoming essential. Ceftriaxone and azithromycin are being increasingly used for complicated and uncomplicated typhoid, respectively.[2,6,7] Over the counter use of these medications can cause emergence of resistance to these subsequently limiting their efficacy to treat. Consequently, this study investigates to analyse the current pattern of antibiotic susceptibility among Salmonella isolates from cases of enteric fever seen at ESIC Medical College & Hospital, Faridabad.

Methods

This is a retrospective, cross-sectional study. Blood cultures from patients with suspected enteric fever from Jan 2017 to Dec 2019 were included. The blood cultures were processed using the BacT/Alert automated blood culture system. Organisms were isolated and identified using standard microbiological methods.[8] Antimicrobial Susceptibility Test (AST) was done using the Kirby Bauer disc diffusion method and interpreted using CLSI guidelines.[3]

Statistical Analysis: The Statistical Package for Social Sciences was used to enter and analyse information on the bacterial isolates, their susceptibility to different antibiotics, and other details (SPSS). Distribution based on percentages is used to illustrate the results. "Significant" was defined as a p value less than 0.05.

Results

During the study period, a total of 4064 blood culture specimens were received from the patients suspected for fever, out of which 66.85% (2717/4064) showed blood culture positive and remaining 33.14% (1347/4064) samples were showed no growth on blood culture media.

Out of a total of 2717 culture positive samples, 373 (13.73%) were found positive for the growth of *Salmonella enterica* [*Salmonella typhi 87.13% (325/373), Salmonella paratyphi A (12.86%)]*, confirming the enteric fever. Other non-enteric pathogens that were isolated included Methicillin Resistant *Staphylococcus aureus* (MRSA) *12.59%*, Acinetobacter species 5.89%, *Klebsiella pneumoniae* 8.91%, *Escherichia coli* 9.42%, *Enterococcus* species 9.16%, *Citrobacter* species 5.37%, Coagulase-negative *Staphylococcus 9.16%, and Pseudomonas aeruginosa* 10.97% (Table 1).

Table 2 showed AST data of the *Salmonella* isolates. Among the *Salmonella Typhi,* majority isolates were resistant to Nalidixic acid. Ampicillin and Ciprofloxacin resistance was observed in more than 60% isolates. Moderate resistance to Amikacin, Azithromycin & Chloramphenicol (24%). Low level resistance was seen towards Cotrimoxazole, Meropenem, Ertapenem & Sulfamethoxazole. Whereas, 100% sensitivity was shown by a number of drugs, i.e., Ofloxacin, Cefixime, Cefotaxime, Ceftriaxone, Tetracycline, Imipenem, and Ticarcillin Clavulanate.

In contrast, *Salmonella paratyphi A* isolates showed only nalidixic acid (NA(R)) resistance was (75%), followed by ciprofloxacin (50%). The *Salmonella paratyphi A* were susceptible to majority of the other drugs testing. Table 3 showed statistically significant resistance of the Salmonella isolates to Nalidixic acid.

Table 1 Distribution of total number of isolates on the basis of gram staining

Organism	Number of isolates	Positive Percentage
Gram Negative bacilli	1475	54.29
Salmonella	373	13.73
Pseudomonas	298	10.97
E coli	256	9.42
Klebsiella	242	8.91
Acinetobacter	160	5.89
Citrobacter	146	5.37
Gram Positive Cocci	1242	45.71
MSSA	365	13.43
MRSA	342	12.59
CONS	286	10.53
Enterococcus	249	9.16
Total	2717	100

Table 2 Antimicrobial susceptibilities of *Salmonella enterica*.

Antibiotics	*Salmonella serotype Typhi* (n=325)			*Salmonella serotype Paratyphi* (n=48)		
	S (%)	*I* (%)	*R* (%)	*S* (%)	*I* (%)	*R* (%)
Ampicillin	235 (72.30%)	8 (2.46%)	82(25.23%)	48 (100%)	0	0
Nalidixic acid	17 (5.23%)	0	308 (94.77%)	12 (25%)	0	36 (75%)
Ciprofloxacin	95 (29.23%)	16 (4.92%)	214 (65.85%)	12 (25%)	12 (25%)	24 (50%)
Ofloxacin	325 (100%)	0	0	48 (100%)	0	0
Cotrimoxazole	257 (79.08%)	43 (13.23%)	25 (7.69%)	36 (75%)	12 (25%)	0
Cefixime	325 (100%)	0	0	48 (100%)	0	0
Cefotaxime	325 (100%)	0	0	48 (100%)	0	0
Ceftriaxone	325 (100%)	0	0	48 (100%)	0	0
Azithromycin	248 (76.31%)	0	77 (23.69%)	24 (50%)	24 (50%)	0
Tetracycline	325 (100%)	0	0	48 (100%)	0	0

Chloramphenicol	240 (73.85%)	8 (2.46%)	77 (23.69%)	48 (100%)	0	0
Imipenem	325 (100%)	0	0	48 (100%)	0	0
Amikacin	248 (76.31%)	8 (2.46%)	69 (21.23%)	36 (75%)	12 (25%)	0
Meropenem	317 (97.54%)	0	8 (2.46%)	48 (100%)	0	0
Ertapenem	283 (87.08%)	0	42 (12.92%)	48 (100%)	0	0
Sulfamethoxazole	274 (84.31%)	0	51 (15.69%)	48 (100%)	0	0
Ticarcillin-Clavulanate	325 (100%)	0	0	48 (100%)	0	0
Polymyxin B	325 (100%)	0	0	48 (100%)	0	0

S: sensitive, *I*: intermediate sensitive, *R*: resistant.

Table 3 Distribution of nalidixic acid (NA) resistant *S. Typhi* and *S. Paratyphi.*

Species	Nalidixic Acid (NA) Resistant		
	Resistant (%)	Sensitive (%)	p-value
Salmonella serotype Typhi (n=325)	308 (94.76%)	17 (5.23%)	
Salmonella serotype Paratyphi (n=48)	36 (75%)	12 (25%)	<0.05
Total(n=373)	344(92.22%)	29(7.77%)	

Discussion

Enteric fever is the most common cause of pyrexia of unknown origin. Limited laboratory diagnosis is the reason for under estimation of the true incidence of the disease in India. Data on culture positive typhoid cases is required to estimate the prevalence of the disease, its aetiology and antimicrobial susceptibilities.[9] Such data is must to formulate & focus policy decisions for control, preventing and managing the diseases. Over the counter use of antibiotics is also impact the AST data of the isolates in question. The study generated data by examining data of 373 Salmonella isolates over a period of 3 years. Among the positive blood cultures, *Salmonella enterica* was isolated in highest number [*Salmonella Typhi* and *Salmonella paratyphi* were 87.15% and12.86%, respectively].

The traditional 1st line agents (Ampicillin, Chloramphenicol, Cotrimoxazole), were found to have a better susceptibility profile. The current data shows a good response to the 1st line agent. This observation is also reported by studies done in India by Veeraraghavan B, Pragasam AK *et al* [10] and neighbouring countries i.e., Nepal.[11,12]

The postulated hypothesis for the recovery to the drug effect can be because of decrease clinical use of these agents for years, thus decreasing the selection pressure on bacteria. Such data strengthens the concept and importance of Antimicrobial Stewardship.

Among the 2nd line agents, ceftriaxone was universally susceptible in all isolates whereas, Azithromycin showed moderate level resistance. These agents are currently used for empirical therapy by most clinicians in India for typhoid cases. The data in our study corroborates with data projected from North India showing emergence of resistance towards Azithromycin among Salmonella isolates. In contrast, South Indian states have observed higher MIC of isolates towards ceftriaxone. The reason has been attributed to the prescribing practices in these areas.[13]

Nalidixic acid resistance has been used as indirect evidence of increased Minimum Inhibitory Concentration (MIC) for Ciprofloxacin in *Salmonella Typhi* [14]. The present study reports very high number of NARST (Nalidixic Acid Resistance *Salmonella Typhi*) (>94%).

Similar to study in Central India showing 96% NARST isolates. These are higher in comparison to other Indian studies, which reports isolates in the range of 60-78%. [15,16,17] The limitation of this study was disc diffusion-based AST data, where MIC were not available. There Ciprofloxacin MIC of the NARST isolates cannot be correlated. But, considering the data reported in literature, NARST isolates found to have high chances of Ciprofloxacin failure in clinical use.[14] The untreated case mortality rate for typhoid fever is >10%, when patients with typhoid fever are treated with appropriate antibiotics, the rate should be <1.1. However, increasing resistance can cause difficulty in clinical management. Therefore, AST data survey and Antimicrobial Stewardship policies are need of the hour to control Typhoid related morbidity and mortality.

Conclusion

Treatment with appropriate antimicrobial drugs is crucial for patients with typhoidal infections and the antimicrobial susceptibility of such isolates must be reported as soon as possible. The changing trends to resistance to 1st and 2nd line drug can help formulate empirical therapy plans as per the epidemiologic profile of any given geographic area. Antibiotic Stewardship steps like rotation of drugs can be evidently useful to manage these cases. Evidence of antimicrobial resistance supports the need for continuous surveillance. Antibiotic resistance is here to stay, and our communities can only be saved by wise planning and an appropriate antibiotic policy.

Conflicts of Interest

The author started there is no conflict of interest

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