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ANTIMICROBIAL SUSCEPTIBILITY IN CULTURE POSITIVE ENTERIC FEVER

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Abstract

INTRODUCTION: Enteric fever includes typhoid and paratyphoid fever. Peak incidence is seen in children 5–15 years of age; but in regions where the disease is highly endemic, as in India, children younger than 5 years of age may have the highest infection rates. There are about 22 million new typhoid cases occur each year. Young children in poor, resource limited areas, who make up the majority of the new cases and there is a mortality figures of 215,000 deaths annually. A sharp decline in the rates of complications and mortality due to typhoid fever is observed as a result of introduction of effective antibiotic therapy since 1950s. MDR-ST became endemic in many areas of Asia, including India soon after multidrug-resistant strains of *Salmonella enterica* serotype *typhi* (MDR-ST) that were resistant to all the three first-line drugs then in use, namely chloramphenicol, amoxycillin and co-trimoxazole emerged in early 1990s.

MATERIAL AND METHODS: Only blood culture or bone marrow culture positive cases were included. The patients with culture isolated enteric fever were included in the study. Antimicrobial susceptibility testing was carried out by disk diffusion method using antibiotic discs. The analysis of the antimicrobial susceptibility was carried out as per CLSI interpretative guidelines.

RESULTS: A total of 82 culture positive cases were included in the present study. 80 culture isolates were from blood culture and 2 from the bone marrow culture. *Salmonella enterica*subspecies *enterica* serovartyphi (S *typhi*) was isolated from 67 (81.70%) patients while *Salmonella enterica* subspecies *enterica*serovarparatyphi (S *paratyphi A*) was isolated from 13 (15.85%) cases and 2 (2.44%) were *Salmonella enterica* subspecies *enterica*serovarschottmuelleri (S *paratyphi B).* Of the 82 cases 65(79.3%) isolates were resistant to ciprofloxacin, 17 (20.7%) were resistant to nalidixic acid, one (1.2%) case each was resistant to Cefotaxime and ceftriaxone, 2 (2.4%) were resistant to chloramphenicol, 10 (12.2%) were resistant and to cotrimoxazole 3 (3.7%) were resistant.

CONCLUSION: In a culture positive cases 65(79.3%) isolates were resistant to ciprofloxacin and 17 (20.7%) were resistant to nalidixic acid. Multidrug resistant isolates were 65(79.3%).

Introduction:

In disease-endemic areas, the annual incidence of enteric fever is about 1%. Peak incidence is seen in children 5–15 years of age; but in regions where the disease is highly endemic, as in India, children younger than 5 years of age may have the highest infection rates[i].

Enteric fever includes typhoid and paratyphoid fever. Typhoid fever is caused by a Gramnegative bacilli, Salmonella enterica subspecies entericaserovarTyphi (Salmonella typhi), whereas paratyphoid fever is caused by any of the three serovars of Salmonella enterica subspecies enterica, namely S. paratyphi A, S. schottmuelleri (also called S. paratyphi B), and S. hirschfeldii (also called S. paratyphi C). World wideType A is the most common pathogen worldwide, whereas Type B predominates in Europe. Type C is rare, and is seen only in the Far East. The overall ratio of the disease caused by S. typhi to that caused by S. paratyphi is about 10 :1 ratio[ii].

There are about 22 million new typhoid cases occur each year. Young children in poor, resourcelimited areas, who make up the majority of the new cases and there is a mortality figures of 215,000 deaths annually[iii].

A systemic infection caused by *Salmonella enterica*subspecies *enterica* serovarstyphi

(S *typhi)* and paratyphi (S *paratyphi*) is known as enteric fever. The disease is endemic in India with an incidence ranging from 102 to 2219 per 100,000 population.[iv] In developing countries like India, typhoid fever is a common illness.[v]

A sharp decline in the rates of complications and mortality due to typhoid fever is observed as a result of introduction of effective antibiotic therapy since 1950s.[vi] MDR-ST became endemic in many areas of Asia, including India soon after multidrug-resistant strains of *Salmonella enterica* serotype *typhi* (MDR-ST) that were resistant to all the three first-line drugs then in use, namely chloramphenicol, amoxycillin and co-trimoxazole emerged in early 1990s.[vii]Fluoroquinolones are currently the first-line drug for the treatment of enteric fever. It is found that fluoroquinolones are very effective against MDR-ST, with cure rates more than 96% and fever clearance achieved in less than four days.[viii]

It was observed that fever took longer than before to clear, and at times surprisingly failed to respond to ciprofloxacin therapy towards the end of last decade.[ix]Strains of *S. typhi* are resistant to nalidixic acid and an inferior clinical response to fluoroquinolones was noted in patients infected with nalidixic acid-resistant *S. typhi* (NARST) compared to response in those infected with nalidixic acid-sensitive *S. typhi* (NASST) strains.[x]An increase in prevalence of Nalidixic Acid Resistant Salmonella (NARS) in India has been observed. Fluroquinolone resistance is predicted by Nalidixic acid resistance.[xi]

Present study was carried out toexplore and evaluate antimicrobial susceptibility pattern in culture positive cases.

MATERIAL AND METHODS:

This was a retrospective study was conducted in the Dept. of Medicine in collaboration with Dept. of Microbiology. The patients admitted with enteric fever at Ananta Institute of Medical Science and Research Centre Rajsamand.

Only blood culture or bone marrow culture positive cases were included. The patients with culture isolated enteric fever were included in the study.

Antimicrobial susceptibility testing was carried out by disk diffusion method using antibiotic discs for chloramphenicol (30 µg), amoxicillin (10 µg), cotrimoxazole (1.25/23.75 µg), ciprofloxacin (5 µg), cefixime (30 µg) and ceftriaxone (30 µg). The analysis of the antimicrobial susceptibility was carried out as per CLSI interpretative guidelines[xii]. Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 were used for the quality control of antimicrobial susceptibility testing.

Statistical analysis was done by using SPSS software. An excel sheet was used to analyse data extracted from the case sheets. P value of < 0.05 was considered as statistically significant.

RESULTS:

A total of 82 culture positive cases were included in the present study

Table 1: Culture positive Enteric fever cases

	Positive	%	P value
Male	48	48.54%	0.3705 (NS)
Female	34	41.46%	95% CI: -8.0952% to 21.6178%
Total	82	100%	

NS: Not significant, CI: Confidence Interval

80 culture isolates were from blood culture and 2 from the bone marrow culture. *Salmonella enterica*subspecies *enterica* serovartyphi *(S typhi)* was isolated from 67 (81.70%) patients while *Salmonella enterica* subspecies *enterica*serovarparatyphi (S *paratyphi A*) was isolated from 13 (15.85%) cases and 2 (2.44%) were *Salmonella enterica* subspecies *enterica*serovarschottmuelleri (S *paratyphiB)*. All blood cultures positive with a mean of 6.8 days after the onset of fever.

Table 2: species identified

Species	N=82	%
Salmonella typhi	67	81.70%
Salmonella paratyphi A	13	15.85%
Salmonella paratyphi B	2	2.44%

Table 3: Antibiotic sensitivity pattern of Salmonella isolated from the patients

Antibiotic	Resistant cases	Percentage
Ciprofloxacin	65	79.3%
Nalidixic acid	17	20.7%
Cefotaxime	1	1.2%
Ceftriaxone	1	1.2%
Chloramphenicol	2	2.4%
Ampicillin	10	12.2%
Cotrimoxazole	3	3.7%

Of the 82 cases 65(79.3%) isolates were resistant to ciprofloxacin, 17 (20.7%) were resistant to nalidixic acid, one (1.2%) case each was resistant to Cefotaxime and ceftriaxone, 2 (2.4%) were resistant to chloramphenicol, 10 (12.2%) were resistant and to cotrimoxazole 3 (3.7%) were resistant.

Multidrug resistant isolates were 65(79.3%). No pan resistant isolate was observed in the present study.

DISCUSSION

Among total of 82 culture positive cases 48(48.54%) were males and 34(41.46%) were females. No statistically significant difference is observed between genders in cultured positive cases.

Majority of strain species identified was salmonella typhi in 67(81.7%) cases. Salmonella paratyphi A and B were identified in 13(15.85%) and 2(2.44%) cases respectively. In a study bt Joshi RD et al[xiii]159 strains of Salmonella typhi and paratyphi were isolated in Kathmandu. Out of 159 isolated, 125 (78.6%) were Salmonella typhi and 34 (21.4%) were paratyphi. In a studyone fifth of the isolates were *S paratyphi A*[xiv].*In* a retrospective analysis done for the 12 years it was observed that the etiological agent was *S*. Typhi in 72% of cases. *S.* Paratyphi A was the second causative agent as also found in studies from other parts of India[xv],[xvi].

In our study it is observed that 79.3% isolates were resistant to Ciprofloxacin al whereas 20.7% were resistant to Nalidixic acid in contrast to 1.6% resistant to Ciprofloxacin and 57% resistant to Nalidixic acid in a study conducted by Upadhyay R et.al[xvii]. Nalidixic acid resistance predicts fluroquinolone resistance. Prevalence of Nalidixic Acid Resistant Salmonella (NARS) in India has increased[11],[xviii]. Joshi RD et al demonstrated co-trimoxazole, chloramphenicol, ceftriaxone, cefotaxime, cefixime, and ofloxacinas 100% sensitive. Similarly, amoxicillin sensitivity was 98.1% (n=156) while ciprofloxacin was sensitive in 6.3% (n=10), intermediately sensitive in 49.1% (n=78) and resistance in 44.7% (n=71).The newer quinolone levofloxacin showed 78.5% (n=11) sensitivity.

Azithromycin was sensitive in 99.2% (n=132) of total isolated Salmonella species both typhi and paratyph[13].The susceptibility to ciprofloxacin was high in 2005 followed by a gradual decrease from 96.4% in 2005 to 89% in 2011. Subsequently, in 2012 the susceptibility reduced to only 4.6% with the revision of CLSI breakpoints[xix].

CONCLUSION

In a culture positive cases 65(79.3%) isolates were resistant to ciprofloxacin and 17 (20.7%) were resistant to nalidixic acid. Multidrug resistant isolates were 65(79.3%). A high degree of sensitivity was noted to chloramphenicolshowing sensitivity has returned to conventional antibiotics which were not used commonly by the physicians in recent years.

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