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Paratyphoid Fever - A Comprehensive Study of Clinical, Laboratory Profile and Antibiotic Sensitivity

Medicine

KEYWORDS: Renal Resistive index (RI), cirrhosis, renal dysfunction.

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ABSTRACT

Enteric fever is a major multi-systemic bacterial infection which remains an important public problem in developing nations. More recently paratyphoid fever has become the frequent cause of enteric fever in some areas. Fluoroquinolones and third-generation cephalosporins are currently the drugs of choice for the treatment of paratyphoid fever, although decreased susceptibility to these antimicrobials have also been reported in some areas. In this retrospective study, the records of culture positive paratyphoid fever cases during the period of march 2016 to august 2016 were obtained. Antibiotic sensitivity patterns were assessed based on culture and sensitivity, all the patients were sensitive to Ampicillin and Chloramphenicol. All the patients were resistant to Quinolones (ciprofloxacin) and Aminoglycosides. Sensitivity to Ceftriaxone is seen in 16/18 (88.8%). The existence of multidrug - resistant bacteria is a serious and growing problem. This situation has been further complicated by the emergence of quinolone resistant strains.

Introduction: Enteric fever is a major multi-systemic bacterial infection. Although enteric fever is not common in industrialized countries, it remains an important and persistent health problem in developing nations[1]. When enteric fever is caused by Salmonella enterica serovar Typhi, it is known as typhoid fever and when due to S. enterica serovar Paratyphi A, B, or C, it is called paratyphoid fever. The clinical differences in signs, symptoms and outcome between typhoid and paratyphoid fever are subtle [2]. Traditionally typhoid fever is believed to be more common, have a more severe clinical course, and result in more frequent and severe sequelae than paratyphoid fever. More recent studies suggest that paratyphoid fever has become the most frequent cause of enteric fever in some areas [3]. Currently, fluoroquinolones and third-generation cephalosporins are the drugs of choice for the treatment of paratyphoid fever, although decreased susceptibility to these antimicrobials have also been reported.[4] Similar observations in our institute prompted us to study the clinical profile of paratyphoid fever and review the antimicrobial drug susceptibility pattern.

Materials and methods: This is a retrospective study conducted at Baby Memorial Hospital, Kerala, a tertiary care hospital in Kozhikode district. The records of culture positive paratyphoid fever cases during the period of march 2016 to august 2016 were obtained from the medical records section. Cases of paratyphoid fever diagnosed on the basis of only clinical examination and Widal test were excluded from the study. 18 cases were identified during the period of 6 months. Clinical presentation, laboratory profile, complications, antibiotic susceptibility patterns and response to treatment were analysed. Laboratory investigations like Total count, differential count, platelet count, liver biochemistry were analysed. Widal test was performed with standardized *S. typhi* O and H antigens. The positive cut-off was taken as ≥ 1:100 for AH agglutinin titer. Blood culture and sensitivity was done in all patients by standard BACTEC blood culture system.

Results: In this retrospective study we had 18 cases of paratyphoid fever during a period of six months, all of which are positive on blood culture for Salmonella paratyphi A. Out of 18 patients, 10 were male and 8 were female of various age groups as depicted in **Table 1.**

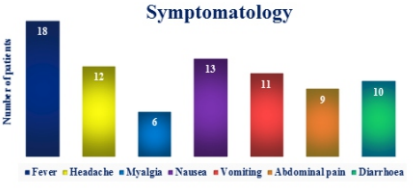
Table 1: Sex and age distribution among paratyphoid positive cases

Sex	Male	10/18	55.5%
	Female	8/18	44.4%
Age	<10yrs	3/18	16.6%
	10-20yrs	2/18	11.1%
	20-30yrs	5/18	27.7%
	30-40yrs	2/18	11.1%
	40-50yrs	3/18	16.6%
	50-60yrs	3/18	16.6%

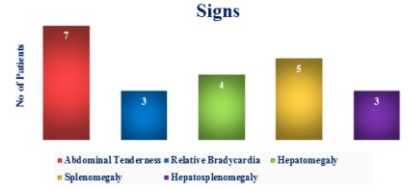
Fever was present in all the patients. Nausea(13/18, 72.2%), Headache(12/18, 66.6%) and vomiting(11/18, 61.1%) are the most common presenting symptoms. Followed by diarrhoea (10/18, 55.5%) and abdominal pain (9/18, 50%). Relative bradycardia is seen only in 3 patients(16.6%). **(Table 2, Graph 2 & 3)**

Table 2: Clinical variables among paratyphoid positive cases

Symptoms	Fever	18/18	100%
	Headache	12/18	66.6%
	Diarrhoea	10/18	55.5%
	Abdominal pain	9/18	50%
	Nausea	13/18	72.2%
	Vomiting	11/18	61.1%
	Myalgia	6/18	33.3%
Signs	Abdominal tenderness	7/18	38.8
	Hepatomegaly	4/18	22.2
	Spleenomegaly	5/18	27.2
	Hepatospleenomegaly	3/18	16.6%
	Relative Bradycardia	3/18	16.6%



Graph 1: Presenting symptoms among paratyphoid patients



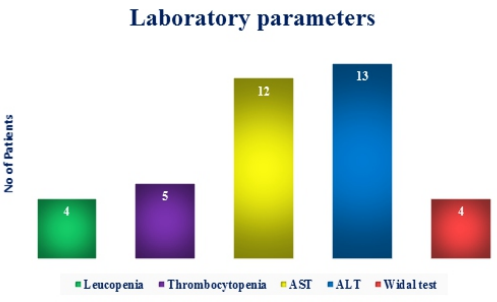
Graph 2: Clinical signs elicited among paratyphoid patients

In the laboratory evaluation, elevated liver enzymes is the most common finding with AST (12/18, 66.6%) and ALT (13/18, 72.2%). Leucopenia (22.2%) and thrombocytopenia (27.7%) are less common. In all the patients widal test was performed initially, which turned out to be positive in only 4 patients (22.2%), which shows decreased sensitivity of this test. **(Table 3, Graph 3)**

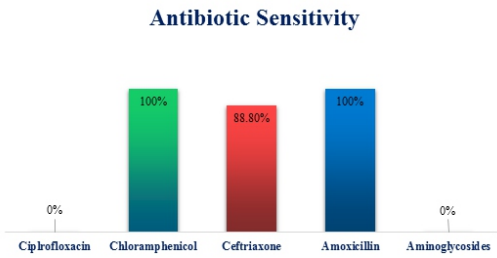
Antibiotic sensitivity patterns were assessed based on culture and sensitivity. All the patients were sensitive to Ampicillin and Chloramphenicol. All the 18 patients were resistant to Quinolones (Ciprofloxacin) and Aminoglycosides. Sensitivity to Ceftriaxone is seen in 16/18 (88.8%). **(Table 3, Graph 4)** Majority of the patients were treated with Ceftriaxone alone and some with combination of Ceftriaxone and Azythromycin. Duration of hospital stay was around 3-6 days in most patients, with 3 patients admitted beyond 10 days. All the patients recovered completely.

Table 3: Laboratory parameters and Antibiotic susceptibility

Lab value	Leucopenia (<4,000/cmm)	4/18	22.2%
	Thrombocytopenia (<1,50,000/cmm)	5/18	27.7%
	SGOT (AST) (>45U/L)	12/18	66.6%
	SGPT (ALT) (>45U/L)	13/18	72.2%
	Widal test (Positive AH>100)	4/18	22.2%
Antibiotic sensitivity	Ciprofloxacin	0/18	0%
	Chloramphenicol	18/18	100%
	Ceftriaxone	16/18	88.8%
	Amoxicillin/Clavulanate	18/18	100%
	Aminoglycosides	0/18	0%



Graph 3: Laboratory profile among Paratyphoid patients



Graph 4: Antibiotic sensitivity patterns in Paratyphoid patients

Discussion: In our study, we have analysed 18 cases, that are positive on blood culture for paratyphoid A over a period of 6 months. The symptoms of paratyphoid fever were nonspecific and could not be differentiated from other fevers. Most of our patients presented with nausea(13/18, 72.2%), Headache(12/18, 66.6%) and vomiting(11/18, 61.1%), followed by diarrhoea (10/18, 55.5%) and abdominal pain (9/18, 50%). The physical examination was relatively uninformative in giving a clinical diagnosis. Features like hepatosplenomegaly and relative bradycardia are seen only in 16.6% patients. Even the Laboratory findings are poorly specific with elevation of AST (12/18, 66.6%) and ALT (13/18, 72.2%) are more common than leucopenia (22.2%) and thrombocytopenia (27.7%). Widal test which is most widely used investigation in India for diagnosis of enteric fever is positive only in four patients(22.2%), which confirms that this classical investigation is unreliable for current clinical practice.

Our study showed increase in number of paratyphoid cases in the recent past with decreased sensitivity of these strains to Quinolones and Aminoglycosides. In fact, all the 18 patients were resistant to Quinolones and Aminoglycosides. Sensitivity to Chloramphenicol and Ampicillin is preserved. Interestingly, the current first line agent in the treatment of enteric fever Ceftriaxone, has shown less sensitivity than Chloramphenicol. This shows that the irrational use of this antibiotic led to the emergence of resistant strains and we need to be cautious before it becomes completely resistant. Fortunately, multidrug resistant strains are not reported in our region so far. Our observation is in contrast to a study conducted at Ludhiana, which revealed that there was a steady increase in the number of paratyphoid cases but the antibiotic sensitivity was 91.48% for Chloramphenicol, 95% for Ampicillin, and 100% sensitive to Ciprofloxacin, Cefotaxime and Gentamicin[5,6]. This was similar to the study done at Rourkela and Nagpur in India[5,7]. But findings of our study is similar to a study done by Chandel *et al.* which showed that 32% isolates of S. *paratyphi* A had decreased susceptibility to Ciprofloxacin [5,8]. However, 86 (90.5%) isolates were susceptible to Chloramphenicol, which is similar to the results seen in a study done by Varsha *et al*[5,9]. In a study conducted in Mumbai, 36 cases showed positive culture report for *S. paratyphi* and none of the isolates showed resistance to Ampicillin, Chloramphenicol and Cotrimoxazole[5,10].

In a review done by Effa *et al.* comprising twenty-six studies, involving 3033 patients, concluded that the newer Fluoroquinolone like Gatifloxacin, remains effective in some regions where resistance to older Fluoroquinolones has developed[5,11]. The study highlights the trials on children infected with Nalidixic acid-resistant strains, older Fluoroquinolones (Ofloxacin) produced more clinical failures than Azithromycin (2.67 (1.16 to 6.11), $n = 125$, 1 trial), but there were no differences with newer Fluoroquinolones (Gatifloxacin, $n = 285$, 1 trial)[5,12]. In a study done by Effa EE, Bukirwa H to compare Azithromycin with other antibiotics for treating uncomplicated enteric fever, it was observed that Azithromycin appears better than Fluoroquinolone drugs in populations that included participants with drug-resistant strains. It was also noted that Azithromycin may perform better than Ceftriaxone.[5,13]

The emergence of isolates resistant to Fluoroquinolones demands to have a good clinical practice with rational use of antibiotics. In a study done by John A, the optimal antimicrobial treatment of patients with enteric fever depends on an understanding of antimicrobial resistance and antimicrobial susceptibility testing of the Salmonella isolated from the individual patients. Patients infected with Salmonella with decreased Ciprofloxacin susceptibility may not respond adequately.[5,14] Chloramphenicol and other antimicrobials like Ampicillin, Sulphonamides and Aminoglycosides may still be utilized in treatment of paratyphoid fever, as the organism is sensitive to these drugs. The existence of multidrug - resistant bacteria is a serious and growing problem in the treatment of paratyphoid fever, especially in the developing countries[15]. With increasing resistance to Fluoroquinolones and possibility of re-emergence of sensitivity to Chloramphenicol, the policy of treatment of enteric fever needs to be rationalized.

Conclusion: There has been steady increase in the number of paratyphoid cases in some regions. The existence of multidrug - resistant bacteria is a serious and growing problem in the treatment of paratyphoid fever, especially in the developing countries. This situation has been further complicated by the emergence of Quinolone resistant strains with reduced susceptibility. In future, measures to control enteric fever are expected to combine an effective bivalent vaccine against both serovars (typhoid and paratyphoid) with public health measures that improve sanitation and access to clean water.

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