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Original Research Article

Clinical profile of enteric fever in tertiary care hospital of Kashmir

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ABSTRACT

Background: Enteric fever is common cause of pyrexia in children and its diagnosis poses several problems, the diagnosis most often remains either as an unsubstantiated clinical impression or a serological diagnosis and occasionally confirmed by blood culture. Typhoid fever is a commonly encountered systemic disease caused by the gram-negative bacteria *Salmonella enterica* serovar typhi. It is a major public health problem in India. The incidence of enteric fever can be regarded as an index of sanitary measure practiced in our country. Aim of our study was to know the clinical profile, hematological features of clinically and serologically suspected typhoid cases, antibiotic pattern in use, the time to defervescence with the treatment received and over all hospital stay days.
Methods: This was a retrospective record file review of all admitted children for pyrexia under evaluation who were clinically suspected as cases of enteric fever and serologically proven by significant titres of O and H antigen and few were culture proven cases of enteric fever carried out at a tertiary care children hospital in Kashmir valley over the period January 2012 to January 2016.
Results: During this period, a total of 129 children with typhoid fever were admitted to Pediatric ward. Of the 129 children, 69 (53.5%) were boys and 60 (46.5%) were girls. The age range of the study population was 1 year to 15 years. The predominant symptoms of typhoid fever were fever 123 (95.3%), anorexia/weakness 58 (45.0%), abdominal pain 53 (41.1%), pallor 47 (36.4%), coated tongue 42 (32.6%), headache 30 (23.3%) and gastrointestinal symptoms/ dysentry 9 (7.0%). Diarrhea 25 (19.4%) was more common than constipation 5 (3.9%) in this study. Hepatomegaly 26 (20.2%) and splenomegaly 67 (51.9%), lymphadenopathy 24 (19.4%) and seizure in 5 cases (3.9%) were other major physical findings. Typhoid complications were seen in the form of jaundice (deranged LFTs) 25 (19.4%), abdominal distention 20 (15.5%) and tenderness 14 (10.9%), encephalopathy 5 (3.9%), shock 3 (2.3%) and UTI 4 (3.1%). Blood culture was positive in 36 (27.9%), 20 (15.5%) percent of the isolates were *Salmonella typhi*, while 16 (12.4%) were *Salmonella paratyphi A*. low yield was attributed to oral antibiotics received outside hospital setting. Ceftriaxone was used to treat all the patients diagnosed with enteric fever. Oral Azithromycin was added to treatment regime in those patients who were persistently febrile after 6 days. Those patients who were discharged before 14 days, therapy was completed with oral cefixime. The mean duration of hospital stay was 9.6 days for uncomplicated cases. Leukopenia was seen in majority of the patients with mean cell count of 6492.7cubic/mm. The mean time to defervescence in patients who received prior antibiotics was 4 days while that in those who did not receive prior antibiotics was 5 days.
Conclusions: Atypical presentations are seen in typhoid fever patients so we need to be cautious about it, clinical symptoms and signs can vary with different regional studies, may be attributed to use of empirical oral antibiotic that alter the clinical presentation of enteric fever. Low culture positivity is due to prior or ongoing antibiotic treatment outside hospital setting. Leucopenia could be an important marker of typhoid. Ceftriaxone is important available cephalosporin for sensitive cases. Combination treatment was used to treat persistently febrile child.

Keywords: Children, Enteric fever, *Salmonella*, Typhoid

INTRODUCTION

Typhoid fever is a systemic illness caused by *Salmonella enterica* serotype *typhi* or *paratyphi A/B.* Poor sanitation, poor clean water supply, dirty eating and poor hygiene are linked to typhoid fever.[1] In India the disease is endemic with an incidence ranging from 102 to 2219 per 100,000 population.[2] It results in huge morbidity, absenteeism and enough resource utilization. History, physical findings and fever pattern are suggestive of typhoid. Blood culture is the 'gold standard' for diagnosis and also gives information about antibiotic sensitivity of the isolate.[3,4] However, prior oral antibiotics use and the cost of cultures, limits its use in the diagnostic approach. The Widal test is very commonly used in our set up but has very variable sensitivity and specificity and problems in interpretation. By the end of 1990s, *Salmonella enterica* developed resistance simultaneously to all first line drugs like chloramphenicol, cotrimoxazole and ampicillin. Fluoroquinolones initially were very effective but the time over a decade has shown high incidence of clinical failure to quinolones. The beta lactams such as cefixime and ceftriaxone are now being increasingly used but these are expensive drugs and are associated with a long time to defervescence and high rates of relapse. These drugs also add to cost for management of typhoid fever. Irrational use of antibiotics in management of suspected typhoid fever will poor hazardous as certain repots of emerging cephalosporin resistance are available and experience with new drugs such as azithromycin is at present little.[5-7] Enteric fever now a day in OPD patients arise several questions about diagnosis and treatment with early antibiotic therapy which change disease course and presentation. Hence this retrospective review of patients of enteric fever at our hospital was carried out to asses some of these clinical features.

The primary aim of the study was to study the clinical profile of enteric fever and response to antimicrobial therapy.

METHODS

This was a retrospective study in which record files of all cases of enteric fever were evaluated at a tertiary care children hospital in Kashmir, India. The records of all patients discharged from our hospital between January 2012 and January 2016 with a diagnosis of enteric fever, typhoid fever or paratyphoid fever were included in our study. These records were retrieved from the Medical Records Section of the hospital. Detailed history, duration of fever, prior antibiotic use, general and systemic examination, investigation, treatment received, defervescence period and total duration in hospital was recorded clinically suspected, serologically or culture proven cases of enteric fever were included in the study. The two-sample t test was used to compare continuous variables and the chi square test was used to compare categorical variables. A p value of less than 0.05 was considered significant. The Ethics Committee of the hospital had no objection for retrospective data analysis, as the data collected was based on routine clinical practice. Further, the committee had no objection to publish a paper based on this retrospective data.

RESULTS

During this period, a total of 129 children with typhoid fever were admitted to Paediatrics ward. Of the 129 children, 69 (53.5%) were boys and 60 (46.5%) were girls. The age range of the study population was 1 year to 15 years.

Table 1: Characteristics and presenting symptoms.

Characteristics and presenting symptoms		129 (number %)
Gender	Male	69 (53.5%)
	Female	60 (46.5%)
Fever	No	6 (4.7%)
	Yes	123 (95.3%)
Coated tongue	No	87 (67.4%)
	Yes	42 (32.6%)
Anorexia/ weakness	No	71 (55.0%)
	Yes	58 (45.0%)
Cough	No	124 (96.1%)
	Yes	5 (3.9%)
Vomiting	No	92 (71.3%)
	Yes	37 (28.7%)
Loose motions	No	104 (80.6%)
	Yes	25 (19.4%)
Abdominal pain	No	76 (58.9%)
	Yes	53 (41.1%)
Seizure	No	124 (96.1%)
	Yes	5 (3.9%)
Headache	No	99 (76.7%)
	Yes	30 (23.3%)
Dysentry	No	120 (93.0%)
	Yes	9 (7.0%)
	Yes	25 (19.4%)
	Yes	25 (19.4%)
Constipation	No	124 (96.1%)
	Yes	5 (3.9%)
Pallor	No	82 (63.6%)
	Yes	47 (36.4%)
Lymphadenopathy	No	105 (81.4%)
	Yes	24 (18.6%)
Hepatomegaly	No	103 (79.8%)
	Yes	26 (20.2%)
Spleenomegaly	No	62 (48.1%)
	Yes	67 (51.9%)

The predominant symptoms (Table 1) of typhoid fever were fever 123 (95.3%), anorexia/weakness 58 (45.0%), abdominal pain 53 (41.1%), pallor 47(36.4%), coated tongue 42 (32.6%), headache 30 (23.3%) and gastrointestinal symptoms/ dysentry 9 (7.0%). Diarrhoea 25 (19.4%) was more common than constipation 5 (3.9%) in this study. Hepatomegaly 26 (20.2%) and

splenomegaly 67 (51.9%), lymphadenopathy 24 (19.4%) and seizure in 5 cases (3.9%) were other major physical findings.

Table 2: Complications observed in patients in hospital.

Complications		
Abdominal tenderness	No	115 (89.1%)
	Yes	14 (10.9%)
Abdominal distention	No	109 (84.5%)
	Yes	20 (15.5%)
Jaundice/Deranged LFT	No	104 (80.6%)

Typhoid complication (Table 2) were seen in the form of jaundice (deranged LFTs) 25 (19.4%), abdominal distention 20 (15.5%) and tenderness 14 (10.9%), encephalopathy 5 (3.9%), shock 3 (2.3%) and UTI 4 (3.1%). Blood culture was positive in 36 (27.9%), 20 (15.5%) percent of the isolates were *Salmonella typhi*, while 16 (12.4%) were *Salmonella paratyphi A*.[8] Low yield was attributed to oral received outside hospital setting.[9-11] The cultures were sent after a mean period of 7 days after the onset of fever, BACTEC method was used for processing blood culture which again added to cost. Widal test results were available for all 129 patients, obtained after mean duration of 4 days in hospital. Widal test was positive (defined as *S. typhi* O antigen >120 and either *S. typhi* H or *S. paratyphi* H antigen titres >120), were positive 108 (91.5%) (Table 3).

Table 3: Descriptive statistics.

Widal titre	Negative	10 (8.5%)
	Positive	108 (91.5%)
Blood culture	No growth	93 (72.0%)
	S. parathyphi	16 (12.4%)
	Salmonella	20 (15.5%)
Single Antibiotic	Ceftriaxone	129 (100.0%)
Combination antibiotics	Ceftriaxone and Azithromycin	16 (72.7%)

All patients received Ceftriaxone and its sensitive was tested. All culture proven enteric cases were sensitive to Ceftriaxone, Azithromycin sensitivity was not evaluated. Oral Azithromycin was added to treatment regime in those patients who were persistently febrile after 6 days. Those patients who were discharged before 14 days, therapy was completed with oral cefixime. The mean duration of hospital stay was 9.6 days for uncomplicated cases. The mean time to defervescence in patients who received prior antibiotics was 4.5 days while that in those who did not receive prior antibiotics was 5 days. Leukopenia was seen in majority of the patients with mean cell count of 6492.7cubic/mm. Majority of patients had received antibiotics before being admitted to the hospital. Beta lactams (cefixime, ceftriaxone, amoxycillin, Cefopodoxime, amoxycillin-clavulanate) were taken by 89 (68%) patients before admission. 8 (6%) patients gave history of having taken azithromycin.

Ceftriaxone was the most common antibiotic used to treat patients in hospital, in 129 (100%) patients. A combination of ceftriaxone and azithromycin was used in 16 patients (12.4%). The mean duration of receipt of antimicrobials after hospitalization was 5 days. The mean time to defervescence defined as time period in days from the day of onset of the antibiotic treatment in the hospital to the disappearance of fever was calculated for various patient groups. The mean time to defervescence in the group of patients who had received antibiotics prior to admission was 4 days (95% CI 3.9, 5.1 days) while in the patients who did not receive prior antibiotics was 5 days (95% CI 4.3, 5.7 days). The overall mean time to defervescence when ceftriaxone alone was used as therapy was 4 days. The mean time to defervescence in those patients who received a combination of ceftriaxone and Azithromycin was 5 days and did not differ significantly from those who received Ceftriaxone alone.

DISCUSSION

This study is from north India, one of the retrospective studies on enteric fever. Other large series include those by Chowta et al, S. jog et al and Walia et al.[2,12,13] Most of the clinical symptoms and signs reported by us are similar to those reported earlier.[14-16] Children in this study commonly presented with fever, headache and gastrointestinal symptoms and diarrhea was more common than constipation. Our observation of fever as a common complaint in all the children and diarrhea being more common than constipation, similar findings were also observed by other author.[9,10] Our data showed that most common clinical findings was coated tongue followed by hepatomegaly (77.55%) and splenomegaly (38.77%). This coincides with findings of other studies.[11,12] In our study leucopenia was predominate lab finding on CBC which differs with Deshmukh et al in their study on paediatric patients with bacteriologically and/or serologically diagnosed typhoid fever found absolute eosinopenia in 71.4% of patients.[10] Leucopenia, eosinopenia, thrombocytopenia and anemia in enteric can be attributed to the myeloid maturation arrest, decrease in the number of erythroblasts and megakaryocytes and increased phagocytic activity of histiocytes in the bone marrow.[11] As many as 74% patients in our study received antibiotics before being admitted to the hospital. This resulted in low yield of blood here study differs gain with S jog et al.[9-12] Despite of low yield for blood culture, culture of sending cultures in pyerexia should be practiced by clinicians, though it adds to cost of management, blood cultures should be sent in suspected enteric fever even if the patient is on antimicrobials. 16% of the isolates in our study were *S paratyphi A* as against 20% in literature.[8] This may be a consequence of increasing immunization with the Vi antigen vaccine that does not protect against *S. paratyphi*.[17] The sensitivity pattern of the isolates obtained in this study is in

accordance with the other studies from India.[1,18] There is high prevalence of nalidixic acid resistance and return of sensitivity to chloramphenicol, ampicillin and cotrimoxazole. We did not observe any resistance to third generation cephalosporins as in other studies by Chowta et al, Safdar et al, etc.[1,19] Chande et al observed resistance to cefotaxime in one isolate in their study from central India.[20] The mean fever clearance time with ceftriaxone used as single therapy observed in our study was 4. days (95% CI 3.7, 4.7 days) as against 6.1 days in literature.[4] Receipt of antibiotic therapy prior to admission was found to have no significant impact on the time to defervescence. Our study however suggest that combination therapy may be superior to single drug therapy, but we did not observe any significant difference in the time to defervescence in those patients who received ceftriaxone alone or in combination with azithromycin.

The main limitation of this study is its retrospective nature and that it was not protocol driven. Patients were receiving various antimicrobials singly or in combination for varying periods prior to hospitalization, which could impact the time to defervescence. Also, the inability of the study to detect a difference in efficacy of various antimicrobial regimes chiefly single versus combination therapy may be due to the small sample size.

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