



Age Related Clinical and Laboratory Manifestations of Enteric Fever in Children

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Abstract

Scanty literature is available on age related clinical features in children in Western India. A study was thereby conducted to evaluate the clinical profile of enteric fever patients admitted in our hospital in the year 2007. All patients with fever with Widal positive and/or with culture grown salmonella were included. A retrospective analysis of their clinical features, laboratory parameters and antimicrobial therapy was done. A total of 33 patients were included and divided into two age groups; < 5 years and > 5 years. Mean age of presentation was 5 ± 3 years. Male: Female ratio was 2:1. Common clinical features were fever (100%), hepatomegaly (82%), elevated liver enzymes (85%), anemia (88%) and elevated ESR (80%). None of the patients had constipation. In the age group of <5 years, diarrhea was more common in ($P = 0.05$), whereas relative bradycardia ($P = 0.018$) and gall bladder sludge on USG ($P = 0.04$) was seen only in > 5 years age group. Of all the first line antibiotics used, Ceftriaxone was used in 29 (87.88%) patients, Ciprofloxacin in 3 (9.1%) patients, and Cefotaxime in 1 (3%) patient. Failure of first line antibiotics was seen in 10 (30.3%) patients. Complications were seen in 6 (18.18%) patients, of which 2 (33.33%) had serositis, 1 (16.67%) each had osteomyelitis, synovitis, splenic abscess and shock. 31 (93.9%) patients recovered. 1 (3%) died and 1 (3%) was lost to follow-up. Recovery was faster in < 5 years age group (Mean 6.1 ± 2.1 days) as compared to > 5 years old (9.4 ± 4.5 days) ($P = 0.01$). Fever, hepatomegaly, elevated liver enzymes, anemia and elevated ESR are the common clinical features of enteric fever in children. Diarrhea is more common in younger children whereas relative bradycardia and gall bladder sludge is more common in older children. Constipation is not a feature. Recovery is better in younger children. 30% of our patients had resistance to third generation cephalosporins as first line antibiotics.

Key Words

Enteric Fever, Clinical Manifestations, Pediatrics

Introduction

Common clinical features of enteric fever are fever, vomiting, abdominal pain, diarrhea, cough, hepatosplenomegaly, anemia, and thrombocytopenia (1-4). Similar clinical presentation is also seen with dengue fever and malaria (5). Enteric fever is reported more frequently in children above 5 years of age and complications are seen in over 1/3 rd of patients (2, 4). However in children less than 5 years of age clinical features may differ and thus it is important to know clinical manifestations of typhoid fever and whether there is any age related difference in clinical presentations of typhoid.

We thus conducted a study of clinical profile of enteric fever in children admitted in our hospital in the year 2007. All patients with fever with Widal positive and/or culture grown salmonella were included in the study. Age related clinical manifestations and laboratory parameters were studied.

Materials and Methods

33 patients with fever with either positive Widal (O and H titres more than 1:80 and *S.paratyphi A* and *B* > 1: 120) (6, 7) or blood culture grown salmonella infection admitted in our pediatric indoor wards from January

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through December 2007 were included in this study. Detailed history with clinical examination was undertaken in all patients. Relative bradycardia was defined as normal heart rate inspite of fever. All patients underwent investigations such as complete hemogram, liver and renal function tests, stool and urine examination, Widal test and blood culture on admission and thereafter if the children's condition warranted it. Additional investigations like echocardiography, Chest X-ray, ultrasound of abdomen were done where it was indicated. Other tests such as OptiMAL for malaria, Leptospira IgM and IgG & Dengue IgM were done to exclude other causes of fever. Anemia was defined as hemoglobin less than 12 gm/dL. Neutrophilia was defined as absolute neutrophil count (ANC) more than 7000/cu.mm. Neutropenia was defined as ANC less than 1500/cu.mm. Leucopenia was defined as total leucocyte count (TLC) less than 4000/cu.mm. Leucocytosis was defined as TLC more than 11500/cu.mm. Thrombocytopenia was defined as platelet count less than 1.5 lakh/cumm. Elevated ESR was defined as ESR more than 15mm at the end of one hour. Elevated SGOT was defined as SGOT more than 40 IU/L, and elevated SGPT as more than 26 IU/L.

Patients with clinical diagnosis of typhoid fever were initially treated with third generation cephalosporins or ciprofloxacin. The clinical course was closely monitored and the period of defervescence recorded. The time to defervescence was defined as time interval from starting an appropriate antimicrobial therapy until the documentation of normal body temperature. The clinical response to therapy was considered inadequate if there was deterioration or no clinical improvement within 7 days of starting specific therapy. Persistence of fever for more than 7 days after antibiotics treatment was taken as a sign to start second line antibiotics. Common clinical & laboratory features of typhoid were noted. Patients were divided into 2 age groups of < 5 years and > 5 years & age related clinical & laboratory manifestations were noted.

Statistical Analysis

It was done on the basis of 't' test for quantitative data and 'chi square test' for qualitative data. P value was applied to assess the probability and significance of the data. P value of < 0.05 was considered significant.

Results

Mean age of presentation was 5 (5.0 ± 3.0) years and 16 (48.5%) patients were < 5 years old whereas 17 (51.5%) were > 5 years of age. Male: Female ratio was 22 : 11. Only 1(3%) patient was immunized for typhoid. The various clinical features are depicted in *Table-1*.

Constipation was not seen in any of the patients. Laboratory parameters are depicted in *Table-2*. The clinical features and laboratory parameters in the two age groups is shown in *Table-3 & 4*. Children in < 5 years age group recovered much faster than those in > 5 years age group (Mean 6.1 ± 2.1 days Vs 9.4 ± 4.5 days respectively, $p = 0.01$). Diarrhea was mainly seen in < 5 years age group, whereas relative bradycardia and gall bladder sludge on USG was seen mainly in > 5 years age group (*Table 3 & 4*). Twenty eight (84.8%) patients had positive Widal test, of which 23 (82.14%) had elevated O titres, 19 (67.86%) had elevated H titres, 4 (14.29%) had elevated AH titres, and 1 (3.57%) had elevated BH titres. Isolated *S.typhi* infections were seen in 29 (87.88%) and isolated *S.paratyphi* infections were 4 (12.12%). Blood cultures were positive in 8 (24.2%) patients. 3 (9.09%) patients had both Widal and blood cultures positive. Of all the first line antibiotics used, Ceftriaxone was used in 29 (87.88%) patients, Ciprofloxacin in 3 (9.1%) patients, and Cefotaxime in 1 (3%) patient. Second line antibiotics were required in 10 (30.3%) patients, of which Amikacin was used in 4 (12.12%) patients, Ofloxacin in 3 (9.1%) patients, Ciprofloxacin in 3 (9.1%) and Piperacillin-Tazobactam in 3 (9.1%) patients, and Metronidazole in 1 (3.03%) patient. Multi-drug resistant infection was seen in 1 (12.5%) out of the 8 blood culture positive patients. Co-infections like *Pseudomonas*, pharyngitis, and leptospirosis was seen in 1 (3.03%) patient each. Complications were seen in 6 (18.18%) patients of which 2 (33.33%) had serositis, and 1 (16.67%) each had osteomyelitis, synovitis, splenic abscess, shock. One patient (3%) died and 1 (3%) was lost to follow-up and remaining all recovered completely.

Table 1. Common Clinical Features of Typhoid in Children

Clinical Feature	No. of Patients
Fever	33 (100%)
Hepatomegaly	27 (81.8%)
Splenomegaly	16 (48.5%)
Vomiting	13 (39.4%)
Abdominal pain	9 (27.3%)
Cough	9 (27.3%)
Diarrhea	6 (18.2%)
Relative bradycardia	5 (15.2%)
Rose spots	3 (9%)

Discussion

There has been very little data available on a related age related clinical manifestations in children with only one study from Walia et al from Delhi (1). In most of the studies, children with enteric fever were more than 5

**Table 2. Laboratory Features of Enteric Fever**

Laboratory parameter	Mean \pm 2SD	Median	Laboratory parameter	No. of patients
SGOT (IU/L)	138.6 \pm 134.5	86.5 (97.9% CI=48-179)	Elevated SGOT	16/16 (100%)
Hemoglobin (gm/dL)	9.6 \pm 2.1	10.2 (96.5% CI=9.2-10.5)	Anemia	29/33 (87.9%)
SGPT (IU/L)	122.7 \pm 290.4	43.5 (97.1% CI = 28-79)	Elevated SGPT	22/26 (84.6%)
ESR (mm at the end of 1 hr)	51 \pm 27.7	50 (95.7% CI = 35-70)	Elevated ESR	20/25 (80%)
Total leucocyte count (cells/cumm)	11453 \pm 6164	10500 (96.5% CI=8000-12400)	Leucocytosis	14/33 (42.4%)
Absolute neutrophil count (cells/cumm)	6448 \pm 4944	4900 (96.5% CI = 3416-7626)	Leucopenia	3/33 (9%)
			Neutrophilia	12/33 (36.4%)
Platelet count (cells/cumm)	315700 \pm 235000	236500 (98% CI= 142000-430000)	Neutropenia	2/33 (6.1%)
			Thrombocytopenia	11/33 (33.33%)
Prothrombin Time (sec)	15.9 \pm 5.1	13.5 (98.8% CI = 12-19.5)	Prolonged PT	2/11 (18.2%)
Partial thromboplastin Time (sec)	29.9 \pm 6.9	31.6 (98.8% CI = 23.5-34.7)	Prolonged PTT	1/11 (9.1%)
			GB sludge on USG	4/29 (13.8%)

Table 3. Age Related Clinical Features

	< 5 years	> 5 years	P value
Duration of fever (days)	14.8 \pm 13.8	9.1 \pm 4.6	0.11
Vomiting (days)	5.4 \pm 3.3	3.6 \pm 2.6	0.33
Abdominal pain (days)	9.3 \pm 10.2	4.2 \pm 0.8	0.22
Diarrhea (days)	4.6 \pm 2.7	6.0	0.66
Cough (days)	8 \pm 8.7	4.8 \pm 1.8	0.44
Hemoglobin (gm/dL)	8.9 \pm 2.4	10.3 \pm 1.6	0.06
White cell count (cells/cumm)	13.2 \pm 7.3	9.8 \pm 4.5	0.11
Polymorphs (%)	55.4 \pm 2.3	55 \pm 16.5	0.94
Lymphocytes (%)	43 \pm 22.5	43.6 \pm 16.5	0.93
Platelet count (cells/cumm)	347400 \pm 254700	287800 \pm 220200	0.48
ESR (mm at end of 1 hour)	50.8 \pm 26.1	51.3 \pm 30.6	0.96
SGOT (IU/L)	174.8 \pm 170.6	116.8 \pm 112.2	0.42
SGPT (IU/L)	75.3 \pm 102.7	163.4 \pm 386.5	0.45
Prothrombin time (sec)	15.7 \pm 3.7	16 \pm 5.5	0.94
Partial thromboplastin time (sec)	29.9 \pm 6.2	29.8 \pm 7.2	0.98
Duration of 1 st line antibiotics	15.6 \pm 4.9	14.9 \pm 11	0.84
Duration of 2 nd line antibiotics	7.7 \pm 2.1	11.8 \pm 3.2	0.09
Recovery (days)	6.1 \pm 2.1	9.4 \pm 4.5	0.01

years of age at the time of presentation (1,2,8) with children less than 5 years ranging from 22.5% to 24.8%. In our study, however children less than 5 years constituted 48.5% of the total patients with enteric fever. Thus in western India, Enteric fever may be seen commonly in children less than 5 years. Also in our patients, males were more common affected as compared to females though not statistically significant whereas Abdel Wahab *et al* found equal distribution between the

boys and girls (3). Fever, hepatomegaly, elevated liver enzymes, anemia, elevated ESR were the most common clinical features of enteric fever in children seen in our study similar to that reported by Malik *et al* (2) and others (4,9,10). The other clinical manifestations like abdominal pain and diarrhea were less commonly seen in our study comparable to that by Tohme *et al* (4). Relative bradycardia was not a major feature of enteric fever in our study similar to that reported by Kumar *et al* (10).

**Table 4. Age Related Laboratory Parameters**

	< 5 years	> 5 years	P value
Males	10 (45.46%)	12 (54.54%)	0.62
Females	6 (54.54%)	5 (45.46%)	
Vomiting	8 (61.53%)	5 (38.47%)	0.22
Abdominal pain	3 (33.33%)	6 (66.67%)	0.28
Diarrhea	5 (83.33%)	1 (16.67%)	0.05
Cough	4 (44.44%)	5 (55.56%)	0.77
Hepatomegaly	13 (48.15%)	14 (51.85%)	0.93
Splenomegaly	8 (50%)	8 (50%)	0.86
Rose spots	1 (33.33%)	2 (66.67%)	0.58
Relative bradycardia	0	5 (100%)	0.018
Anemia	15 (51.72%)	14 (48.28%)	0.31
Neutropenia	1 (50%)	1 (50%)	0.96
Neutrophilia	8 (66.67%)	4 (33.33%)	0.11
Leucopenia	2 (66.67%)	1 (33.33%)	0.50
Leucocytosis	9 (64.29%)	5 (35.71%)	0.12
Thrombocytopenia	5 (45.46%)	6 (54.54%)	0.80
Elevated ESR	10 (50%)	10 (50%)	0.68
Elevated SGPT	10 (45.46%)	12 (54.54%)	0.86
Widal positive	14 (50%)	14 (50%)	0.68
Blood culture positive	4 (50%)	4 (50%)	0.92
Gall bladder sludge	0	4 (100%)	0.04
2 nd line antibiotics required	3 (42.86%)	7 (57.14%)	0.16
Recovered	15 (100%)	15 (100%)	0.36

However, it is more commonly seen in children above 5 years of age. This finding has not been noted in any previous study. Leucopenia was also not commonly seen similar as that reported by Lefebvre *et al* (11) and Malik *et al* (2) respectively. Thus leucopenia, abdominal pain and diarrhea may not be common features of enteric fever in children. Gall bladder sludge was seen in 13.8% of patients in our study similar to that reported by Mateen *et al* (12). However in our study it as seen in mainly children above 5 years of age which has not been noted in previous studies. Blood culture was positive in one-quarter of the cases of cases. Only one multi drug resistant case was observed. However one-third of the patients required second line antibiotic therapy in our study inspite of receiving treatment with ciprofloxacin and cephalosporins as first line antibiotic. Thus it is likely that drug resistance to these drugs may be seen in the future and there may be emergence of multi-drug resistant typhoid as has been reported by Kumar *et al* (10). Mean time for fever defervescence was 9.4 ± 4.5 days in > 5 years old and 6.1 ± 2.1 days in < 5 years old in our study as compared to 7.85 ± 4.95 days in > 5 years old and 9.87 ± 6.26 days in < 5 years as reported by Oh *et al* (8). Complications of enteric fever were seen in 18.18% of patients which is less than those reported in other studies where complications have been seen in over 30% of the patients (2,4,10). Common complications of typhoid that have been reported are bone marrow suppression, paralytic ileus (2,8), gastrointestinal complications (4,11), pneumonia (8), cholecystitis, endocarditis, osteomyelitis

(11), CNS complications (13) and splenic abscess (14,15). Similarly, in our patients common complications were pleural effusion, splenic abscess and osteomyelitis. Other complications that were noted in our patients were synovitis and shock. Mortality was minimal in our study as has been reported by other studies (9,11)

Conclusion

Common clinical features of enteric fever include fever, hepatomegaly, elevated liver enzymes and anemia. Diarrhea is more common in children < 5 years and recovery takes place in less than one week, whereas relative bradycardia and gall bladder sludge is seen mainly in children > 5 years and recovery time is longer.

References

1. Walia M, Gaind R, Paul P, Mehta R, Aggarwal P, Kalaivani M. Age-related clinical and microbiological characteristics of enteric fever in India. *Trans R Soc Trop Med Hyg* 2006;100(10):942-48.
2. Malik AS, Malik RH. Typhoid fever in Malaysian children. *Med J Malaysia* 2001 ;56(4):478-90.
3. Abdel Wahab MF, el-Gindy IM, Sultan Y, el-Naby HM. Comparative study on different recent diagnostic and therapeutic regimens in acute typhoid fever. *J Egypt Public Health Assoc* 1999;74(1-2):193-205
4. Tohme A, Zein E, Nasnas R. Typhoid fever. Clinical and therapeutic study in 70 patients. *J Med Liban* 2004;52(2):71-77
5. Shah I, Katira B. Clinical & Laboratory Profile of Dengue, Leptospirosis and Malaria in Children- A Study from Mumbai. *Arch Dis Child* 2007;92:561.
6. Taiwo SS, Fadiora SO, Oparinde DP, Olowe OA. Widal agglutination titres in the diagnosis of typhoid fever West. *Afr J Med* 2007 ;26(2):97-101
7. Itah AY, Akpan CJ. Correlation studies on Widal agglutination reaction and diagnosis of typhoid fever. *Southeast Asian J Trop Med Public Health* 2004 ;35(1):88-91
8. Oh HM, Masayu Z, Chew SK. Typhoid fever in hospitalized children in Singapore. *J Infect* 1997;34(3):237-42
9. Yap YF, Puthuchery SD. Typhoid fever in children—a retrospective study of 54 cases from Malaysia. *Singapore Med J* 1998;39(6):260-62
10. Kumar R, Gupta NS. Multidrug-resistant typhoid fever. *Indian J Pediatr* 2007 ;74(1):39-42.
11. Lefebvre N, Gning SB, Nabeth P, *et al*. Clinical and laboratory features of typhoid fever in Senegal. A 70-case study. *Med Trop (Mars)* 2005; 65(6):543-48.
12. Mateen MA, Saleem S, Rao PC, Reddy PS, Reddy DN. Ultrasound in the diagnosis of typhoid fever. *Indian J Pediatr* 2006; 73 (8):681-85.
13. Biswal N, Mathal B, Bhatia B D, Srinivasan S *et al*. Enteric fever. A changing perspective. *Indian Pediatr* 1994; 31: 813-19
14. Thapa R, Mukherjee K, Chakrabarty S Splenic abscess as a complication of enteric fever. *Indian Pediatr* 2007 ;44(6):438-40
15. Malik AS. Complications of bacteriologically confirmed typhoid fever in children. *J Trop Pediatr* 2002 ;48(2):102-08