Clinico – Laboratory Profile of Enteric fever in Children

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Abstract :

Introduction: Enteric fever remains an unresolved public health problem in India chiefly due to improper sanitary conditions and deficient supply of safe drinking water. **Aims:** The aim of the study was to study the clinical profile, laboratory parameters and antibiotic sensitivity pattern in culture positive enteric fever cases in pediatric age group. **Materials and Methods:** The study was designed as prospective study in tertiary care hospital in Ahmedabad from April 2015 to September 2015. All the patients who were clinically suspected for enteric fever were investigated by blood culture and Widal test. **Results:** Culture positivity rate in our study was 65.97%(64,N=97), of which 89.06%(57) were positive for S.Typhi and 10.93%(7) were positive for S.Paratyphi A. Common clinical features seen along with fever were abdominal pain (53.85%), vomiting (41.76%) and diarrhea (19.78%). All the isolates were sensitive to third generation cephalosporins and fluoroquinolones. The mean time to defervescence was 3.98 days. Conclusions: Enteric fever is major cause of febrile illness in children (especially school going). Fever with abdominal pain, vomiting and diarrhea were major clinical manifestations. There was 100% sensitivity to ceftriaxone, which was highly effective as monotherapy.

Key words: Children, Clinical profile, Culture, Enteric fever.

Introduction:

Enteric fever is a systemic bacterial infection caused by Salmonella enteric serotype Typhi or Paratyphi A or B.[1] Symptoms may vary from mild to severe. Often there is gradual onset of a high fever over several days. Weakness, abdominal pain, constipation and headaches also commonly occur. As enteric fever is a disease transmitted by the feco-oral route, its greatest burden is in resource-limited countries where water supply and sanitary conditions are poor. Enteric fever is the most common cause of fever lasting for more than 7 days in clinical practice in India. [2] It is endemic in India and reported data for the year 2014 shows 1.53 million cases and 361 deaths. [1]

Diagnosis of enteric fever is fraught with problems. History, physical findings and fever pattern are suggestive but can neither confirm nor exclude typhoid. Blood culture is the 'gold standard' for diagnosis and also gives information about antibiotic sensitivity of the isolate; however the cost of cultures and administration of prior antibiotics are hindrance in this diagnostic approach. The Widal test is very commonly used in Indian set up for diagnosis of enteric fever, but has problems in its interpretation.[3] Since 1990's, S. Typhi has developed resistance simultaneously to all the drugs used in first line treatment (chloramphenicol, co-trimoxazole and ampicillin). [4] Fluoroquinolones when first introduced in early 1990's were very effective but the past decade has seen a progressive increase in the MICs of ciprofloxacin and 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.[3] Recently, azithromycin is being used as an alternative agent for treatment of uncomplicated typhoid fever (World Health Organization, 2003; Parry et al., 2002) [5] The fluoroquinolones, other second-line antibiotics, such as third-generation cephalosporins (eg, ceftriaxone and cefixime), and azithromycin are currently regarded as the antibiotics of choice for treating MDR strains. However, an issue of great concern is the emergence of strains of S. Typhi and S.

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Paratyphi with reduced susceptibility to fluoroquinolones. [4]

A prospective study was undertaken to analyze the varied clinical presentations, culture positivity and correlation with lab investigations, with special reference to antibiotic sensitivity in a tertiary care hospital in Ahmedabad.

Methods:

This was a prospective study carried out in the department of pediatrics at a tertiary care private hospital in Ahmedabad, Gujarat, India, from April to September 2015. Pediatric patients aged 1 to 14 years with clinically suspected enteric fever (fever for 5 days or more with no primary focus on clinical examination) and proven either by positive blood culture or Widal test with significant titre (level of both H or O antibodies of 1 in 160 dilution or more by tube method) were enrolled in the study. Others who were clinically diagnosed with enteric fever but had negative widal test or titre less than the significant titre or negative blood culture were excluded from the study. Clinical, laboratory and treatment information were taken on a detailed proforma and analyzed.

Results:

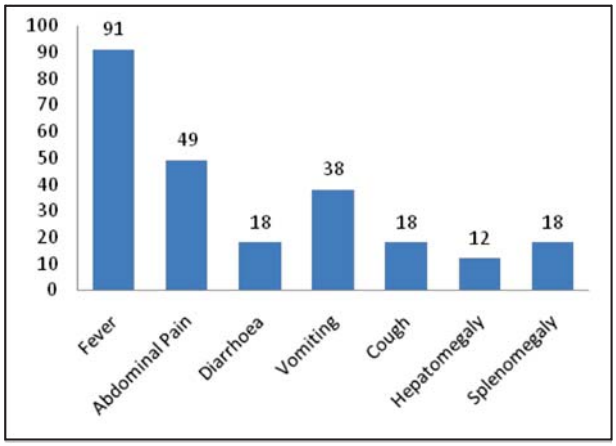
Out of the total 97 suspected patients of enteric fever, 91 patients were diagnosed as having enteric fever and were included in the study, during the period of six months, between April 2015 to September 2015. The confirmation of the diagnosis was made either by positive blood culture or widal test with significant titre. 53(58.24%) of the 91 study patients were males and 38(41.75%) were females. Mean age of the study group was 7.74 years. Table 1 shows the distribution of enteric fever in various pediatric age groups.

Table 1: Age Distribution of patients with Enteric Fever

Age Group	No.of patients (n= 91)
Toddlers (1 – 3 years)	18
Pre-school Children (3 – 5 years)	14
School going Children (5 –14 years)	59

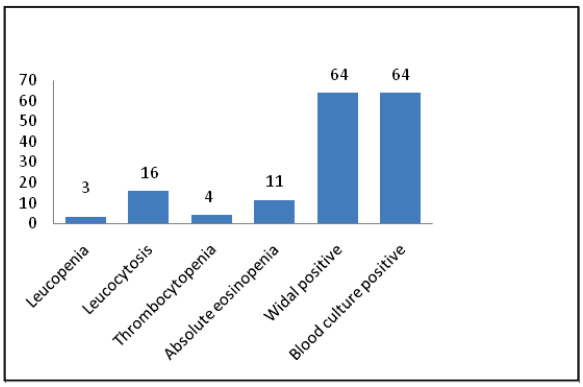
All patients presented with fever with mean duration of 9.25 days, the range being 5 to 30 days. Out of 91 patients, Abdominal pain in 49(53.85%), vomiting in 38 (41.76%), diarrhea in 18(19.78%) and cough in 18(19.78%) were the common associated symptoms found in our study group. Clinically, hepatomegaly was seen in 12(13.19%), splenomegaly in18 (19.78%) and hepatosplenomegaly in 6(6.6%). Complications noticed during hospitalization were hepatitis in 14(15.38%) and myocarditis in 5(5.49%) patients.

Figure 1: Clinical features of enteric fever in Children



The mean white blood cell (WBC) count was 8395 cells/cumm. Out of 91 patients, 72(79.12%) had WBC count within the normal range (4000-11000 cells/cumm). 3(3.29%) had leucopenia, while 16(17.58%) had leucocytosis. 4(4.39%) had thrombocytopenia (platelet count <1.5 lacs/cumm). Absolute eosinopenia (<40 cells/cumm eosinophils) was found in 11(12.08%). SGPT was elevated (>45 IU/ml) in 25(27.47%) patients. Widal test was positive in 64(70.32%) out of 91 patients, of which titre was significant in 61(67.03%) patients for S.Typhi and 4(4.39%) for S.Paratyphi A. The culture positivity rate was 65.97% (64,n=97), of which 89.06%(57) were positive for S.Typhi and 10.93%(7) were positive for S.Paratyphi A. Both Widal and Blood culture were positive in 37(40.65%) patients.

Figure 2: Laboratory Findings of Enteric fever in Children



Antibiotic sensitivity was tested in all 64 culture positive patients by using disc diffusion method (Kirby-Bauer method) and results were obtained by standard CLSI guideline. Resistance to chloramphenicol, azithromycin and trimethoprim-sulphmethoxazole was 6.25%, 14.06% and 7.81%, respectively. No isolates were found to be resistant to ceftriaxone, nalidixic acid, ciprofloxacin, ofloxacin and other third generation cephalosporins. As per current recommendations, ceftriaxone was used to treat all the patients diagnosed with enteric fever. In those patients who were discharged before 14 days, therapy was completed with cefixime. The mean time to defervescence (time period in days from the day of onset of the antibiotic therapy in the hospital to the disappearance of fever) was 3.98 days. The mean duration of hospitalization in our study group was 6.6 days.

Discussion:

This is a single centre study of enteric fever cases studying the clinical features, laboratory findings and sensitivity patterns of the strains isolated from the patients. There are few studies for clinical features of enteric fever in pediatric patients. 64.83% of the patients in our study group are above 5 years (school going) which is similar to other studies. [3]

Fever was the most common clinical feature (100%) in the patients of our study group which is similar to previous studies. [3, 4, 6, 7, 8, 9] Abdominal pain was present in 53.85% which is higher than other studies, wherein it ranged from 16 – 46%. [3, 4, 6] Vomiting (41.76%) is in the same range as other studies (37–49%). [3, 6, 7] Diarrhoea was present in 19.78% which is similar to other studies, wherein it ranged from 8-29%. [3, 6, 7] Relative bradycardia was not seen and it is consistent with other studies. [3, 6, 8] Hepatomegaly was seen in 13.19% patients which is lesser than other studies (21-71%). [3, 6, 7] Splenomegaly (19.78%) is comparatively lower than other studies (34%). [6, 7] Normal leucocyte count was seen in most of our patients which is similar to earlier studies. [3, 6] Thrombocytopenia is reported in 4.39% of cases which is lesser than earlier studies (10-15%). [3, 6]

Table 2: Sensitivity patterns of Salmonella enterica isolates

Sr. No.	Antibiotic Sensitivity	Salmonella Typhi N=57 (%)	Salmonella Paratyphi A N=7(%)
1	Chloramphenicol	53(92.98%)	7(100%)
2	Trimethoprim/Sulfamethoxazole	52(91.22%)	7(100%)
3	Nalidixic acid	57(100%)	7(100%)
4	Ciprofloxacin	57(100%)	7(100%)
5	Ofloxacin	57(100%)	7(100%)
6	Ceftriaxone	57(100%)	7(100%)
7	Cefixime	57(100%)	7(100%)
8	Cefotaxime	57(100%)	7(100%)
9	Azithromycin	50(87.71%)	5(71.42%)

Table 3: Comparison of antibiotic sensitivity for S.Typhi

Antibiotics	Current study	Chandrashekhar et al	Jeeyani et al
Chloramphenicol	92.98%	*	95.11%
Azithromycin	87.71%	84%	97.04%
Trimethoprim/sulfamethoxazole	91.22%	90.3%	*
Ciprofloxacin	100%	83.3%	100%
Ceftriaxone	100%	87.5%	100%
Cefixime	100%	91.7%	100%
Nalidixic acid	100%	23.1%	100%

* sensitivity was not tested.

12.08% of our patients had absolute eosinopenia which is lesser than the previous studies (70-80%). [4, 6, 10] SGPT was elevated in 27.47% of cases which is comparable to earlier studies. [6])

Widal positivity rate with significant titre of 1:160 or more, was 70.32% in our study which is higher than other studies wherein, positivity rate ranges from 35%-60%. [3, 6, 8] Out of the total isolates, 8% were S. Paratyphi A and remaining 92% were S. Typhi. All the isolates were sensitive to ciprofloxacin, ofloxacin and nalidixic acid which is contradictory to previous studies where resistance to these drugs was seen. [4, 8, 9] For S.Typhi, sensitivity patterns have been compared in the following table. [3, 6]

According to guidelines given by IAP national task force, patients in our study were treated with ceftriaxone. [10] No resistance to ceftriaxone is found in our study which explains its use as first line drug in treatment of enteric fever cases. Mean time to defervescence is 3.98 days in our study. In studies conducted by Jog et al, Jeeyani et al and Chowta et al, the mean defervescence time was found to be 4.2, 5.9 and 6 days, respectively. [4, 6, 11]

Conclusion:

Enteric fever is an important cause of febrile illness in children (especially school going). Fever with abdominal pain, vomiting, diarrhea, hepatomegaly and splenomegaly were the common clinical manifestations of enteric fever. Culture positivity rate was 65.97%. There is 100% sensitivity to ceftriaxone, cefixime, fluoroquinolones and other third generation cephalosporins. Resistance to azithromycin was 14.06%. Ceftriaxone as a monotherapy has been highly competent in treatment of enteric fever. Mean time to defervescence is 3.98 days in our study.

References:

1. K. Park. Park's textbook of preventive and social medicine. 21 edition, Banarsidas Bhanot Publishers; 2011. pp 234.
2. Vinod K Paul, Arvind Bagga. Ghai essential paediatrics.8 ed.CBS Publishers and distributors;2013.pg243.
3. Chandrashekar, Anil Kumar YC, Kirandeep Sodhi, Dalal S.S. Study of Clinical and Laboratory Profile of Entertic Fever in Pediatric age group. International Journal of Basic and Applied Medical Sciences 2013 vol 3; pp 16-23.
4. S Jog, R Soman, T Singhal, C Rodrigues, A Mehta, FD Dastur. Enteric fever in Mumbai – Clinical Profile, Sensitivity Patterns and Response to Antimicrobials. Journal of Association of Physicians of India 2008 April; 65: 237-40.
5. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. N Engl J Med 2002; 347:1770-82.
6. Hetal N. Jeeyani, Baldev S. Prajapati, Afroz Bloch. Enteric Fever in Children-Clinical Profile, Sensitivity Patterns and Response to Antimicrobials. GCSMC Journal of Medical Sciences 2015 vol 4.pp 40-43.
7. Ganesh R, Janakiraman L, Thiruvengadam V, Sathiyasekeran M. Profile of typhoid fever in children from a tertiary care hospital in Chennai – South India. Indian J Pediatrics (2010) 77:1089 -1092.
8. Gupta A, Swarnkar NK, Choudhary SP. Changing antibiotic sensitivity in enteric fever. J Trop Ped 2001; 47: 369-371.
9. Walia M, Gaind R, Paul P, Mehta R, Aggarwal P, Kalaivani M.Current perspectives of enteric fever: a hospital based study from India. Ann Trop Paediatrics. 2005 Sep; 25(3):161-74.
10. Kundu R, Ganguly N, Ghosh TK, Yewale VN, Shah RC, Shah NK; IAP Task Force. IAP Task Force Report: Management of enteric fever in children. Indian Pediatr 2006; 43:883-887.
11. Chowta MN, Chowta NK. Study of clinical profile and antibiotic response in typhoid fever. Indian Journal of Medical Microbiology (2005) 23 (2):125-127.