Original Research Article

Clinico-epidemiological profile and patterns of antibiotic sensitivity of among paediatric patients diagnosed with enteric fever

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Received: 12-11-2020 / Revised: 29-12-2020 / Accepted: 08-01-2021

Abstract

Background: Enteric fever (typhoid and paratyphoid fever) is a major public health concern in developing countries including India. Wide variation in clinical presentations makes its diagnosis on clinical ground a challenging task. Emergence of strain with polymicrobial resistance is a matter of serious concern. **Aims:** This study was conducted to evaluation of clinic-epidemiological profile and patterns of antibiotic sensitivity of enteric fever cases among paediatric patients. **Methods:** A prospective observational study was conducted in the Department of Paediatric, Kalawati Saran Children Hospital, New Delhi, India for 18 months. Total 200 Children aged below 18 years with history of fever of more than 7-10 days duration were included in this study. In each case, age, sex, presenting complaint, laboratory investigations and antibiotic sensitivity pattern are collected and analysed. **Results:** Out of 200 cases, 135 cases (67.5%) were males and 65 cases (32.5%) were females. Most of the cases were aged between 6 and 12 years. 49 cases were below 6 years, representing 23.5%. 51 cases were aged above 12 years, representing 25.5%. 100 cases were aged between 6 and 12 years (50%). The most common symptom was fever (100%), followed by anorexia (63.5%), vomiting (43.5%), pain abdomen (19%), diarrhea (11%), headache (10.5%), and cough (6%). The most common sign we observed in physical findings, was toxic look in 70% of the cases followed by coated tongue in 48.5%, hepatomegaly 42%, splenomegaly 20.5%, hepatosplenomegaly in 14.5% of cases and pallor in 6% of cases. Anemia found in 42 (21%) cases, leucopenia and leucocytosis was observed in 64(32%) cases and 35(17.5%) cases respectively. Neutropenia found in 85(42.5%) cases and neutrophilia was found in 61(30.5%) cases. Eosinopenia was seen in 91(45.5%) cases, eosinophilia in 17(8.5%) cases and thrombocytopenia in 30(15%) cases. SGOT levels was elevated (>200IU/ml) in 25(12.5%) cases and SGPT (>200IU/ml) in 29(14.5%) cases. The elevated levels of liver enzymes lasted only few days. *Salmonella typhi*O titres>1:100 was seen in 192(96%) cases and TH titres>1:200 in 151(75.5%) cases. Blood culture positive for *Salmonella typhi*noted in 44(22%) cases. Out of 200 cases only 62 cases had been immunized with typhoid vaccine. All of them had taken typhoid polysaccharide vaccine more than 3 years prior to illness. The most common sensitivity was seen in all the cases ceftriaxone (97%) and followed by cefixime(95%) , ofloxacin (93%), ciprofloxacin (80%), chloramphenicol (79%), cefotaxime (76%),amoxicillin (63%) and azithromycin in (51%). *S. typhi*was more sensitive to ceftriaxone, cefixime followed by ofloxacin. Least sensitivity was seen with azithromycin. **Conclusion:** Typhoid fever is a multisystem disease with variable clinical presentations. No sign or symptom is specific for its diagnosis which needs correlation with lab investigations which again are not always helpful. Polymicrobial resistance mandates heightened focus on preventive measures.

Keywords: Children, Clinical profile, Coated tongue, Typhoid fever.

Introduction

Assessment of a child presenting with fever without an obvious focus is a challenge to most of us. To determine the etiology and plan the management in the first few days is always difficult and yet imperative. In view of the anxiety of the parents, most paediatricians have the tendency to start some antibiotics before any real clue about the etiology irrespective of the act that most of these fevers might just be of viral etiology. In enteric fever this initial antibiotic might modify the course of the disease and pose significant difficulty in interpretation of lab investigations. The term enteric fever includes typhoid fever caused by S.typhi and paratyphoid fever caused by S.paratyphi A, B and C. Detailed study of enteric fever was presented by Bretonneau (1826) who identified intestinal lesions.The name typhoid fever was given by Louis (1829) to distinguish it from typhus fever. Eberth (1880) described typhoid bacillus[1].According to WHO Confirmed case of typhoid fever is defined, as a patient with fever (> 38°C) that has lasted for at least three days, with a laboratory confirmed positive culture of S. typhi.[2] Probable case of typhoid fever is a patient with fever (>38°C) that has lasted for > 3 days, with a positive serodiagnosis or antigen detection test but without S. typhi isolation[2]. The world sees approximately 22 million new typhoid cases occur each year. In India in disease-endemic areas, the annual incidence of enteric fever is about 1%.[3] Complete blood counts in enteric fever are found to be unremarkable. The hemoglobin is normal in the initial stages but drops with progressing illness. Severe anemia is unusual and should make one suspect intestinal hemorrhage or hemolysis or an alternative diagnosis like malaria. The WBC count is normal in most cases and leucocytosis makes the diagnosis less probable. Leukopenia is perceived to be an important feature of typhoid fever and has been reported in only 20-25% cases[4].The differential count is usually unremarkable except for eosinopenia. Eosinopenia often absolute may be present in 70-80% cases[5]. Presence of absolute eosinopenia offers a clue to diagnosis but does not differentiate enteric fever from other acute bacterial or viral infections. A normal eosinophil count does make typhoid fever a less likely possibility. Platelet counts are normal to begin with and fall in some cases by the second week of illness. Overall prevalence of thrombocytopenia is around 10-15%.[4]The emergence of strains of S*almonella typhi* resistant to multiple antibiotics poses a serious

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problem. Chloramphenicol was considered the antimicrobial gold standard for the treatment of typhoid fever till 1948[6]. But in the last two decades there has been increase in the resistance of strains of *S. typhi* to chloramphenicol. It was first reported in Britain, in 1950[7] and in India in 1972[8]. Gradually, resistance to multiple antibiotics developed[9]. The first major epidemic of multidrug resistant *S. typhi* was reported in 1972[10] in Mexico. Since then, an increasing frequency of antibiotic resistance has been reported from all parts of the world, but more so from the developing countries[9].The uses of chloramphenicol, ampicillin and co-trimoxazole have become infrequent and quinolones have become the first line of treatment of typhoid fever. It is one of the common causes of fever in children with varied presentation and significant difference in the signs and symptoms compared to adults. The classic Widal agglutination test is one of the most utilized diagnostic tests for typhoid fever, especially in developing countries. This study was conducted to evaluation of clinic-epidemiological profile and patterns of antibiotic sensitivity of enteric fever cases among paediatric patients.

Materials and Methods

A prospective observational study was conducted in the Department of Paediatric, Kalawati Saran Children Hospital, New Delhi, India for 18 months. After taking the approval of the protocol review committee and institutional ethics committee.

Methodology

Total 200 Children aged below 18 years who presented to the Paediatric department with history of fever of more than 7-10 days duration were included in this study. Previously antibiotic treated patients and patients with proven localised infection were excluded. These cases were either Widal positive (Widal test TO Titer>1:100 or TH titre >1:200) or blood culture positive for Salmonella species. The cases which were discharged against medical advice and cases for which consent was not obtained were excluded from the study. Antibiotics were started in each case after blood was drawn for Widal test and blood culture for Salmonella species. Each case was followed up clinically for improvement. For those cases which did not show improvement after 5 days of antibiotics, changes made according to the culture reports. Antibiotic sensitivity pattern was noted for culture positive cases. Cases were followed till discharge. The data collected was analyzed with respect to age, sex and presenting complaints.

Results

In this study, all the cases presented to OPD with a median of 7-10 days duration of fever. 150 cases (75%) had received antibiotics for a minimum period of 3-5 days prior to admission. Table 1 shows Out of 200 cases, 135 cases (67.5%) were males and 65 cases (32.5%) were females. Table 2 shows, most of the cases were aged between 6 and 12 years. 49 cases were below 6 years, representing 23.5%. 51 cases were aged above 12 years, representing
25.5%. 100 cases were aged between 6 and 12 years (50%). In all the above age groups male predominance was seen.

Table 1: Sex Distribution of patients

Sex	N=200	%
Male	135	67.5
Female	65	32.5

Table 2: Age wise distribution

Age (years)	N=200	%
0-6 years	49	24.5
6-12 years	100	50
12-18 years	51	25.5

Duration of hospital stay varied from up to two Week. As shown in Table-3, most of the cases (71.5%) stayed in hospital up to two Week after admission. 28.5% cases stayed up to one Week day in hospital. In these cases, fever persisted beyond one Week. No mortality was observed during our study period. Although mild elevated liver enzymes were observed in some cases, no complications were seen in any case.

Table 3: Duration of hospital stay

Duration of hospital stay	No. Of cases	P-value
One Week	57 (28.5%)	0.19
More than one Week	143 (71.5%)	0.00

Typhoid fever presents with a wide range of symptoms. Due to the use of antibiotics prior to diagnosis, children may not present with typical symptoms. However, in our study, the most common symptom was fever (100%), followed by anorexia (63.5%), vomiting (43.5%), pain abdomen (19%), diarrhea (11%), headache (10.5%), and cough (6%)

Table 4: Common presenting symptoms

Presenting symptom	No. of Cases	P-value
Fever	200 (100%)	0.001
Anorexia	127 (63.5%)	0.000
Vomiting	87 (43.5%)	0.001
Pain abdomen	38 (19%)	0.017
Diarrhea	22 (11%)	0.070
Headache	21 (10.5%)	0.91
Cough	12 (6%)	0.163

Table 5: Various physical findings

Signs	No. of Cases	P-value
Toxic look	140 (70%)	0.001
Coated tongue	97(48.5%)	0.001
Hepatomegaly	84 (42%)	0.002
Splenomegaly	41 (20.5%)	0.055
Hepatosplenomegaly	29 (14.5%)	0.085
Pallor	12(6%)	0.212

Coming to physical findings, the most common sign we observed was toxic look in 70% of the cases followed by coated tongue in 48.5%, hepatomegaly 42%, splenomegaly 20.5%, hepatosplenomegaly in 14.5% of cases and pallor in 6% of cases.

Table 6: Laboratory parameters

Laboratory parameters	Abnormal values	No. of cases	P-value
Hemoglobin	Anemia (Hb<11g%)	42(21%)	0.031
Total leukocyte count	Leucocytosis(>11000cells/mm^3)	35(17.5%)	0.029
	Leucopenia(<4000cells/mm^3)	64(32%)	0.00
Polymorphs	Neutropenia	85(42.5%)	0.00
	Neutrophilia	61(30.5%)	0.00
Eosinophils	Eosinophilia	17(8.5%)	0.17
	Eosinopenia	91(45.5%)	0.00
Platelets	Thrombocytopenia	30(15%)	0.01
SGOT	Elevated SGOT	25(12.5%)	0.21
SGPT	Elevated SGPT	29(14.5%)	0.27
Widal titres	TO >1:100	192(96%)	0.00
	TH >1: 200	151(75.5%)	0.00
Blood culture positive	Salmonella	44(22%)	0.01

Table 6 depicts the laboratory parameters. Anemia found in 42 (21%) cases, leucopenia and leucocytosis was observed in 64(32%) cases and 35(17.5%) cases respectively. Neutropenia found in 85(42.5%) cases and neutrophilia was found in 61(30.5%) cases. Eosinopenia was seen in 91(45.5%) cases, eosinophilia in 17(8.5%) cases and thrombocytopenia in 30(15%) cases. SGOT levels was elevated (>200IU/ml) in 25(12.5%) cases and SGPT (>200IU/ml) in 29(14.5%) cases. The elevated levels of liver enzymes lasted only few days. There were no complications observed during our study period. *Salmonella typhi*O titres >1:100 was seen in 192(96%) cases and TH titres >1:200 in 151(75.5%) cases. Blood culture positive for *Salmonella typhi*noted in 44(22%) cases. Out of 200 cases only 62 cases had been immunized with typhoid vaccine. All of them had taken typhoid polysaccharide vaccine more than 3 years prior to illness.

Table 7: Antibiotic sensitivity pattern

Drug	Sensitivity	P-value
Ceftriaxone	97%	0.000
Cefixime	95%	0.000
Ofloxacin	93%	0.000
Chloramphenicol	79%	0.000
Cefotaxime	76%	0.002
Azithromycin	51%	0.109
Ciprofloxacin	80%	0.001
Amoxicillin	63%	0.043

Significant p<0.01

Table 7 depicts antibiotic sensitivity patterns among culture positive cases. the most common sensitivity was seen in all the cases ceftriaxone (97%) and followed by cefixime(95%) , ofloxacin (93%), ciprofloxacin (80%), chloramphenicol (79%), cefotaxime (76%),amoxicillin (63%) and azithromycin in (51%). *S. typhi*was more sensitive to ceftriaxone, cefixime followed by ofloxacin. Least sensitivity was seen with azithromycin.

Discussion

Typhoid fever is a common infectious disease presenting as acute multisystem febrile illness. Our study has presented detailed study of 200 cases of typhoid fever about symptoms, clinical signs, investigations and in vitro antibiotics sensitivity/resistance pattern and treatment response. The definitive diagnosis of typhoid fever requires a confirmed diagnosis based on the blood or bone marrow culture. However, blood culture has several limitations including amount of blood required due to low levels of bacteremia and prior antibiotic use[11]. All the cases presented to OPD with a median of 7-10 days duration of fever. 150 cases (75%) had received antibiotics for a minimum period of 3-5 days prior to admission. Out of 200 cases, 135 cases (67.5%) were males and 65 cases (32.5%) were females .Similar results were reported in other studies[12].Most of the cases were aged between 6 and 12 years. 49 cases were below 6 years, representing 23.5%. 51 cases were aged above 12 years, representing 25.5%. 100 cases were aged between 6 and 12 years (50%). In all the above age groups male predominance was seen. A study done by R Modi et al also reported maximum incidence of typhoid in the age group 6 to 10 year[13]. Another study also reported maximum number of cases in the age group above 5 years[14].The duration of hospital stay varies, with maximum number of cases staying in hospital between 8-10 day. Cases were discharged after 3 consecutive days of afebrile period without antipyretics. These results were in accordance with study done by Hyder et al[15]. We observed high incidence of typhoid fever in lower class, lesser in middle class society and least in higher class. This can be explained by differences in drinking water sources and hygienic practices like hand washing and sanitary latrine facilities. Similar results were reported in other study[16] in our study, the most common symptom was fever (100%), followed by anorexia (63.5%), vomiting (43.5%), pain abdomen (19%), diarrhea (11%), headache (10.5%), and cough (6%). A study done by Sinha A et al.[17] Kapoor JP et al also reported similar results[18].Other studies also showed similar clinical picture[19-21].Contradictory to this, a study done by Joshi et alreported headache as the most common symptom next to fever[22]. In our study the most common sign we observed was toxic look in 70% of the cases followed by coated tongue in 48.5%, hepatomegaly 42%, splenomegaly 20.5%, hepatosplenomegaly in 14.5% of cases and pallor in 6% of cases. Study done by Laishram et al reported coated tongue (80%) as the most common sign followed by Hepatomegaly (76%) and splenomegaly (38%)[23]. In other study they had reported relative bradycardia and hepatomegaly as the most common sign[24].

During our study, all cases were positive for Widal. Blood culture was positive in 22% of cases. Other study also reported 16% culture

positive cases[15].A study done by Banu et al also reported 28% culture positive cases[24].Due to prior use of antibiotics, the culture positive cases are decreasing. Thus, need for relay on other serological tests for diagnosis of typhoid exists. Study done by Modi et al reported 97% Widal positive cases[13].Anemia was seen in 22.5% of cases. The other studies reported little higher percentage of anemias. A study done by Raj C et al reported anemia in 41.8% of patients and Lefebvre et al reported anemia in 78% of cases[25,26] in our study Leucocytopenia and Eosinopenia found in 32% and 45.5% respectively. Similar results reported in Lefebvre et al.[26] Although leucocytosis and eosinophilia are rare in typhoid, our study reported leucocytosis in 17.5% of cases and eosinophilia in 8.5% cases respectively. Thrombocytopenia was found in 15% of cases. Elevated SGOT is seen 12.5 % of cases and SGPT was raised in 14.5% of the cases. The other study reported elevated liver enzymes in 70% of cases[27].

Antibiotic sensitivity was similar to other studies. Most of the culture positive cases showed sensitivity to ceftriaxone, cefixime, ofloxacin, ciprofloxacin. Similar sensitivity pattern reported in other study[22].However sensitivity pattern varies from place to place. Other studies showed return of sensitivity pattern with chloramphenicol, cotrimoxazole, amoxicillin[20,28,29]. A study done by Mishra et al reported 100% sensitivity to azithromycin[30]. In our study the sensitivity to azithromycin was 51%. A Study done by Hyder et al reported 100% sensitivity to ceftriaxone and ciprofloxacin[16].

Conclusion

Typhoid fever is a multisystem disease with variable clinical presentations. No sign or symptom is specific for its diagnosis which needs correlation with lab investigations which again are not always helpful. Polymicrobial resistance mandates heightened focus on preventive measures.

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Conflict of Interest: Nil
Source of support:Nil