Original research article

Clinico-demographic profile and antibiotic sensitivity pattern of enteric fever cases among paediatric

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Abstract

Aim: the aim of this study was to determine the Clinico-Epidemiological Profile among Paediatric Patients in Bihar region.

Material and methods: A prospective observational study was conducted in the Department of Paediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India for 14 months. Total 110 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 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Most of the cases were aged between 6 and 12 years (50%). The most common symptom was fever (100%), followed by anorexia (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhea (13.64%), headache (11.82%), and cough (8.18%). The most common sign we observed was toxic look in 70.90% of the cases followed by coated tongue in 50.90%, hepatomegaly 44.55%, splenomegaly 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% of cases. Table 6 depicts the laboratory parameters. Anemia found in 23 (20.90%) cases, leucopenia and leucocytosis was observed in 39(35.45%) cases and 16(14.55%) cases respectively. Neutropenia found in 45(40.90%) cases and neutrophilia was found in 30(27.27%) cases. Eosinopenia was seen in 51(46.36%) cases, eosinophilia in 7(6.36%) cases and thrombocytopenia in 18(16.36%) cases. SGOT levels was elevated (>200IU/ml) in 17(15.45%) cases and SGPT (>200IU/ml) in 15(13.63%) cases. There were no complications observed during our study period. *Salmonella typhi* O titres >1:100 was seen in 103(93.63%) cases and TH titres >1:200 in 82(74.54%) cases. Blood culture positive for *Salmonella typhi* noted in 27(24.55%) cases. The most common sensitivity was seen in all the cases ceftriaxone (94%) and followed by cefixime(92%) , ofloxacin (90%), ciprofloxacin (81%), chloramphenicol (78%), cefotaxime (75%),amoxicillin (59%) and azithromycin in (46%). *S. typhi* was more sensitive to ceftriaxone, cefixime followed by ofloxacin. Least sensitivity was seen with azithromycin.

Conclusion: Typhoid fever is most commonly observed with unhygienic practices and eating of unhealthy outside food. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.

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

Introduction

Enteric fever, representing a systemic infection caused by Salmonella enteric serovar Typhi (S. typhi) and Salmonella enteric serovar Paratyphi (S. paratyphi), is a common cause of morbidity in the developing world, particularly in South and South–East Asia.[1,2] It is estimated that over 22 million cases and more than 200000 deaths of typhoid fever occurred in the year 2000, with the majority of disease burden being borne by children and adolescents in South and South–East Asia.[1] Highest incidence has been documented in impoverished, overcrowded areas with poor access to sanitation such as the urban slum areas of North Jakarta (Indonesia), Kolkata (India) and Karachi (Pakistan) with annual incidence rates of blood culture–confirmed enteric fever ranging from 180–494/100000 among 5–15 year-olds and 140–573/100000 among those 2–4 years old.[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 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. Treatment of typhoid includes proper hydration, correction of electrolyte imbalance, antipyretic therapy and appropriate antibiotics. Soft and easily digestible food should be continued.

Materials and Methods

A prospective observational study was conducted in the Department of Paediatrics Nalanda Medical College and Hospital, Patna, Bihar, India for 14 months, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

Total 110 Children aged below 18 years who presented to the Pediatric 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 titre >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. 74 cases (67.27%) had received antibiotics for a minimum period of 3-5 days prior to admission. Table 1 shows Out of 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Table 2 shows, most of the cases were aged between 6 and 12 years. 27 cases were below 6 years, representing 24.55%. 28 cases were aged above 12 years, representing 25.45%. 55 cases were aged between 6 and 12 years (50%). In all the above age groups male predominance was seen.

Table 1: Gender Distribution of patients

Gender	N=110	%
Male	75	68.18
Female	35	31.82

Table 2: Age wise distribution

Age(years)	N=110	%
0-6 years	27	24.55
6-12 years	55	50
12-18 years	28	25.45

Duration of hospital stay varied from up to two Week. As shown in Table-3, most of the cases (68.89%) stayed in hospital up to two Week after admission. 31.81% 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	35 (31.81%)	0.19
More than one Week	75(68.89%)	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 (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhea (13.64%), headache (11.82%), and cough (8.18%).

Table 4: Common presenting symptoms

Presenting symptom	No. of Cases	P-value
Fever	110 (100%)	0.001
Anorexia	71 (64.55%)	0.000
Vomiting	53 (48.18%)	0.001
Pain abdomen	21 (19.09%)	0.019
Diarrhea	15 (13.64%)	0.072
Headache	13 (11.82%)	0.94
Cough	9(8.18%)	0.175

Table 5: Various physical findings

Signs	No. of Cases	P-value
Toxic look	78(70.90%)	0.001
Coated tongue	56(50.90%)	0.001
Hepatomegaly	49 (44.55%)	0.003
Splenomegaly	23 (20.90%)	0.069
Hepatosplenomegaly	14(12.73%)	0.079
Pallor	8(7.27%)	0.224

Coming to physical findings, the most common sign we observed was toxic look in 70.90% of the cases followed by coated tongue in 50.90%, hepatomegaly 44.55%, splenomegaly 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% of cases.

Table 6: Laboratory parameters

Laboratory parameters	Abnormal values	No. of cases	P-value
Hemoglobin	Anemia (Hb <11g%)	23 (20.90%)	0.039
Total leukocyte count	Leucocytosis (>11000cells/mm^3)	16 (14.55%)	0.036
	Leucopenia (<4000cells/mm^3)	39 (35.45%)	0.00
Polymorphs	Neutropenia	45 (40.90%)	0.00
	Neutrophilia	30 (27.27%)	0.00
Eosinophils	Eosinophilia	7 (6.36%)	0.22
	Eosinopenia	51 (46.36%)	0.00
Platelets	Thrombocytopenia	18 (16.36%)	0.01
SGOT	Elevated SGOT	17 (15.45%)	0.37
SGPT	Elevated SGPT	15 (13.63%)	0.30
Widal titres	TO >1:100	103 (93.63%)	0.00
	TH >1: 200	82 (74.54%)	0.00
Blood culture positive	Salmonella	27 (24.55%)	0.01

Table 6 depicts the laboratory parameters. Anemia found in 23 (20.90%) cases, leucopenia and leucocytosis was observed in 39(35.45%) cases and 16(14.55%) cases respectively. Neutropenia found in 45(40.90%) cases and neutrophilia was found in 30(27.27%) cases. Eosinopenia was seen in 51(46.36%) cases, eosinophilia in 7(6.36%) cases and thrombocytopenia in 18(16.36%) cases. SGOT levels was elevated (>200IU/ml) in 17(15.45%) cases and SGPT (>200IU/ml) in 15(13.63%) 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 103(93.63%) cases and TH titres >1:200

in 82(74.54%) cases. Blood culture positive for *Salmonella typhi* noted in 27(24.55%) cases. Out of 110 cases only 29 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	94%	0.000
Cefixime	92%	0.000
Ofloxacin	90%	0.000
Chloramphenicol	78%	0.000
Cefotaxime	75%	0.002
Azithromycin	46%	0.119
Ciprofloxacin	81%	0.001
Amoxicillin	59%	0.042

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 (94%) and followed by cefixime(92%) , ofloxacin (90%), ciprofloxacin (81%), chloramphenicol (78%), cefotaxime (75%),amoxicillin (59%) and azithromycin in (46%). *S. typhi* was more sensitive to ceftriaxone, cefixime followed by ofloxacin. Least sensitivity was seen with azithromycin.

Discussion

Although typhoid continues to be seen in large numbers, documented typhoid cases are reducing in recent years. 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. 74 cases (67.27%) had received antibiotics for a minimum period of 3-5 days prior to admission. Out of 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Similar results were reported in other studies.[12] most of the cases were aged between 6 and 12 years. 27 cases were below 6 years, representing 24.55%. 28 cases were aged above 12 years, representing 25.45%. 55 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 (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhea (13.64%), headache (11.82%), and cough (8.18%). 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] [14-16].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 70.90% of the cases followed by coated tongue in 50.90%, hepatomegaly 44.55%, splenomegaly 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% 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 24.55% 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 20.90% 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 35.45% and 46.36% respectively. Similar results reported in Lefebvre et al.[26] Although leucocytosis and eosinophilia are rare in typhoid, our study reported leucocytosis in 14.55% of cases and eosinophilia in 6.36% cases respectively. Thrombocytopenia was found in 16.36% of cases. Elevated SGOT is seen 15.45% of cases and SGPT was raised in 13.63% 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 46%. A Study done by Hyder et al reported 100% sensitivity to ceftriaxone and ciprofloxacin.[15]

Conclusion

Typhoid fever is most commonly observed with unhygienic practices and eating of unhealthy outside food. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.

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