

## Original research article

**Evaluation Of Clinico-Biochemical Profile And Antibiotic Sensitivity Pattern Of Children Diagnosed With Typhoid Fever****Dr. Dheeraj Kumar<sup>1</sup>, Dr. Bankey Behari Singh<sup>2</sup>****<sup>1</sup> Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.****<sup>2</sup> Associate Professor & HOD, Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India****Corresponding Author: Dr. Dheeraj Kumar****Abstract**

**Aim:** This study was conducted to evaluation of Clinical & Laboratory Profile of Typhoid Fever in Children in Bihar Region.

**Methods:** A prospective observational study was conducted in the Department of Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 18 months. Total 120 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 120 cases, 80 cases (66.67%) were males and 40 cases (33.33%) were females. Most of the cases were aged between 6 and 12 years. 59 cases were aged between 6 and 12 years (49.17%). In all the above age groups male predominance was seen. The most common symptom was fever (100%), followed by anorexia (65.83%), vomiting (47.5%), pain abdomen (20%), diarrhea (11.67%), headache (9.17%), and cough (6.67%). The most common sign we observed was toxic look in 69.17% of the cases followed by coated tongue in 49.17%, hepatomegaly 45.83%, splenomegaly 20.83%, hepatosplenomegaly in 13.33% of cases and pallor in 5.83% of cases. Table 6 depicts the laboratory parameters. Anemia found in 26 (21.67%) cases, leucopenia and leucocytosis was observed in 41(34.17%) cases and 19(15.83%) cases respectively. Neutropenia found in 50(41.67%) cases and neutrophilia was found in 35(29.17%) cases. Eosinopenia was seen in 56(46.67%) cases, eosinophilia in 8(6.67%) cases and thrombocytopenia in 19(15.83%) cases. SGOT levels was elevated (>200IU/ml) in 14(11.67%) cases and SGPT (>200IU/ml) in 17(14.17%) cases. The elevated levels of liver enzymes lasted only few days.

**Conclusion:** Public health interventions like supply of safe drinking water, appropriate sanitation, awareness of the disease and its transmission, and good personal hygiene practices may be employed.

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

**Introduction**

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.<sup>1</sup> 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*.<sup>2</sup> 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.<sup>2</sup> The world sees approximately 22 million new typhoid cases occur each year<sup>6</sup> . In India in

disease-endemic areas, the annual incidence of enteric fever is about 1%.<sup>3</sup> 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.<sup>4</sup> The differential count is usually unremarkable except for eosinopenia. Eosinopenia often absolute may be present in 70-80% cases.<sup>5</sup> 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%.<sup>4</sup> The emergence of strains of *Salmonella typhi* resistant to multiple antibiotics poses a serious problem. Chloramphenicol was considered the antimicrobial gold standard for the treatment of typhoid fever till 1948.<sup>6</sup> 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.<sup>7</sup> and in India in 1972.<sup>8</sup> Gradually, resistance to multiple antibiotics developed.<sup>9</sup> The first major epidemic of multidrug resistant *S. typhi* was reported in 1972.<sup>10</sup> 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.<sup>9</sup> 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 Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 18 months, after taking the approval of the protocol review committee and institutional ethics committee.

#### Methodology

Total 120 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. 80 cases (66.67%) had received antibiotics for a minimum period of 3-5 days prior to admission. Table 1 shows Out of 120 cases, 80 cases (66.67%) were males and 40 cases (33.33%) were

females. Table 2 shows, most of the cases were aged between 6 and 12 years. 29 cases were below 6 years, representing 24.17%. 32 cases were aged above 12 years, representing 26.66%. 59 cases were aged between 6 and 12 years (49.17%). In all the above age groups male predominance was seen.

**Table 1: Gender Distribution of patients**

Gender	N=120	%
Male	80	66.67
Female	40	33.33

**Table 2: Age wise distribution**

Age( years)	N=120	%
0-6 years	29	24.17
6-12 years	59	49.17
12-18 years	32	26.66

Duration of hospital stay varied from up to two Week. As shown in Table-3, most of the cases (70.83%) stayed in hospital up to two Week after admission. 29.17% 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 (29.17%)	0.16
More than one Week	85(70.83%)	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 (65.83%), vomiting (47.5%), pain abdomen (20%), diarrhea (11.67%), headache (9.17%), and cough (6.67%).

**Table 4: Common presenting symptoms**

Presenting symptom	No. of Cases	P-value
Fever	120 (100%)	0.001
Anorexia	79 (65.83%)	0.000
Vomiting	57 (47.5%)	0.001
Pain abdomen	24 (20%)	0.016
Diarrhea	14 (11.67%)	0.069
Headache	11 (9.17%)	0.91
Cough	8(6.67%)	0.172

**Table 5: Various physical findings**

Signs	No. of Cases	P-value
Toxic look	83(69.17%)	0.001
Coated tongue	59(49.17%)	0.001
Hepatomegaly	55 45.83%)	0.002
Splenomegaly	25 (20.83%)	0.066
Hepatosplenomegaly	16(13.33%)	0.076
Pallor	7(5.83%)	0.221

Coming to physical findings, the most common sign we observed was toxic look in 69.17% of the cases followed by coated tongue in 49.17%, hepatomegaly 45.83%, splenomegaly 20.83%, hepatosplenomegaly in 13.33% of cases and pallor in 5.83% of cases.

**Table 6: Laboratory parameters**

Laboratory parameters	Abnormal values	No. of cases	P-value
<b>Hemoglobin</b>	Anemia (Hb <11g%)	26 (21.67%)	0.036
<b>Total leukocyte count</b>	Leucocytosis (>11000cells/mm <sup>3</sup> )	19 (15.83%)	0.033
	Leucopenia (<4000cells/mm <sup>3</sup> )	41 (34.17%)	0.00
<b>Polymorphs</b>	Neutropenia	50 (41.67%)	0.00
	Neutrophilia	35 (29.17%)	0.00
<b>Eosinophils</b>	Eosinophilia	8 (6.67%)	0.19
	Eosinopenia	56 (46.67%)	0.00
<b>Platelets</b>	Thrombocytopenia	19 (15.83%)	0.01
<b>SGOT</b>	Elevated SGOT	14 (11.67%)	0.34
<b>SGPT</b>	Elevated SGPT	17 (14.17%)	0.27
<b>Widal titres</b>	TO >1:100	115 (95.83%)	0.00
	TH >1: 200	91 (75.83%)	0.00
<b>Blood culture positive</b>	Salmonella	31 (25.83%)	0.01

Table 6 depicts the laboratory parameters. Anemia found in 26 (21.67%) cases, leucopenia and leucocytosis was observed in 41(34.17%) cases and 19(15.83%) cases respectively. Neutropenia found in 50(41.67%) cases and neutrophilia was found in 35(29.17%) cases. Eosinopenia was seen in 56(46.67%) cases, eosinophilia in 8(6.67%) cases and thrombocytopenia in 19(15.83%) cases. SGOT levels was elevated (>200IU/ml) in 14(11.67%) cases and SGPT (>200IU/ml) in 17(14.17%) 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 115(95.83%) cases and TH titres >1:200 in 91(75.83%) cases. Blood culture positive for *Salmonella typhi* noted in 31(25.83%) cases. Out of 120 cases only 34 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	81%	0.000
Cefotaxime	78%	0.002
Azithromycin	49%	0.122
Ciprofloxacin	84%	0.001
Amoxicillin	62%	0.045

**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 (84%), chloramphenicol (81%), cefotaxime (78%), amoxicillin (62%) and azithromycin in (49%). *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.<sup>11</sup> All the cases presented to OPD with a median of 7-10 days duration of fever. 80 cases (66.67%) had received antibiotics for a minimum period of 3-5 days prior to admission. Out of 120 cases, 80 cases (66.67%) were males and 40 cases (33.33%) were females. Similar results were reported in other studies.<sup>12</sup> Most of the cases were aged between 6 and 12 years. 29 cases were below 6 years, representing 24.17%. 32 cases were aged above 12 years, representing 26.66%. 59 cases were aged between 6 and 12 years (49.17%). 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.<sup>13</sup> Another study also reported maximum number of cases in the age group above 5 years.<sup>14</sup> 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.<sup>15</sup> 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.<sup>16</sup> in our study, the most common symptom was fever (100%), followed by anorexia (65.83%), vomiting (47.5%), pain abdomen (20%), diarrhea (11.67%), headache (9.17%), and cough (6.67%). A study done by Sinha A et al.<sup>17</sup> Kapoor JP et al also reported similar results.<sup>18</sup> Other studies also showed similar clinical picture.<sup>19-21 14-16</sup>. Contradictory to this, a study done by Joshi et al reported headache as the most common symptom next to fever.<sup>22</sup> In our study the most common sign we observed was toxic look in 69.17% of the cases followed by coated tongue in 49.17%, hepatomegaly 45.83%, splenomegaly 20.83%, hepatosplenomegaly in 13.33% of cases and pallor in 5.83% of cases. Study done by Laishram et al reported coated tongue (80%) as the most common sign followed by Hepatomegaly (76%) and splenomegaly (38%).<sup>23</sup> In other study they had reported relative bradycardia and hepatomegaly as the most common sign.<sup>24</sup>

During our study, all cases were positive for Widal. Blood culture was positive in 25.83% of cases. Other study also reported 16% culture positive cases.<sup>15</sup> A study done by Banu et al also reported 28% culture positive cases.<sup>24</sup> 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.<sup>13</sup> Anemia was seen in 21.67% 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.<sup>25,26</sup> in our study Leucocytopenia and Eosinopenia found in 34.17% and 46.67% respectively. Similar results reported in Lefebvre et al.<sup>26</sup> Although leucocytosis and eosinophilia are rare in typhoid, our study reported leucocytosis in 15.83% of cases and eosinophilia in 6.67% cases respectively. Thrombocytopenia was found in 15.83% of cases.

Elevated SGOT is seen 11.67% of cases and SGPT was raised in 14.17% of the cases. The other study reported elevated liver enzymes in 70% of cases.<sup>27</sup>

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.<sup>22</sup> However sensitivity pattern varies from place to place. Other studies showed return of sensitivity pattern with chloramphenicol, cotrimoxazole, amoxicillin.<sup>20,28,29</sup> A study done by Mishra et al reported 100% sensitivity to azithromycin.<sup>30</sup> In our study the sensitivity to azithromycin was 49%. A Study done by Hyder et al reported 100% sensitivity to ceftriaxone and ciprofloxacin.<sup>15</sup>

### Conclusion

Typhoid fever varies in presentation with abdominal distension more common in younger children whereas abdominal pain and headache were more common in older children. There is re-emergence of sensitivity of *S.typhi* for Chloramphenicol, Ampicillin and Cotrimoxazole. Public health interventions like supply of safe drinking water, appropriate sanitation, awareness of the disease and its transmission, and good personal hygiene practices may be employed.

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