

# Histopathological and Haematological Manifestations of Typhoid Fever in Pediatric Age Group

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## ABSTRACT

**Background:** Typhoid fever is an acute systemic infection caused by *Salmonella Enterica* Serovar Typhi. Organism is transmitted by fecal-oral route.

**Aim:** To determine frequency of various histopathological & hematological manifestations of typhoid fever in pediatric age group.

**Study design:** Cross-sectional survey.

**Methodology:** Complete blood count, pro-thrombin time and activated partial thromboplastin time were performed on the patients (n=140) to find out various hematological manifestations. Histopathological findings of patients undergoing colonoscopy and biopsy due to gastrointestinal presentations were also noted.

**Results:** Present study had 65% males with 35% females. Almost 65.7% cases presented with anemia. Around 50.7% patients had leucopenia while eosinopenia was 67.1%. Cases (39.3%) presented with prolonged activated partial thromboplastin time while 32.1% cases had prolonged pro-thrombin time. Among histopathological manifestation, 3(2.14%) presented with Typhoid colitis/enteritis, 2(1.43%) with gastrointestinal bleeding due to ulcers and only 1(0.71%) with peritonitis.

**Conclusion:** It was concluded that most common haematological manifestation in typhoid fever was eosinopenia which was most frequently found in coexistence with thrombocytopenia. However, histopathological abdominal complications were quite rare but could be dreadful and should be kept in mind.

**Keywords:** Typhoid Fever, Hematological, Histopathological Manifestations, Abdominal complications and Children.

## INTRODUCTION

Causative agent for Typhoid fever is salmonella enterica serovartyphi<sup>1</sup>. Feco-oral route is its mode of transmission<sup>2,3</sup>. This is a systemic infection that is insidious in onset and manifested by symptoms like fever, headaches, malaise, anorexia and a non-productive cough<sup>4</sup>. Other cardinal signs include bradycardia, splenomegaly, abdominal discomfort, macular rash (red-spots) on trunk<sup>5,6</sup>. Typhoid fever is associated with anemia, elevated erythrocyte sedimentation rate (ESR), thrombocytopenia<sup>7</sup>, low PCV, leucopenia, eosinopenia<sup>8</sup> and subclinical intravascular disseminate coagulation<sup>9</sup>.

Complications such as ulceration of Peyer's patches in the ileum<sup>10</sup> causing intestinal hemorrhage or perforation<sup>11</sup> can occur, especially late in untreated cases or in patients with multiple drug resistance. Relapses can occur. Disease is often associated with poor sanitation and housing. Personal hygiene and recent use of antimicrobials are further risk factors.<sup>3</sup> *Salmonella enterica* serovar Paratyphi causes a similar, although less severe syndrome. The most serious complication of typhoid fever, intestinal bleeding or holes (perforations) may develop in the third week of illness.

Isolation of causative agent from blood, bone marrow or a specific anatomical lesion is required for its definitive diagnosis. However, presence of clinical symptoms and/or an antibody response is suggestive of its diagnosis. Positive blood culture is the main tool for its correct diagnosis. Stool cultures is another test but a positive stool culture can occur in carriers as well<sup>11,12</sup>.

Typhoid ulcers on endoscopy and histological slides appear as multiple superficial punched out oval lesions with slightly elevated margins. Microscopical hypertrophy of ileal mucosa occur due to diffuse presence of monocytes, macrophages and polymorphic neutrophils as documented by many studies<sup>11,13</sup>.

For better treatment and prevention of life threatening complications like perforation and peritonitis, correct diagnosis with early colonoscopy and histopathological examination is a need of hour. Apart from diagnosis, these manifestations can help physician for accurate choice of antibiotics that prevent multidrug resistance and to monitor response of antibiotics therapy hence current study was planned.

The objective of the study was to determine frequency of various histopathological and hematological manifestations of typhoid fever in paediatric age group.

## METHODOLOGY

This cross sectional study was conducted at Pathology Department, Children's Hospital and Institute of Child Health, Lahore after approval from Ethical Review Board. Patients (n=140) who fulfilled the inclusion criteria were selected with 95% confidence level, 7% margin of error and taking expected prevalence of prolonged prothrombin time 21.6%. Patients (both genders) were diagnosed with typhoid fever on widal test or typhidot and positive culture sensitivity report having age from six months to 15 years were included. Children who were diagnosed with infectious conditions other than typhoid fever while having preceding pancytopenia were excluded. Complete blood count and prothrombin time and activated partial thromboplastin time were performed on the patients to find out various hematological manifestations. Histopathological and endoscopic ultrasound findings were noted in patients with GI symptoms undergoing the relevant procedures. All this information was recorded on proforma. All data was analyzed through SPSS version 20.0. All categorical variables were calculated and expressed as frequencies and percentages. Numerical variables like age was expressed as mean±SD.

## RESULTS

Total 140 children were enrolled. The patients mean age was 7.83±2.92 year. Children were distributed in three groups according to their age brackets as shown in Table-1.

Table-1: Parameter of all subjects (n=140)

Groups	Frequency	%age
<b>Gender</b>		
Males	91	65
Females	49	35
<b>Age group in years</b>		
0-5	25	18.6
6-10	86	61.4
11-15	28	20
Mean + SD	7.83±2.92	

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Very few cases had histopathological manifestations; however, all patients had at least one or more haematological problems at the time of presentation which were summarized as frequency and percentage in Table-2.

Table 2: Overall frequency of different hematological & histopathological manifestations

Variables	Frequency	%age
Anemia	92	65.7
Leucopenia	71	50.7
Eosinopenia	94	67.1
Thrombocytopenia	56	40.0
Prolonged prothrombin time	45	32.1
Prolonged APTT	55	39.3
Typhoid colitis/enteritis	03	2.14
Gastrointestinal hemorrhage	02	1.43
Peritonitis	01	0.71

Different manifestations in different age groups were summarized as frequency and percentage in Table-3. Majority 5(3.57%) of cases with GI complication and endoscopic histopathological diagnosis were found in 6-10 years age group, while among 11-15 years old patients, no histopathological GI complication was noticed as shown in Table-3.

Table-3: Different histopathological & haematological manifestations among different age groups

Variables	0-5 Years (n= 26)	6-10 Years (n= 86)	11-15 Years (n= 28)
Anemia	16(61.5%)	56 (65.1%)	20(71.4%)
Leucopenia	15(57.7%)	42(48.8%)	14(50.0%)
Eosinopenia	17(65.4%)	55(64.0%)	22(78.6%)
Thrombocytopenia	9(34.6%)	34(32.6%)	13(28.6%)
Prolonged PT	9 (34.6%)	28(54.1%)	8(57.8%)
Prolonged APTT	12(46.2%)	33(38.4%)	10(35.7%)
Typhoid enteritis/colitis	01(0.71%)	02(1.43%)	NIL
GI-Bleed	NIL	02(1.43%)	NIL
Peritonitis	NIL	01(0.71%)	NIL

## DISCUSSION

Anemia is a common finding in most typhoid fever patients. It is mostly secondary to endotoxemia caused by bacteria and inadequate food intake but may be multi-factorial in etiology.<sup>14,15</sup> The prevalence of anemia in typhoid fever varies greatly according to different reports and has been found in 15% to 61.3% of newly diagnosed patients with typhoid fever.<sup>7</sup> In this study the overall frequency of anemia found was 65.7%; majority of such cases were male and between 6-10 years age (62.5%). One study concluded that 61.3% of their typhoid fever patients presented with anemia<sup>5</sup>. Many studies concluded that anemia was seen in majority patients of typhoid fever<sup>16,17</sup>.

The results of the current study revealed that 50.7% of typhoid fever cases presented with leucopenia. The exact cause of leucopenia is a shift in leukocytes from the circulation into the marginal zone by salmonella typhi, resulting in leucopenia<sup>14,18</sup>. The previous literature has reported leucopenia 19-53.3% of typhoid patients<sup>7,16</sup>.

In our study eosinopenia was found in 67.1% typhoid patients, most were males aged 6-10 years (61.8%). Eosinopenia, as a response to acute infection, is well known. Absolute eosinopenia in the proper clinical settings can give a strong clue to the diagnosis of enteric fever. In other study 73% patients were presented with eosinopenia.<sup>7</sup>

The previous studies have reported thrombocytopenia as a common manifestation of typhoid fever, seen in 35 to 61.5% of patients<sup>7,14</sup>. In the present study frequency of thrombocytopenia was found to be 40%, among which it mostly coexisted with anemia. A study conducted in typhoid fever children reported 37% cases with thrombocytopenia.<sup>18</sup>

In this study, 32.1% cases had prolonged prothrombin time while 39.3% had prolonged activated partial thromboplastin time but none of them had an active bleed. Our results were in line with

previous study that showed prolonged prothrombin time in 21.6% while 46.1% patients with prolonged activated partial thromboplastin time<sup>18</sup>.

Very few histopathological manifestations due to gastrointestinal complications were seen in our study, out of which typhoid colitis was seen in only 1(0.71%) typhoid enteritis were seen in only 2(1.43%) patients. Colitis is an infrequent presentation in typhoid fever in pediatric age group. This is in accordance with study conducted by Arun Babu T et al<sup>19</sup>. After effects of enteric fever such as gastrointestinal bleeding and bowel perforation are hardly seen<sup>20</sup>.

In the present study, 2(1.43%) children presented with gastrointestinal bleeding and typhoid ulcers and only one (0.71%) presented with peritonitis due to intestinal perforation. All of these patients were having drug resistance and history of recurrent enteric fever that usually result in ulcer formation with ultimate hemorrhage and perforation as proved by Azmatullah A et.al in their study<sup>21</sup>. Most of these cases were found in 6 to 10 years age group. Incidence in similar age group was noticed in another study by Iftikhar A<sup>22</sup>.

**Limitations:** Our study had limitations like financial constraints, lack of resources, short duration of study and lack of genetic workup.

## CONCLUSION

It was concluded that most common hematological manifestation in typhoid fever was eosinopenia which was most frequently found in coexistence with thrombocytopenia. Histopathological display of the disease is rare but important to keep in mind to avoid the gastrointestinal life threatening complications.

**Authors' contribution:** FR&FS: Conceptualized the study, analyzed the data, and formulated the initial draft.

ZK&MUR: Contributed to the proof reading.

SSA&SZW: Collected data.

**Conflict of Interest:** None to declare

**Financial Disclosure:** None

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