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Original Research Article

Association Between Hepatosplenomegaly and Hematological Abnormalities in Children with Typhoid Fever

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Abstract

Background: Typhoid fever is a systemic bacterial infection that commonly affects children and may be associated with hematological abnormalities and hepatosplenomegaly. The presence of organomegaly may reflect systemic involvement and could be associated with greater hematological derangement. This study was undertaken to evaluate the association between hepatosplenomegaly and hematological abnormalities in children with typhoid fever.

Methods: A hospital-based observational study was conducted in the Department of Paediatrics of a tertiary care teaching hospital over a period of one year. A total of 100 children aged 1–18 years diagnosed with typhoid fever were included. Clinical examination was performed to assess hepatomegaly and splenomegaly. Hematological parameters including hemoglobin, total leukocyte count, differential leukocyte count, platelet count and red cell indices were evaluated. The association between hepatosplenomegaly and hematological abnormalities was analyzed using appropriate statistical tests, with $p<0.05$ considered statistically significant.

Results: Among the 100 children, 28 (28%) had hepatosplenomegaly, while 18 (18%) had isolated hepatomegaly and 12 (12%) had isolated splenomegaly. Anemia was observed in 46% of children, thrombocytopenia in 34%, leukopenia in 31%, neutropenia in 19% and leukocytosis in 12%. Children with hepatosplenomegaly had a significantly higher frequency of anemia (71.4% vs. 36.1%, p=0.004), leukopenia (53.6% vs. 22.2%, p=0.006) and thrombocytopenia (53.6% vs. 26.4%, p=0.012) compared with those without hepatosplenomegaly. Mean hemoglobin, total leukocyte count and platelet count were also significantly lower in children with hepatosplenomegaly.

Conclusion: Hepatosplenomegaly was significantly associated with anemia, leukopenia and thrombocytopenia in children with typhoid fever. Its presence may serve as a useful clinical indicator of increased hematological involvement and may warrant closer hematological monitoring.

Keywords: Typhoid fever; Children; Hepatosplenomegaly; Hepatomegaly; Splenomegaly; Anemia; Leukopenia; Thrombocytopenia.

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Introduction

Typhoid fever is a systemic bacterial infection caused predominantly by *Salmonella enterica* serovar Typhi and remains an important public health problem, particularly in developing countries where inadequate sanitation, unsafe drinking water and limited access to healthcare contribute to continued transmission [1,2]. Children are an important population affected by enteric fever, and the disease may range from uncomplicated febrile illness to severe systemic infection with involvement of multiple organs [3].

The clinical presentation of typhoid fever in children is variable. Prolonged fever is the most characteristic feature and may be accompanied by headache, weakness, anorexia, nausea, vomiting, abdominal pain, diarrhoea or constipation [2,4]. Because these manifestations overlap with several other childhood febrile illnesses, clinical diagnosis may be challenging. Blood culture remains an important method for microbiological confirmation, although its sensitivity may be affected by prior antibiotic exposure and the timing of specimen collection [5].

Typhoid fever is a systemic infection with prominent involvement of the reticuloendothelial system. The liver and spleen may become involved during the course of infection, resulting in hepatomegaly, splenomegaly or simultaneous

enlargement of both organs [3,6]. Hepatosplenomegaly is therefore an important clinical finding in children with enteric fever and may reflect the extent of systemic involvement.

Hematological abnormalities are frequently observed in children with typhoid fever. Anemia, leukopenia and thrombocytopenia are among the commonly reported abnormalities, while some patients may develop leukocytosis, neutropenia or other changes in complete blood count parameters [4,7,8]. These abnormalities are likely to be multifactorial and may result from infection-associated bone marrow suppression, altered hematopoiesis, reticuloendothelial activation, inflammatory responses and, in severe cases, direct bone marrow involvement [8,9].

The relationship between hepatosplenic involvement and hematological abnormalities is of particular clinical interest. Enlargement of the liver and spleen may indicate greater involvement of the reticuloendothelial system, while associated hematological changes may reflect the systemic effects of infection. Children presenting with hepatosplenomegaly may therefore have a greater frequency or severity of cytopenias compared with children without organomegaly [6,8].

Previous studies have described hepatomegaly, splenomegaly and hematological abnormalities as important manifestations of pediatric enteric fever [4,6,7]. However, the specific association between hepatosplenomegaly and individual hematological abnormalities such as anemia, leukopenia and thrombocytopenia has not been adequately characterized in many hospital-based pediatric populations.

Identifying this association may have clinical relevance because hepatosplenomegaly can be detected during routine physical examination, while hematological abnormalities can be identified through complete blood count testing. Recognition of children at increased risk of cytopenias may help clinicians institute appropriate hematological monitoring and assess the severity of systemic involvement.

Therefore, the present study was undertaken to evaluate the association between hepatosplenomegaly and hematological abnormalities among children with typhoid fever, with particular emphasis on anemia, leukopenia, thrombocytopenia and changes in major complete blood count parameters.

Materials and Methods

Study Design and Setting: The present study was designed as a hospital-based observational study to evaluate the association between hepatosplenomegaly and haematological abnormalities among children diagnosed with typhoid fever. The study was conducted in the Department of Paediatrics of a tertiary care teaching hospital, over a period of one year.

Study Population: The study population comprised pediatric patients diagnosed with typhoid fever who attended the outpatient department or were admitted to the pediatric wards during the study period. A total of 100 eligible children were included in the study.

Sample Size: A total of 100 pediatric patients with typhoid fever were enrolled during the study period based on predefined eligibility criteria and the feasibility of recruitment at the study centre.

Inclusion Criteria

Children fulfilling the following criteria were included:

- Children aged 1–18 years.
- Patients with a clinical diagnosis of typhoid fever supported by appropriate laboratory investigations.
- Children presenting to or admitted in the Department of Paediatrics during the study period.
- Patients for whom clinical examination and complete blood count data were available.
- Parents or legally authorized guardians willing to provide written informed consent.

Exclusion Criteria

Patients were excluded if they had:

- Pre-existing hematological disorders such as leukaemia, aplastic anemia or known hemoglobinopathies.
- Chronic liver disease or chronic splenic disease diagnosed before the current illness.
- Known malignancy or chronic systemic disease likely to influence hematological parameters.
- Other confirmed acute infections known to cause significant hematological abnormalities.
- Incomplete clinical or laboratory records.
- Previous enrollment during the same episode of illness.
- Parents or guardians unwilling to provide informed consent.

Data Collection: After obtaining written informed consent from the parents or legally authorized guardians, relevant demographic, clinical and laboratory information was collected using a structured data collection proforma.

The following information was recorded:

- Age and sex
- Residence

- Duration of fever
- Relevant presenting symptoms
- Previous history of typhoid fever
- Relevant medical history
- Drug and treatment history
- General physical examination findings
- Presence or absence of hepatomegaly
- Presence or absence of splenomegaly
- Presence or absence of hepatosplenomegaly
- Complete blood count parameters
- Peripheral blood smear findings
- Relevant biochemical investigations
- Microbiological/serological evidence supporting typhoid fever
- Clinical outcome during hospitalization, where applicable

Diagnosis of Typhoid Fever: Typhoid fever was diagnosed on the basis of the clinical presentation and supported by appropriate laboratory investigations according to institutional practice.

Patients presenting with prolonged or persistent fever along with clinical features suggestive of enteric fever were evaluated using relevant investigations. Blood culture, where performed, was considered the microbiological reference method for confirmation. Appropriate serological testing may also have been used as supportive evidence according to clinical requirements and institutional protocol.

The final diagnosis was established by the treating pediatrician after considering the clinical presentation and available laboratory findings.

Clinical Assessment of Hepatomegaly and Splenomegaly: All enrolled children underwent a detailed physical examination.

Hepatomegaly was assessed by abdominal examination, particularly palpation of the liver below the right costal margin. The liver span and extent of palpable enlargement were recorded when clinically feasible.

Splenomegaly was assessed by palpation of the spleen below the left costal margin. The presence and approximate extent of splenic enlargement were documented. Hepatosplenomegaly was defined as the simultaneous clinical presence of both hepatomegaly and splenomegaly.

Children were categorized into the following groups for analysis:

- No hepatosplenomegaly
- Hepatomegaly alone
- Splenomegaly alone
- Hepatosplenomegaly

Clinical examination was performed by qualified pediatric clinicians using standard examination techniques.

Hematological Investigations: Venous blood samples were collected under aseptic precautions from each enrolled child. Complete blood count was performed using an automated hematology analyzer according to the laboratory's standard operating procedures.

The following hematological parameters were recorded:

- Hemoglobin concentration
- Total leukocyte count
- Differential leukocyte count
- Platelet count
- Red blood cell indices, including mean corpuscular volume where available

Peripheral blood smear examination was performed when clinically indicated or as part of routine laboratory evaluation.

Assessment of Hematological Abnormalities: Hematological abnormalities were categorized according to age-appropriate pediatric reference ranges.

The following abnormalities were specifically assessed:

Anemia; Anemia was defined according to the applicable age-specific hemoglobin reference range.

Leukopenia; Leukopenia was defined as a total leukocyte count below the age-appropriate reference range.

Leukocytosis; Leukocytosis was defined as a total leukocyte count above the age-appropriate reference range.

Thrombocytopenia; Thrombocytopenia was defined as a platelet count below the laboratory's accepted reference range.

Other Hematological Abnormalities: Other abnormalities, including neutropenia, lymphocytosis or abnormalities in red blood cell indices, were documented when present.

Grouping of Study Participants: For evaluating the relationship between organomegaly and hematological abnormalities, participants were categorized according to the presence or absence of hepatosplenomegaly. The haematological parameters of children with hepatosplenomegaly were compared with those of children without hepatosplenomegaly. The frequency of individual hematological abnormalities was also compared between the groups.

Additional Laboratory Investigations: Additional investigations such as liver function tests, renal function tests and other biochemical investigations were performed when clinically indicated as part of routine patient management.

These investigations were used to assess associated systemic involvement and were not mandatory for inclusion unless required by the study protocol.

Outcome Assessment: The primary outcome of the study was to determine whether the presence of hepatosplenomegaly was associated with hematological abnormalities in children with typhoid fever.

The primary hematological outcomes included:

- Anemia
- Leukopenia
- Leukocytosis
- Thrombocytopenia
- Other clinically relevant abnormalities in complete blood count parameters

Secondary observations included the demographic and clinical characteristics of children with and without hepatosplenomegaly.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using appropriate statistical software.

Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation for normally distributed data or as median with interquartile range for non-normally distributed data. The association between hepatosplenomegaly and categorical hematological abnormalities was assessed using the Chi-square test or Fisher's exact test, as appropriate. For comparison of continuous hematological parameters between groups, the independent samples t-test was used for normally distributed variables, while the Mann–Whitney U test was used for non-normally distributed variables. Where appropriate, correlation analysis was performed to assess the relationship between the degree of organomegaly and hematological parameters.

A p-value <0.05 was considered statistically significant.

Results and Observations

A total of 100 pediatric patients with typhoid fever were included in the present observational study conducted at the Department of Paediatrics, Yadgiri Institute of Medical Sciences, Yadgiri, Karnataka, over a period of one year. Demographic, clinical, hepatosplenic and haematological characteristics were analysed.

Table 1: Demographic characteristics of study participants (n=100)

Characteristic	Category	n	%
Age	1–5 years	18	18.0
	6–10 years	32	32.0
	11–14 years	28	28.0
	15–18 years	22	22.0
Sex	Male	57	57.0
	Female	43	43.0
Residence	Rural	61	61.0
	Urban	39	39.0

The largest proportion of children belonged to the 6–10-year age group (32%). A slight male predominance was observed, and 61% of participants were from rural areas.

Table 2: Clinical characteristics of study participants

Clinical feature	N	%
Fever	100	100.0
Abdominal pain	43	43.0
Weakness/fatigue	39	39.0
Loss of appetite	35	35.0
Diarrhea	32	32.0
Vomiting	28	28.0
Headache	25	25.0
Nausea	21	21.0
Constipation	17	17.0

Fever was present in all children. Abdominal pain, weakness/fatigue and loss of appetite were among the commonly reported associated symptoms.

Table 3: Duration of fever and diagnostic evidence

Parameter	Category	n	%
Duration of fever	≤7 days	29	29.0
	8–14 days	48	48.0
	>14 days	23	23.0
Diagnostic evidence	Blood culture positive	54	54.0
	Serological/supportive laboratory evidence	28	28.0
	Clinical diagnosis with supportive investigations	18	18.0

Nearly half of the children (48%) presented with fever of 8–14 days duration. Blood culture confirmation was available in 54% of cases.

Table 4: Distribution of hepatomegaly and splenomegaly

Clinical finding	N	%
No organomegaly	42	42.0
Hepatomegaly alone	18	18.0
Splenomegaly alone	12	12.0
Hepatosplenomegaly	28	28.0
Total	100	100.0

Some form of hepatomegaly or splenomegaly was present in 58% of children. Hepatosplenomegaly was observed in 28% of the study participants.

Table 5: Hematological parameters among study participants

Hematological parameter	Mean ± SD
Hemoglobin (g/dL)	10.8 ± 1.5
Total leukocyte count (cells/mm³)	5,920 ± 2,140
Neutrophils (%)	57.4 ± 9.6
Lymphocytes (%)	35.2 ± 8.7
Platelet count (×10³/μL)	168 ± 61
MCV (fL)	78.6 ± 6.9

The mean hemoglobin was 10.8 ± 1.5 g/dL, mean total leukocyte count was 5,920 ± 2,140 cells/mm³ and mean platelet count was 168 ± 61 ×10³/μL.

Table 6: Frequency of hematological abnormalities

Hematological abnormality	n	%
Anemia	46	46.0
Thrombocytopenia	34	34.0
Leukopenia	31	31.0
Neutropenia	19	19.0
Lymphocytosis	16	16.0
Leukocytosis	12	12.0
No major abnormality	21	21.0

Anemia was the most common hematological abnormality (46%), followed by thrombocytopenia (34%) and leukopenia (31%).

Table 7: Severity of anemia and platelet abnormalities

Parameter	Category	n	%
Anemia (n=46)	Mild	29	63.0
	Moderate	15	32.6
	Severe	2	4.4
Platelets (n=100)	Normal	66	66.0
	Mild thrombocytopenia	25	25.0
	Moderate thrombocytopenia	8	8.0
	Severe thrombocytopenia	1	1.0

Among children with anemia, mild anemia was the most common. Thrombocytopenia was present in 34% of participants, predominantly in the mild category.

Table 8: Total leukocyte count and peripheral smear findings

Parameter	Category	n	%
TLC	Leukopenia	31	31.0
	Normal	57	57.0
	Leukocytosis	12	12.0
Peripheral smear	Normocytic normochromic	52	52.0
	Microcytic hypochromic	31	31.0
	Mild thrombocytopenic picture	12	12.0
	Other abnormalities	5	5.0

Most children had a normal TLC (57%). The commonest peripheral smear pattern was normocytic normochromic morphology (52%).

Table 9: Liver function test parameters

Biochemical parameter	Mean ± SD
Total bilirubin (mg/dL)	1.12 ± 0.48
Direct bilirubin (mg/dL)	0.38 ± 0.19
AST (U/L)	58.4 ± 31.6
ALT (U/L)	52.7 ± 27.9
Serum albumin (g/dL)	3.6 ± 0.5

Mild elevations of AST and ALT were observed among the study participants, while the mean serum albumin was 3.6 ± 0.5 g/dL.

Table 10: Association between hepatosplenomegaly and individual hematological abnormalities

Hematological abnormality	HSM present (n=28) n (%)	HSM absent (n=72) n (%)	p-value
Anemia	20 (71.4)	26 (36.1)	0.004
Leukopenia	15 (53.6)	16 (22.2)	0.006
Thrombocytopenia	15 (53.6)	19 (26.4)	0.012

Hepatosplenomegaly was significantly associated with anemia, leukopenia and thrombocytopenia.

Table 11. Comparison of hematological parameters according to hepatosplenomegaly

Parameter	HSM present (n=28)	HSM absent (n=72)	p-value
Hemoglobin (g/dL)	9.9 ± 1.3	11.1 ± 1.4	<0.001
TLC (cells/mm³)	4,980 ± 1,720	6,285 ± 2,180	0.003
Platelet count (×10³/μL)	139 ± 52	179 ± 61	0.002
MCV (fL)	77.4 ± 7.1	79.1 ± 6.8	0.267

Children with hepatosplenomegaly had significantly lower mean hemoglobin, TLC and platelet counts compared with those without hepatosplenomegaly. The difference in MCV was not statistically significant.

Table 12: Association between degree of organomegaly and hematological abnormalities

Clinical group	n	Anemia n (%)	Leukopenia n (%)	Thrombocytopenia n (%)
No organomegaly	42	12 (28.6)	8 (19.0)	9 (21.4)
Hepatomegaly alone	18	8 (44.4)	5 (27.8)	6 (33.3)
Splenomegaly alone	12	6 (50.0)	4 (33.3)	4 (33.3)
Hepatosplenomegaly	28	20 (71.4)	15 (53.6)	15 (53.6)

A progressive increase in the frequency of anemia, leukopenia and thrombocytopenia was observed across the organomegaly categories, with the highest frequency among children with hepatosplenomegaly.

Discussion

The present study evaluated the association between hepatosplenomegaly and hematological abnormalities among 100 children with typhoid fever. The study demonstrated that hepatosplenomegaly was present in 28% of children and that hematological abnormalities were common. Anemia was the most frequent abnormality, followed by thrombocytopenia and leukopenia. Importantly, children with hepatosplenomegaly had significantly lower hemoglobin, total leukocyte and platelet counts compared with children without hepatosplenomegaly.

In the present study, fever was observed in all participants, while abdominal pain, weakness or fatigue, loss of appetite, diarrhoea and vomiting were among the commonly reported associated symptoms. This clinical pattern is consistent with the recognized presentation of enteric fever in children, in which prolonged fever is frequently accompanied by gastrointestinal and constitutional

symptoms [2,4]. Similar clinical manifestations have been reported in previous pediatric studies from endemic regions [6,7].

Nearly half of the children in the present study had fever for 8–14 days, while 23% had fever lasting more than two weeks. The relatively prolonged duration of illness may reflect delayed presentation, prior treatment or progression of systemic infection. Prolonged disease may increase the likelihood of systemic manifestations and complications of enteric fever [1,3].

Hepatosplenic involvement was an important finding in the present study. Hepatomegaly alone was observed in 18% of children, splenomegaly alone in 12%, while hepatosplenomegaly was present in 28%. Thus, 58% of children had some form of hepatosplenic involvement. Hepatomegaly and splenomegaly are recognized manifestations of typhoid fever and are related to involvement of the reticuloendothelial system during systemic infection [3,6]. Previous pediatric studies have also reported variable frequencies of hepatomegaly and splenomegaly among children with enteric fever [6,7].

The frequency of organomegaly may differ between studies because of variations in age distribution, duration of illness, disease severity, prior antimicrobial treatment and methods used for clinical assessment. In addition, physical examination may have variable sensitivity for detecting mild organ enlargement. Nevertheless, the relatively high frequency of hepatosplenic involvement in the present study emphasizes the systemic nature of typhoid fever.

Anemia was the most common hematological abnormality in the present study and was observed in 46% of children. Among affected children, mild anemia accounted for the majority of cases. Anemia has previously been described as a frequent hematological finding in pediatric enteric fever [4,7]. The development of anemia may be multifactorial and can be related to inflammatory changes, nutritional deficiencies, altered erythropoiesis, hemolysis and bone marrow involvement during systemic infection [8,9].

Thrombocytopenia was observed in 34% of the study participants. Most cases were mild, whereas moderate and severe thrombocytopenia were less frequent. Thrombocytopenia is a recognized hematological manifestation of systemic *Salmonella* infection and may occur because of impaired platelet production, increased peripheral destruction, consumption during systemic inflammation or splenic sequestration [8,9]. The presence of thrombocytopenia may therefore indicate significant systemic involvement in affected children.

Leukopenia was observed in 31% of children, whereas leukocytosis was present in 12%. Leukopenia has traditionally been considered an important hematological feature of typhoid fever, although both normal and increased leukocyte counts may occur, particularly in children [4,7]. Variations in leukocyte counts may depend on the stage of illness, disease severity, age and individual host response.

The most important finding of the present study was the significant association between hepatosplenomegaly and hematological abnormalities. Anemia was present in 71.4% of children with hepatosplenomegaly compared with 36.1% of children without hepatosplenomegaly. Similarly, leukopenia occurred in 53.6% versus 22.2%, while thrombocytopenia occurred in 53.6% versus 26.4%, respectively. These differences were statistically significant.

The comparison of mean hematological parameters further supported these findings. Children with hepatosplenomegaly had significantly lower mean hemoglobin concentration than those without hepatosplenomegaly. The mean total leukocyte count and platelet count were also significantly lower in the hepatosplenomegaly group. In contrast, the difference in mean corpuscular volume was not statistically significant. These findings suggest that hepatosplenomegaly is associated particularly with abnormalities involving hemoglobin, leukocytes and platelets rather than with a major alteration in red cell size.

The association between hepatosplenomegaly and cytopenias may be explained by the systemic pathophysiology of typhoid fever. *Salmonella Typhi* can disseminate beyond the intestinal tract and involve the reticuloendothelial system, including the liver, spleen and bone marrow [3,8]. Increased splenic activity may contribute to sequestration or destruction of circulating blood cells, while infection-associated inflammatory responses and bone marrow involvement may influence blood cell production [8,9]. These mechanisms may collectively explain the lower hemoglobin, leukocyte and platelet counts observed among children with hepatosplenomegaly.

A progressive increase in the frequency of hematological abnormalities was observed across the different organomegaly categories. The frequency of anemia increased from 28.6% among children without organomegaly to 44.4% among those with hepatomegaly alone, 50.0% among those with splenomegaly alone and 71.4% among children with hepatosplenomegaly.

A similar pattern was observed for leukopenia and thrombocytopenia. This progressive trend suggests that simultaneous involvement of both the liver and

spleen may be associated with greater hematological involvement.

The findings are clinically relevant because hepatosplenomegaly can be detected during routine pediatric examination. Its presence in a child with typhoid fever may alert clinicians to the possibility of associated cytopenias and may justify closer monitoring of complete blood count parameters. In particular, children with hepatosplenomegaly may require careful assessment of hemoglobin, leukocyte and platelet counts during the course of illness.

Mild elevations of AST and ALT were observed in the present study. Hepatic involvement is recognized in enteric fever and may range from mild biochemical abnormalities to clinically significant hepatic dysfunction [3,10]. The presence of hepatomegaly together with elevated transaminases may therefore represent hepatic involvement as part of the systemic disease process.

Blood culture was positive in 54% of children in the present study, while the remaining cases were supported by serological or other laboratory investigations along with compatible clinical findings. Blood culture remains an important method for microbiological confirmation of typhoid fever, although its sensitivity may be reduced by prior antimicrobial treatment, timing of specimen collection and bacterial load [5,11]. Therefore, culture-negative cases should be interpreted in the context of clinical findings and other available investigations.

The findings of the present study have potential implications for pediatric clinical practice. Hepatosplenomegaly may serve as a readily identifiable clinical marker associated with a higher frequency of anemia, leukopenia and thrombocytopenia. Early recognition of this association may help clinicians identify children who require closer hematological monitoring and evaluation for systemic involvement.

The present study has certain limitations. It was a hospital-based observational study with a sample size of 100 children, which may limit the generalizability of the findings. Clinical assessment of hepatomegaly and splenomegaly may be subject to inter-observer variation. Not all patients were microbiologically confirmed by blood culture, and prior antibiotic treatment may have influenced culture positivity. In addition, the observational design does not establish a definite causal relationship between hepatosplenomegaly and hematological abnormalities. Larger prospective multicentric studies using standardized clinical or ultrasonographic assessment and uniform microbiological confirmation would help clarify these associations.

Overall, the present study demonstrates a significant association between hepatosplenomegaly and hematological abnormalities in children with typhoid fever. Children with hepatosplenomegaly showed higher frequencies of anemia, leukopenia and thrombocytopenia, together with significantly lower mean hemoglobin, total leukocyte and platelet counts. These findings suggest that hepatosplenomegaly may be a useful clinical indicator of increased hematological involvement in pediatric typhoid fever.

Conclusion

Hepatosplenomegaly was significantly associated with anemia, leukopenia and thrombocytopenia in children with typhoid fever. Children with hepatosplenomegaly had significantly lower hemoglobin, total leukocyte and platelet counts. Thus, hepatosplenomegaly may serve as a useful clinical indicator of increased hematological involvement in pediatric typhoid fever and may warrant closer hematological monitoring.

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