

# Hematological Changes in Patients Presenting with Typhoid Fever

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## ABSTRACT

**Objective:** To study hematological changes in typhoid fever.

**Study Design:** Observational study

**Place and Duration of Study:** This study was conducted at the pathology department of Bacha Khan Medical College Mardan and Medical Department of Mardan Medical Complex Teaching Hospital Mardan from June, 2015 to February, 2016.

**Materials and Methods:** This study included total of 100 patients of typhoid fever and 50 as a control healthy individuals. Typhoid positive serum was taken as that with visible agglutination at 1:320. To exclude false positive we used rising titer for widal test. These patients were also Typhidot positive and were having step ladder rising of fever. Complete blood counts were performed by hematology analyzer an automated machine (Sismex Japan)

**Results:** In the present study 40% had anemia, Hemoglobin level was  $9.1 \pm 0.879$  g/dl, 20% had thrombocytopenia, platelet count was  $120 \pm 17.897 \times 10^3/\text{ul}$ , 30% had leucopenia, total leucocyte count was  $2.8 \pm 1.557 \times 10^3/\text{ul}$  and 6% patients showed leucocytosis, total leucocyte count was  $14.5 \pm 1.875 \times 10^3/\text{ul}$ . Hemoglobin, white blood cell and platelet count were significantly lowered as compared to control group.

**Conclusion:** The study concluded that hematological abnormalities are significant findings in typhoid fever. Any patient presenting with cytopeneia should be strictly screened for Typhoid fever to avoid unnecessary use of bone marrow aspiration. Moreover full blood counts should be performed on these patients as this gives useful information to the clinician for effective and prompt treatment. Due to high morbidity and mortality in misdiagnosed cases further research work and new diagnostic tests are recommended for diagnosis of the disease

**Key Words:** Anemia, Typhoid fever, Thrombocytopenia, Leucopenia.

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## INTRODUCTION

Typhoid fever is a systemic bacterial infection, caused by salmonella typhi. It develops following ingestion of food or water that is contaminated with the organism and this human pathogen has the ability to survive for several months in soil and water<sup>1</sup>. Typhoid fever constitutes a major public health problem in many developing countries but mortality has been reported from developed countries as well. It has involved 12.6 million cases worldwide and estimated 60,000 deaths annually<sup>2</sup>. It is higher among children however mortality due to enteric fever depends on time taken to diagnose and immediate treatment.

Mortality is 1% if treatment is started before onset of complications and up to 15% if treatment is started after onset of complications<sup>3</sup>. Salmonella typhi infection also

presents as fever of unknown origin<sup>4</sup>. Once untreated typhoid fever is associated with a lot of complications which include intestinal perforation in the distal ileum, septicemia, peritonitis, encephalitis, metastatic abscess, cholecystitis, endocarditis, osteomyelitis and rash<sup>5</sup>. Typhoid fever is also associated with biochemical changes<sup>6</sup>. It is also associated with hematological abnormalities, hepatic dysfunction and high frequency of extrahepatic complications, but these changes are transient and respond well to appropriate antimicrobial therapy<sup>7</sup>. Alteration in hematological parameters include anemia and decrease in platelets and total leucocyte count and reduction in neutrophil and eosinophils. Typhoid fever may be a cause of pancytopenia and is associated with depressed erythropoiesis, myelopoiesis, thrombopoiesis<sup>8</sup>. Sometime typhoid fever presents with atypical manifestations, like burning micturition, diarrhea, isolated hepatomegaly and bone marrow depression which usually occurs in 1<sup>st</sup> week of infection and these cases are multi drug resistant (MDR) which results in high mortality and morbidity<sup>9</sup>. The aim of this study is to evaluate hematological changes in typhoid fever. Typhoid fever is a major public health problem in developing countries including Pakistan, because of poor hygienic measures and dense population; people are at high risk of contracting the diseases. As typhoid fever is associated with hematological and non-hematological complications, so any patient presenting

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with hematological abnormalities, typhoid fever should be kept in mind and proper diagnosis should be done for prompt and immediate treatment to reduce their complications and to avoid unnecessary use of bone marrow aspiration.

## MATERIALS AND METHODS

This study was conducted in the pathology and medical departments of Bacha Khan Medical College and Mardan Medical Complex Teaching Hospital Mardan from June, 2015 to February, 2016.

A total of 100 patients were included in the study. They were positive for typhoid fever diagnosed by Widal test, Typhidot test and on the basis of their clinical presentation, 50 patients were taken as a control group. Typhoid positive serum was taken as that with visible agglutination at 1:320. To exclude false positive we used rising titer for widal test. These patients were also Typhidot positive and were having step ladder rising of fever. Patients having temperature due to malaria, sore throat, chest or urinary tract infection were excluded from the study.

Hemoglobin less than 10g/dl was considered as anemia, platelet count less than  $150 \times 10^3/\text{ul}$  and total leucocyte less than  $3 \times 10^3/\text{ul}$  were defined for thrombocytopenia and leucopenia respectively. Temperature of  $101^\circ\text{F}$  was defined for fever.

Complete blood counts were performed on all these patients by hematology analyzer (Sismex Japan) for which 3ml blood was collected in a tube containing 1.8ml EDTA. All the samples were processed by hematology analyzer for determination of Hemoglobin level, platelets and total leucocyte counts.

All the data was statistically analyzed by using T. Test and chi-square test. Level of significance was set at  $P < .001$ .

## RESULTS

A total of 100 patients of typhoid fever were included in the study and 50 as control healthy individuals.

Complete blood counts were performed on the samples of these individuals for determination of Hemoglobin level, Platelets counts and total leucocyte counts. Forty out of 100 patients (40%) had anemia. Hemoglobin level was  $9.10 \pm 0.879$  g/dl which was significantly lower than the control groups. Twenty out of 100 patients (20%) had thrombocytopenia, platelet count was  $120 \pm 17.897 \times 10^3/\text{ul}$  significantly lower than the control group. Thirty out of 100 patients (30%) had leucopenia, total leucocyte count was  $2.8 \pm 1.507 \times 10^3/\text{ul}$  and 6 out of 100 (6%) patients had leucocytosis.

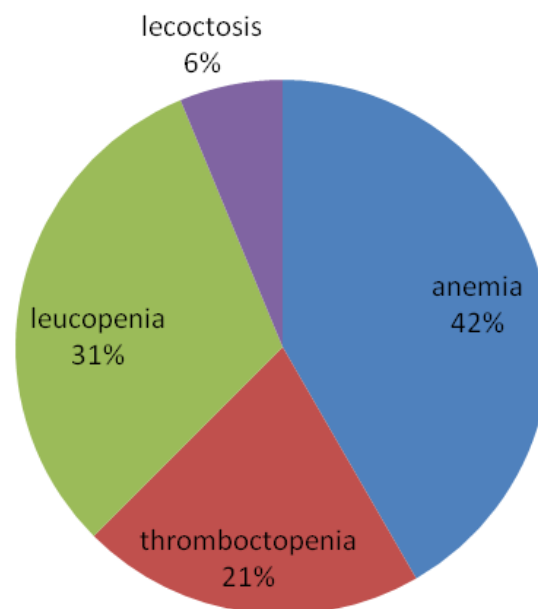
The present study showed that hematological changes are significant findings in typhoid fever and values are significantly lower as compared to control group, pvalue for Hemoglobin, platelet counts and total leucocyte count is  $P < .004$ ,  $P < .0032$ , and  $P < .0035$  respectively.

**Table No.1: Frequency of Hematological Changes in Typhoid fever**

| S.No. |                  |     |
|-------|------------------|-----|
| 1     | Anemia           | 40% |
| 2     | Thrombocytopenia | 20% |
| 3     | Leucopenia       | 30% |
| 4     | Leucocytosis     | 6%  |

**Table No.2: Mean value of Hematological parameters in typhoid fever as compared to control group**

| S.No.            | Mean value of hematological parameter in typhoid fever | Mean value of control group              |
|------------------|--------------------------------------------------------|------------------------------------------|
| Hemoglobin Level | $9.19 \pm 0.879$ g/dl                                  | $12.99 \pm 0.468$ g/dl                   |
| Platelet counts  | $120 \pm 17.578 \times 10^3/\text{ul}$                 | $450 \pm 20.678 \times 10^3/\text{ul}$   |
| Leucopenia       | $2.8 \pm 1.56, \times 10^3/\text{ul}$                  | $5.6 \pm (1.3568 \times 10^3)/\text{ul}$ |
| Leucocytosis     | $14 \pm 1.54 \times 10^3/\text{ul}$                    | $10 \pm 0.567 \times 10^3/\text{ul}$     |



**Figure No.1: Frequency of Hematological Changes in Typhoid fever.**

## DISCUSSION

Typhoid fever is a systemic bacterial infection caused by salmonella typhi (gram negative rods). Infection is usually acquired through the ingestion of contaminated food or water. It is a major public health problem in the developing countries including Pakistan.

Typhoid fever presents with a lot of clinicopathological profile. It may present as fever of unknown origin (FUO)<sup>10</sup>. Clinical features include fever, headache, fatigue, joint pain, splenomegaly, intestinal inflammation and perforation, peritonitis, septicemia and hematological changes<sup>11</sup>.

In the present study 40% patients showed anemia, 20% patients had thrombocytopenia and 30% showed leucopenia. A similar study has been conducted by Lolkchandwala which reported that typhoid fever is associated with anemia, thrombocytopenia and leucopenia<sup>12</sup>. Another study conducted on 42 typhoid patients by Ifeanyi revealed that typhoid fever is associated with significant findings of leucopenia, anemia and thrombocytopenia which shows similar correlation with our study<sup>5</sup>. Another study was conducted by Abro et al on 75 typhoid patients in which 61% patients showed anemia 40% patients showed thrombocytopenia, 10% had leucocytosis and 4% had leucopenia<sup>2</sup>. All these studies showed that typhoid fever is associated with significant hematological changes but all these hematological changes are transient and improve with antimicrobial therapy. Poor disposal of human excreta, poorly equipped latrine, poor hand washing habit and untreated water and poor hygienic conditions are the main causes of transmission of typhoid fever<sup>13</sup>. Endotoxin LPS of the salmonella typhi play important role in pathogenesis of liver injury and other complications<sup>14</sup>. Hematological changes are common in typhoid fever. Bone marrow suppression and hemophagocytosis are possible mechanisms responsible for hematological changes<sup>15</sup>. Microangiopathic hemolytic processes are also involved in the pathogenesis of anemia<sup>16</sup>. It is also suggested that leucopenia (neutropenia) has been caused by increased margination and defective granulopoiesis<sup>17</sup>. The reduction in WBC occurs as a fall in neutrophils and eosinophils counts. Eosinophil count starts declining from six days onwards and eosinopenia has diagnostic value as well<sup>18</sup>. The underlying cause of eosinopenia in typhoid fever is unclear but principally in healthy individual eosinophils reside at mucosal surfaces including gut mucosa<sup>19</sup>. It is possible that increased margination of these cells during infection account for marked decrease in eosinophils in typhoid fever<sup>20</sup>. Some degree of eosinopenia is present in all enteric fever patients<sup>12</sup>. Leucocytosis also occurs in typhoid fever. In our study 6% patients showed leucocytosis. The same has been reported by Abro et al<sup>2</sup>.

## CONCLUSION

The study concluded that typhoid fever is associated with significant hematological changes; therefore full blood counts should be done immediately and could be useful in the diagnosis of typhoid fever. It provides useful information to the clinicians for effective and prompt treatment and diagnosis of typhoid fever. Moreover as the disease cause high morbidity and mortality if untreated or misdiagnosed, further research work is recommended for new reliable diagnostic tests for early diagnosis of the disease.

As typhoid positive patients present with significant hematological changes so any patient presenting with

cytopenia should be strictly screened for typhoid fever to avoid unnecessary use of bone marrow aspiration.

### Author's Contribution:

|                            |                                    |
|----------------------------|------------------------------------|
| Concept & Design of Study: | Dr. Naveed Khan                    |
| Drafting:                  | Dr. Naveed Khan & Dr. Hameed Ullah |
| Data Analysis:             | Dr. Subhan Uddin & Dr. Manzoor     |
| Revisiting Critically:     | Dr. Subhan Uddin & Dr. Manzoor     |
| Final Approval of version: | Dr. Naveed Khan                    |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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