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FREQUENCY OF BIOCHEMICAL AND HEMATOLOGICAL CHANGES OCCURRING IN CHILDREN WITH TYPHOID FEVER

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Abstract:
Objective: *In typhoid fever biochemical and Hematological changes due to multi-organ involvement are very common. The purpose of this analysis was to evaluate the severity and frequency of the changes in children due to typhoid fever admitted in the hospital.*
Study Design: *A hospital based descriptive study.*
Place and Duration: *In the Pediatric Department of People's Medical College Hospital, Nawabshah for one year duration from April 2016 to April 2017.*
Methodology: *The study included clinical information, demographic data, biochemical and hematological changes noted in each children selected for study. Children with positive Salmonella typhi culture in the blood were selected for the study. The complete liver function tests, blood count, urea, blood cultures, malaria parasites, coagulation profile and electrolytes for all patients have been performed. Children with obvious hematological changes in bone marrow examination, whereas patients with normal ALT were tested for hepatitis serology (A, B and C).*
Results: *75 children total with typhoid fever were included in the study. The average age ± standard deviation of the children included in the study was 10.2 ± 4.7 years and the males were 81.3% and females were 17.96%. The most common blood variations noted in investigations; thrombocytopenia (40%), anemia (61.3%), leukopenia (4%) and leukocytosis (10.6%). However, among biochemical changes; elevated AST (62.7%), ALT (73.3%), alkaline phosphatase (44%), bilirubin (30.6%), blood urea (12%) and prothrombin time (57.3) but found that albumin was lower than 40% . Children with elevated ALT had a high incidence of thrombocytopenia (p <0.03), alkaline phosphatase (p <0.02), increased serum bilirubin (p <0.04) and PT (p <0.05). Serum ALT serum bilirubin was 3 mg / dl 10.3%> and the duration of prothrombin was 3 seconds greater than 8% of patients who checked it, 8% was> 10 times higher than normal levels. After the biochemical and hematological changes returned to the normal range, all children were discharged in a healthy manner.*
Conclusion: *Typhoid fever causes significant hematological changes and also liver dysfunction. Liver involvement was linked with high frequency of extra-hepatic problems. Rather than high frequency and serious problems noted in blood and liver involvement, these changes are acute and appropriate antimicrobial therapy resolve these issues.*
Key words: *Hematology, Typhoid fever, changes, biochemistry.*

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INTRODUCTION:

Typhoid fever is a systemic bacterial infection caused by Salmonella Typhi, a gram negative rod. Usually Infection is transmitted by swallowing food contaminated with urine or by contaminated contaminants of water stool or flour. In many developing countries important public health problem is Typhoid fever around the world and is increasingly reported in countries who are fully developed. Children and young adults are mainly affected by Typhoid fever and is considered to be one of the leading causes of worldwide morbidity with more than 12.6 million cases Globally and approximately 6 million deaths per year. About 80% of cases occur in Asia. In the developing world, incidence is up to 1100 cases per one lac people were recorded. A wide range of presentations can be made from uncomplicated typhoid fever to complex complications involving multiple organs during enteric fever. Hematological disorders are common in patients with hepatic fever, while hepatic dysfunction has been reported to vary from 1% to 26% and0-6% of all patients. The purpose of this study was to know the severity and frequency of hematological changes, renal involvement and liver dysfunction in children with typhoid fever.

MATERIALS AND METHODS:

This hospital based descriptive study was held in the Pediatric Department of Peoples Medical College Hospital, Nawabshah for one year duration from April 2016 to April 2017. The study was designed to include demographic data (age, gender, and history), biochemical, and clinical information and blood changes observed in each child. The data is recorded in a separate structured format. In the past, patients were inquired about their past history of medical illness such as kidney diseases, liver diseases, blood diseases. When the typhoid fever was confirmed by a positive blood culture for Salmonella Typhi they were included in the study. During the presentation all patients (performed by Hitachi Machine 912), blood culture (3 samples), complete blood count (performed with Beckman Coulter automatic machine), malaria, coagulation profile, electrolytes, blood sugar random and urea. Children with biochemical and / or clinical features of liver involvement (ALT> 3 times the normal level) were exposed to serology of the viral hepatitis and ultrasonic images of the abdomen; Bone marrow evaluation was done only in patients with unresponsive severe hematological changes. For the treatment of typhoid fever standard protocols were adopted While waiting for sensitivity and culture results, empirical antimicrobial treatment with ceftriaxone at 75 mg / kg / day dose (up to 2 g / day) in two doses until interruption was initiated and continued for five days. At the end of this period or taking ciprofloxacin (200 mg IV / 250 mg BD oral), taking into account the possible sensitivity to antibiotics. Antimicrobial treatment was continued after the sensitivity and culture analysis was obtained. While the antimicrobial therapy was continue for two weeks in most of the patients and for three weeks complicated typhoid fever were treated. As the patients became asymptomatic, the patients were discharged after the biochemical and hematological changes returned to the normal range. Data were analyzed by SAS Enterprise Guide 4.1. P <0.04 was considered static for the variation in all statistical analyzes.

RESULTS:

A total of 75 children were included in the study with typhoid fever. The patients included in the study had a mean SD of 10 ± 4.7 years (10-14 years) and boys (most of the children studied were attending school). There was no major variation in age between the two groups. The past journeys to endemic areas were positive in 42% of patients. The duration of the disease was 4 to 28 days before the children went to the pediatric department of the hospital. Headache, Fever, abdominal pain, vomiting, loss of appetite, general body pain, diarrhea, weight loss, dry cough following main symptoms, constipation, altered sensation, yellowing of the urine and eyes. Fever, toxic and diseased appearance, anemia, relative bradycardia, hepatomegaly, abdominal pain, jaundice and splenomegaly were the main clinical symptoms. Main blood disorders; thrombocytopenia, hemoglobin, leukocytosis and leukopenia reduction (Table-I).

Table-I: Frequency of Hematological changes observed in Typhoid fever.

Parameter	*No of Pts. (%)*
WBC count (Mean ± SD:7.12+3.69x10^3/ul) (Range:1.5-28.8x10^3/ul).	
Normal WBC	64(85.3)
Leucocytosis	8(10.6)
Leucopenia	3(4)
Differential (Absolute count)	
Normal Neutrophils	63(84)
Neutrophilia	9(12)
Neutropenia	3(4)
Normal eosinophils	75(100)
Hemoglobin (Mean ± SD: 12.33±1.78 gm/dl) (Range: 5-15.4 gm/dl).	
Normal Hb	29(38.6)
Anemia	46(61.3)
Platelet count (Mean ± SD:288.93±146.76x10^3/ul) (Range: 11-734x10^3/ul).	
Normal platelets	45(60)
Thrombocytopenia	30(40)

Ref.range: WBC: 3.6-11x10^3 cell/ul, Hb: 13-18gm/dl, Platelets: 150-400x10^3 cell/ul.

ALT levels in 55 (73.3%), 28 (37.3%) were above the reference range 3 times in 6 (8%) children. Other important biochemical changes include; serum bilirubin, AST, prothrombin time, alkaline phosphatase, serum albumin level reduction and blood urea elevation given in(**Table II**).

Table-II: Frequency of biochemical changes observed in Typhoid fever.

Parameter	*No. of Pts.(%)*
ALT (Mean ± SD: 160.8+244.04 U/L) (Rnage: 12-1807 U/L).	
Normal ALT	20(26.6)
Raised ALT	55(73.3)
AST (Mean ± SD: 126.64+161.72 U/L) (Range: 10-889 U/L).	
Normal AST	28(37.3)
Raised ALT	47(62.7)
Bilirubin (Mean ± SD: 1.8+4.04 mg/dl) (Range: 0.2-31.8 mg/dl).	
Normal bilirubin	52(69.3)
Raised bilirubin	23(30.6)
Albumin (Mean ± SD: 3.46+0.55 gm/dl) (Range:1.7-4.8gm/dl).	
Normal Albumin	45(60)
Decreased Albumin	30(40)
Alk. Phosphatase (Mean ± SD: 125.28+123.17 U/L) (Range: 48-934 U/L).	
Normal Alk.Phosphatase	42(56)
Raised Alk.Phosphatase	33(44)
Prothrombin Time (Mean ± SD: 14.73+1.95 sec) (Range: 11.7-25.9sec).	
Normal PT	32(42.6)
Raised PT	43(57.3)
Blood Urea (Mean ± SD: 25.21+13.53 mg/dl) (Range: 7-67 mg/dl).	
Normal B.Urea	64(84.3)
Raised B.Urea	9(12)

Ref.range: ALT: 0-41U/L, Alk.Phos: 40-129 U/L, T.Bil: 0-1mg/dl, Alb.: 3.4-4.8gm/dl, AST: 0-38 U/L, B.Urea: 12-40 mg/dl.

The bilirubin level in the serum was> 3 mg / dl in 9 (> 11.06%) patients. High levels of thrombocytopenia, anemia, elevated serum biirubin, prothrombin time and alkaline phosphatase in patients with elevated ALT levels are shown in Table-III.

Table-III: Associated hematological and biochemical changes in patients with typhoid fever who had normal or raised ALT

Parameter	*Pts. With normal ALT*	*Pts. With raised ALT*	*p value*
Hemoglobin	12.3±2.1gm/dl	12.3±1.6gm/dl	0.9
WBC	8.5±5.6x103/UL	6.6±2.5x103/UL	0.1
Platelets	290.0±167.4x103/UL	206.7±131.0x103/UL	0.04
T. Bilirubin	0.7±0.6mg/dl	2.1±4.6mg/dl	0.02
Al.Phosph.	112.5±59.3U/L	166.7±136.1U/L	0.01
Proth.Time	14.12±1.2 Sec	14.9±2.1 Sec	0.04
Blood Urea	27.7±13.2mg/dl	24.2±13.4mg/dl	0.3

The most common findings in ultrasonography were hepatomegaly and splenomegaly. In addition to supportive therapy, all patients were given intravenous antibiotics at admission. The average stay in hospital was 11.01 ± 4.01

days (7-24 days). Patients with complicated typhoid fever had longer hospital stay in patients with liver dysfunction than controlled patients, p <0.03. The serial evaluation of the biochemical, hematological and physical examination parameters showed a normal return to the normal level after the recovery of the acute disease in all cases. All patients were discharged after normal physical health achievement.

DISCUSSION:

The pathophysiology of typhoid fever is a complex process that develops in several stages. The disease incubation period is 7 to 14 days and mostly asymptomatic; in which reticuloendothelial system have macrophages. In 1st week of typhoid fever symptoms occurs as there is a gradually increase in temperature followed by bacteremia. In 2nd week there were pink spots, splenomegaly and abdominal pain. In third week chances of complications were high and associated with severe inflammatory bowel response with associated necrosis, which can lead to hemorrhage and perforation. They defined the most serious digestive hemorrhage, perforation and encephalopathy among the other complications in 10-15% of cases of bleeding through circumcision. In these case series, anemia was found in 61.3% of the patients, 14 (77.8%) in 13 (77.8%) of Ahmed et al. (38%) and Alamoolinejad et al. (79.4%). According to previous reports, most patients had normal white blood cells. Leukopenia is said to have a general blood changes in typhoid fever. In this analysis, leukopenia was present in 5%, leukopenia in 18%. In 40% of the cases Thrombocytopenia was noted, with a greater number than that reported by other researchers (11% and 10%). In this case series, there was no intravascular coagulopathy evidence and not spreading in any patient; this was an observation supported by previous work. While previous investigators reported eosinophilia in the case of thyroid fever, the number of eosinophils in this study was within the reference range. In our study, jaundice and fever were the main symptom in 11.06% of the cases. In typhoid fever Liver involvement is usually linked with extra-hepatic problems and we have the same results. Clinically obvious kidney disease in typhoid fever is a rare event and the renal complications spectrum includes mild to severe glumerulonepheritis and ARF. In this series of cases, the blood urea level was slightly elevated, and no patient experienced remarkable renal failure except hydration and typhoid fever and return to nine patient reference ranges.

CONCLUSION:

In conclusion it is observed typhoid fever causes major hematological variations as well as impaired liver function. Liver involvement was linked with high rates of extrahepatic complications in children. Despite the high frequency and severe liver involvement and hematological changes, these changes are temporary and respond adequately to appropriate antimicrobial therapy. In addition, the kidneys are less commonly involved and usually special treatment was not required.

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