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Research Article

STUDY TO KNOW THE INCIDENCE AND SEVERITY OF LIVER DAMAGE IN PATIENTS OF TYPHOID FEVER

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ABSTRACT:

Objective: Liver involvement in typhoid fever is common. This study was conducted to determine the incidence and severity of liver damage in patients presenting with typhoid fever.

Study Design: An Observational Study.

Place and Duration: In the Gastroenterology department of Services Hospital Lahore for one year duration from June 2017 to June 2018.

Methods: Only patients with positive blood culture for *Salmonella Typhi* were selected for the study. Liver function tests and complete blood count were performed for all patients with liver function test disorder, viral hepatitis profile and ultrasound as an abdominal cyst.

Results: A total of 52 patients met the inclusion criteria, including hepatic manifestation in 10% of cases, jaundice (13.4%), hepatomegaly (51.9%), high serum alanine aminotransferase levels (85%) more than 10 times the normal value, aspartate aminotransferase (75%), prothrombin time (53.8%). In 15.4% the PT was 3 seconds greater than the reference value, from alkaline phosphatase (44%) and from serum bilirubin (25%); Decreased serum albumin levels (38%). Other symptoms were splenomegaly (36.5%), anemia (55.7%), leukopenia (6%) and thrombocytopenia (44%). The mean hospital stay was 11.5 + 4.3 days. All patients were discharged healthy.

Conclusion: In the presence of high-grade fever, tender hepatomegaly and jaundice, patients who have traveled from tropical countries or have recently had a high frequency of high typhoid fever should induce a suspected clinical diagnosis of enteric fever. In these cases, liver dysfunction is transient, despite its high incidence and severe nature, and responds favorably to appropriate antibiotic therapy.

Key words: typhoid fever, liver dysfunction.

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INTRODUCTION:

Typhoid fever (enteric fever) is an acute febrile disorder, a major public health problem in many developing countries of the world¹⁻³. It has been reported that this disease is also increasing in developed countries. According to a report from the Center for Disease Control and Prevention, each year there are 21.6 million typhoid cases each year, from 100 to 1000 cases per 100,000 people and 600,000 deaths per year⁴⁻⁶. The disease mainly affects children and young adults. During enteric fever, a variety of organs can be involved, from uncomplicated typhoid fever to a complex variety, including multiple organs⁷. The liver is often involved in typhoid fever, and most patients have a lower aminotransferase elevation without jaundice. However, in a small number of patients, the characteristics cannot be distinguished clinically and biochemically from other causes of hepatitis. Typhoid fever-related hepatitis is not only associated with life-threatening extrahepatic complications, but also a higher recurrence rate in patients with liver failure⁸. This study was conducted to determine the severity and incidence of liver dysfunction in typhoid disease.

MATERIALS AND METHODS:

This Observational Study was held in the Gastroenterology department of Services Hospital Lahore for one year duration from June 2017 to June 2018. The study was designed to include demographic data (age, gender, nationality, and travel history), clinical information, and biochemical changes observed in patients. Patients were questioned about past medical jaundice history, medication and travel abroad. For the study, patients with positive blood culture for S.Typhi were enrolled, while patients with chronic liver disease, immune suppressed (HIV / drugs), positive viral hepatitis

profile, recent hepatotoxic drug consumption and active alcohol consumption were recorded. Patients with positive blood culture for S. paratyphi were excluded from the study. Liver function test (LFT) performed by Hitachi Machine 912, complete blood count (CBC), clotting profile, blood culture (3 samples) performed by automatic Beckman Coulter machine were taken from all patients. Viral hepatitis and abdominal ultrasound profile for patients with clinical and / or biochemical evidence of liver dysfunction. The treatment was performed in accordance with standard guidelines for the treatment of typhoid disease and antibiotics (mostly ceftriaxone and ciprofloxacin) and supportive therapy were included. Antibiotic treatment was initiated with the clinical diagnosis of typhoid disease and the possible susceptibility to drugs and treatment was continued after the sensitivity and culture report were obtained. Data were analyzed with SAS Enterprise 4.1 statistical package. P <0.05 was considered significant for all statistical analyzes.

RESULTS:

A total of 52 patients met the inclusion criteria. In general, the mean age of study patients was + SD 27.4 + 7.89 years (14-45 years) and men found women to be superior to 45 (87%) and 7 (13%). There was no significant difference between women and men in terms of age, most of the patients participating in the study were workers in construction companies or agricultural areas, and the majority of travel history to endemic areas was positive. The duration of the patients was 3 to 14 days before going to the hospital and the emergency department of the hospital. Fever, headache, abdominal pain, yellow color change in eyes and urine were present in some patients.

Table.1. Clinical data of 52 patients with Typhoid fever.

Clinical parameter	No	%age
Males	45	87
Females	7	13
Symptoms		
Fever	52	100
Headache	49	94.2
Anorexia	46	88.4
Myalgia	41	78.8
Abdomen pain	36	69.2
Vomiting/Nausea	22	42.3
Diarrhea	8	15.5
Jaundice	5	9.6
Signs		
Fever	52	100
Abdom. Tenderness	36	69.2
Anemia	29	55.7
Hepatomegaly	27	51.9
Splenomegaly	19	36.5
Jaundice	7	13.4
Rose spots	1	1.9

The main clinical findings (Table-1) were toxic appearance and disease, fever, relative bradycardia, anemia, abdominal sensitivity, hepatomegaly, splenomegaly and jaundice. The liver function test showed a high bilirubin level in 13 patients (25%), of which 6 (12%) had bilirubin greater than 3 mg / dl. In general, alanine transaminase (ALT) was above the reference range in 44 (85%) patients, but more than 10 times the reference range in 5 (10%) patients. Alkaline phosphatase was observed in 23 (44%) patients, while prothrombin time was 28 (53.8%) and 8 (15.4%) patients had PT over three seconds of the reference interval. Serum albumin was lower in 20 patients (38%). Hematologic changes were 45 (87%) normal white blood cell count, 4 (8%) leukocytosis and 3 (6%) patients leukopenia. Low hemoglobin and low platelet count (thrombocytopenia) were observed in 29 (55.7%) and 23 (44%) patients, respectively (Table-2).

Table.2. Biochemical and hematological data of 52 patients with Typhoid fever.

Laboratory Parameters	Mean	Range	Normal	Increased	Decreased
ALT	204.4±362.7	18-1924	8(15%)	44(85%)	-
AST	136.8±201.5	13(25%)	39(75%)		-
Alk. Phosp	19.9±130.5	62-934	29(56%)	23(44%)	-
T. Bil	1.9±3.8	0.2-18	39(75%)	13(25%)	
P.T	14.7±2.1	11.7-25.9	24(46.2%)	28(53.8%)	-
Albumin	3.4±0.5	1.7-4.5	32(62%)	-	20(38%)
WBC	6.8±2.5x10 ³	1.5-12.8x10 ³	45(87%)	4(8%)	3(6%)
Hb	12.3±1.9	5-15.6	23(45%)	-	29(55%)
Plates	175.5±102.2x10 ³	11-561x10 ³	29(56%)	-	23(44%)

Ref. range: ALT-0-41U/L, Alk.Phos-40-129 U/L, T.Bil-0-1mg/dl, Alb.-3.4-4.8gm/dl, PT- 11-14 sec, WBC-3.6-11x10³ cell/ul, Hb-13-18gm/dl, Platelets 150-400x10³ cell/ul.

Abdominal ultrasonography revealed hepatomegaly in 27 patients (52%), splenomegaly in 19 patients (36.5%), and thickening of the gallbladder wall suggesting acute gallbladder stone cholecystitis in 3 patients (6%). Except for acute gallbladder cholecystitis and four patients who developed severe hematologic dyscrasias, the course of this disease remained uneventful and was managed jointly by infectious disease and surgery or hematological team. The mean hospital stay was 11.5 + 4.3 days (6-22 days). The serial evaluation of the biochemical and hematological parameters of the physical examination returned to the normal level in all cases after the recovery of the acute disease.

DISCUSSION:

The incidence of complications in typhoid fever is reported to be variable. Parry MC *et al*. Complications were observed in 10-15% of patients with the most severe GI bleeding, perforation and typhoid encephalopathy reported by Van den Bergh *et al* in children 13 percent to 38 percent⁹⁻¹⁰. Choo *et al*. Have reported the most common complications in typhoid disease caused by hepatitis, bone marrow suppression, paralytic ileus, myocarditis, psychosis and cholecystis¹¹. Asymptomatic hepatitis is common in typhoid fever and most patients have lower AST and ALT elevations. Although the pathogenesis of hepatitis remains unclear, it may occur with various mechanisms, including non-specific reactive inflammation, in response to hepatic injury, local or systemic effects of endotoxin, or ulcerations in the intestine, in typhoid fever or *S. typhi* produced cytotoxin due to the effect of Kupffer cells have been infected¹². In peak fever, jaundice tends to occur at the peak different from viral hepatitis, in which case

fever usually occurs after the onset of jaundice. When jaundice occurs in typhoid fever, the most probable cause is hepatitis, collagenite, cholecystitis and hemolysis. Morgestrn *et al*. reported the incidence of jaundice in 9% of typhoid fever. In our study, the symptoms that occurred in 13.4% of the patients were fever and jaundice¹³. Hepatomegaly, probably due to hypertrophy and hyperplasia of Kupffer cells, is seen in enteric fever after the first week of the disease. In this case series hepatomegaly was observed in 51.9% of patients. Patients were compared with 26% and 20% reported by Mirsadraee *et al*¹⁶ and Bhutta ZA¹⁷ respectively. Abnormal AST and ALT are indicative of a hepatocyte disorder in combination; many researchers have used these enzymes to evaluate liver involvement during typhoid fever. Van den Bergh *et al*. reported a 26% increase in the frequency of serum enzyme in 52% of Morgenstern *et al* and 52% in Mirsadraee *et al*¹⁴⁻¹⁵. In our study, abnormal TP and bilirubin levels simulating acute viral hepatitis in our study showed an increase of 5 times more than

normal levels in 5 patients. Hematological disorders are common in typhoid fever. Significant changes include anemia, leukopenia, eosinophilia, thrombocytopenia, and subclinical spreading intravascular coagulation. Suppression of bone marrow and hemophagocytosis is considered an important mechanism for hematological changes.

CONCLUSION:

In conclusion, recognition of typhoid hepatitis is important because it should be distinguished from other conditions such as viral hepatitis, malaria and amoeba disease. Patients with a history of recent travel to endemic areas or patients with tropical disease should be suspected of typhoid fever in the presence of high fever, jaundice and sensitive hepatomegaly. In these cases, liver dysfunction is transient, despite its high incidence and severe nature, and responds favorably to appropriate antibiotic therapy.

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