

# Typhoid Hepatitis

Pages with reference to book, From 317 To 318

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## Abstract

Typhoid Hepatitis is a rare presentation of typhoid fever, clinically suspected in patients with persistent fever hepatomegaly and jaundice and especially in cases where the liver function tests show predominantly conjugated hyperbilirubinemia, modest elevation of liver enzymes and negative serology for viral hepatitis. From January, 1989 to December, 1994, 476 cases were included in this study, 204 with typhoid fever admitted in JPMC Karachi and 272 in Civil Hospital, Quetta. Eleven percent cases had typhoid hepatitis. Nineteen (4%) cases were initially diagnosed as viral hepatitis and 33(7%) developed jaundice later on. As typhoid is prevalent in Pakistan and typhoid hepatitis is a challenging problem, accurate and simple methods are required for diagnosis in all febrile cases. It should particularly be considered as a differential diagnosis for cases with fever, jaundice and hepatomegaly (JPMA 45 :317, 1995).

## Introduction

Mild jaundice and hepatomegaly have been reported in typhoid fever, which has a worldwide distribution<sup>1</sup>. It is particularly prevalent in developing countries<sup>2</sup> due to lack of public health education and failure in communal hygiene<sup>3</sup>. It also becomes a challenging problem, when it presents atypically and jaundice, fever and hepatomegaly is one such presentation which masquerades as infective hepatitis<sup>4</sup>. This study reports prevalence of typhoid hepatitis in cases of typhoid fever.

## Patients and Methods

To determine the prevalence of typhoid hepatitis, all cases diagnosed primarily as typhoid fever and admitted to the Medical Unit of JPMC, Karachi and Civil Hospital, Quetta were included in the study. Pregnant females and patients taking drugs with known hepatotoxic side effects were excluded. Nineteen patients were diagnosed provisionally as hepatitis due to the presence of jaundice whereas 33 became distance at a later stage. A detailed physical examination was carried out Laboratory tests included a complete blood picture, urine analysis, blood urea, serum creatinine, blood smear for malarial parasite, Hepatitis B surface antigen and liver function tests: serology for hepatitis profile was performed when facilities were available. Blood and bone marrow cultures were done and widal test performed on admission and after 2 weeks. Liver biopsy was done in 12 cases only. Blood and bone marrow samples were collected simultaneously and aseptically. Five ml of blood drawn with a disposable syringe was dispensed into culture bottles containing 45 ml of brain heart infusion broth<sup>5</sup>. Similarly, bone marrow aspiration was done according to Keeling's method<sup>6</sup>. About 1 ml of bone marrow aspirate from the syringe was directly transferred to the culture bottle containing 25 ml of 'brain heart infusion broth', which was incubated at 37°C for seven days. In the intervening period, sub-cultures were made every 24 hours (up to 72 hours) on sheep blood agar, MacConkey's agar and Salmonella Shigella agar plates and then incubated at 37°C on the 7th day of incubation. Bacilli were further identified according to the standard techniques<sup>7</sup>. Antimicrobial sensitivity pattern of all the isolates was done by standard disc diffusion method<sup>5</sup>. The susceptibility or resistance was judged on the basis of measurement of zones of growth inhibition around individual discs.

## Results

A total of 476 cases were included in this study. Of these, 52 had typhoid hepatitis. Nineteen (4%) were initially diagnosed as viral hepatitis and 33 (7%) developed jaundice at a later stage. There were 31 males and 21 females with the maximum number of patients (13) being in the age group 10-20 years. Thirty-six subjects belonged to the poor socio-economic class. Most frequent symptoms were fever, headache, nausea, vomiting and abdominal discomfort. Main physical signs were fever, jaundice, tender hepatomegaly, splenomegaly, (41 cases) and toxemia. All patients had fever ranging between 100°F to 103°F. They developed moderate jaundice between 6-10 days. Laboratory investigations showed a raised ESR in 23 (44%) cases. No malarial parasite was reported in the blood smear and the serology for hepatitis was negative in all patients. Widal was positive in the 19 cases presenting as hepatitis giving a high suspicion of typhoid hepatitis. Blood culture was positive in 8 (42%) cases, while bone marrow culture was positive in all 19 cases. The remaining 33 cases presented as a febrile illness and developed jaundice and hepatomegaly at a later period. Bone marrow culture was positive in all cases, irrespective of duration of pyrexia, jaundice and hepatomegaly. The predominant abnormality in the liver function test was a conjugated hyperbilirubinemia. The values ranged between 2.3 and 7.0 mg% with a mean value of 3.82 mg%. Total serum bilirubin was more than 10 mg% in 5 patients with an overall mean value of 6.06 mg%. SGPT levels varied between 43.9 to 160 U/L (mean 91.44 U/L). The alkaline phosphatase was between 76.2 and 180 U/L (mean 14.78 U/L). Liver biopsy was done in 12 cases. All showed intact lobular architecture and swollen hepatocytes with dilatation of sinusoids, which were lined by plump hyperplastic Kupffer cells. Three biopsies done in the acute stage, showed mild mononuclear cell infiltration in the portal triad and the sinusoids contained a large number of mononuclear cells. Three specimens showed moderate fatty infiltration of hepatocytes with some areas of liver necrosis. All cultures were reported sensitive to ofloxacin and ciprofloxacin which gave a 100% cure rate. There was no mortality.

## Discussion

Fever, jaundice and hepatomegaly is a common triad seen in medical outpatients in tropical countries like Pakistan<sup>8,9</sup>. The age in this study ranged from 10-70 years and fifty percent of cases occurred in persons less than 35 years of age which has been reported by other workers also<sup>10</sup>. Typhoid hepatitis was more common in males as compared to the females in a proportion of about 3:2. The initial clinical diagnosis of typhoid hepatitis is largely dependent on a high index of suspicion. The confirmation of the diagnosis of typhoid hepatitis still depends on laboratory investigations in most of the cases<sup>11</sup>. In countries like Pakistan, where febrile illness with jaundice are commonly encountered, it is vital, to carefully differentiate between viral hepatitis, malarial hepatitis and typhoid hepatitis. As the treatment for viral hepatitis is only supportive, for the other two conditions, the treatment has to be prompt and specific.

In this study all 19 (4%) cases presenting with fever, jaundice and hepatomegaly were initially thought to have viral hepatitis. However, the history of pyrexia ranging between 100°F to 103°F and appearance of moderate jaundice between 6 to 10 days gave a suspicion of typhoid hepatitis. This was supported by abnormal LFT's and positive Widal test. It is concluded that typhoid should be considered in patients with persistent fever, jaundice and hepatomegaly, who show conjugated hyperbilirubinemia with mild derangement of enzymes and negative serology for viral hepatitis. Whether Widal test should be used as a screening criteria for typhoid hepatitis in all patients presenting as hepatitis is a matter for speculation and further research because it only becomes positive in the second week of the typhoid fever<sup>12</sup>. Jaundice is not a very common mode of presentation of typhoid fever but is not that rare

either<sup>13-15</sup>. Bone marrow culture is a helpful investigation as Salmonellae persist for prolonged periods in the RE cells of the bone marrow. This provides an early diagnosis<sup>16,17</sup>. Liver histology shows non-specific changes and is therefore not recommended.

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