

HEPATIC MANIFESTATIONS IN TYPHOID FEVER

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ABSTRACT

*Thirty one children with typhoid fever aged 2 months to 12 years and blood culture positive for multidrug resistant *S. typhi* were prospectively studied for their hepatic functions at the time of hospitalization and 2-3 weeks after completion of antibiotic therapy. Hepatic manifestations included hepatomegaly (51.6%); jaundice (16.1%); raised levels of serum glutamic oxaloacetic transaminase (SGOT) (61.3%), serum glutamic pyruvic transaminase (SGPT) 48.4%, alkaline phosphatase (AP) (22.6%) and serum bilirubin (SB) (6.1%); reduced levels of serum albumin (SA) (41.9%); prolonged prothrombin time (PT) (9.7%) and abnormal ultrasound abdomen (19.3%). Hepatic dysfunction was a notable feature even in those cases without hepatomegaly, with raised levels of SGOT (60%), SGPT (40%), AP (20%), SB (6.7%), decreased SA (53.3%) and prolonged PT (6.7%).*

There was no correlation between the degree of hepatic enlargement or hyperbilirubinemia with abnormalities in liver functions. Hepatic dysfunction was noticed to be transient, as all these parameters returned to normal within 2-3 weeks after successful antibiotic therapy.

Key words: *Salmonella typhi, Hepatomegaly, Liver enzymes, Jaundice, Typhoid fever.*

The clinical picture of typhoid fever has changed considerably during recent years with the emergence of multidrug resistant strains of *S. typhi* (MDRST)(1-3). Among the varied clinical spectrum of typhoid fever presentation with jaundice is important as it simulates acute hepatitis. Several workers(4-7) have studied hepatic functions in adults suffering from typhoid fever but there is paucity of such data in children. This prospective study was planned to review the spectrum of hepatic involvement and to evaluate the severity and outcome of various hepatic manifestations of typhoid fever in children.

Material and Methods

Thirty one children of either sex, between 2 months to 12 years age, with culture positive multidrug resistant typhoid fever were selected by purposive sampling. Acute viral hepatitis, malarial hepatitis, any other viral illness in the recent past and drug induced* hepatitis were excluded by history, thorough clinical examination and investigations including detection of IgM malaria antibodies, peripheral blood smear for malarial parasite, IgM anti HAV and Hb-SAg. All the patients were more than 60% of weight/height by NCHS standard. The following investigations were undertaken in all the patients: routine blood and urine,

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serum bilirubin (SB), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum alkaline phosphatase (AP), serum albumin (SA), prothrombin time (PT) and ultrasound examination of abdomen (US). All the cases were treated with appropriate antibiotics for 14 days and investigations were repeated 2-3 weeks after completion of treatment.

Results

Out of 31 children with multidrug resistant typhoid fever, 20 cases (64.5%) had clinical and/or biochemical evidence of hepatic dysfunction. The spectrum of hepatic involvement included hepatomegaly (51.6%), jaundice (16.1%), derangement of various hepatic functions (61.3%) and abnormal US abdomen (19.3%). Out of the 5 cases with jaundice, 2 patients also had tender hepatomegaly but in 1 case liver was not enlarged. It was also interesting to note that hepatic functions were altered even without hepatomegaly (*Table I*).

In 3 out of 5 icteric patients, US abdomen suggested increased echotexture of the

liver and in one of them liver size was normal. Out of 15 patients with increased liver enzymes without jaundice, 2 had increased echotexture of the liver and 1 had distended gall bladder with thickened wall.

The outcome was favorable in all the cases and were discharged after completion of antibiotic therapy. In the follow up, liver size regressed and jaundice disappeared within 7-10 days while in the hospital; and all the liver functions returned to normal 2-3 weeks after successful antibiotic therapy (*Table II*). US abdomen performed during the follow up was normal in all the cases including those 6 patients with abnormal findings at the time of admission.

Discussion

Hepatic dysfunction detected by clinical and/or biochemical parameters was noticed in as many as 64.5% of cases in our study which is higher than that reported by others(6-9). However, those reports are from adults and the organisms were not multidrug resistant. The spectrum of hepatic dysfunction is believed to be more severe in

TABLE I—Spectrum of Hepatic Dysfunction

Alteration in hepatic functions	Total cases (n=32)		Cases with hepatomegaly (n=16)		Cases without hepatomegaly (n=15)	
	No.	%	No.	%	No.	%
SGOT (>40 U/L)	19	61.3	10	62.5	9	60.0
SGPT (>32 U/L)	15	48.4	9	56.3	6	40.0
AP (>250 U/L)	7	22.6	4	25.0	3	20.0
SA (<3 g/dl)	13	41.9	5	31.3	8	53.3
SB (>1 mg/dl)	5	16.1	4	25.0	1	6.7
PT (>3 sec from controls)	3	9.7	2	12.5	1	6.7

TABLE II- *Pre-treatment and Post-treatment Mean Values of Variables in Patients with Clinical/Biochemical Evidence of Hepatic Dysfunction (n=20)*

Parameters	Pre-treatment	Post-treatment	p-value
Serum bilirubin (mg/dl)	1.54 ±2.13	0.44 ±0.47	0.03*
SGOT (U/L)	92.35 ±46.94	28.34 ±12.72	0.00002*
SGPT (U/L)	71.10 ±35.43	20.37 ±6.99	0.00001*
Alkaline phosphatase (U/L)	205.30 ±119.82	146.05 ±49.30	0.05*
Serum albumin (g/dl)	3.17 ±0.56	32.8 ±0.51	0.54
Prothrombin tiem (see)	17.15 ±7.02	14.74 ±0.81	0.14

* Statistically significant.

relapses(6) and due to MDRST(2,10). In all our cases MDRST were isolated but none of them presented with a relapse.

Hepatomegaly is usually observed in enteric fever after the first week of illness, most often persists throughout the period of marked elevation of temperature, becomes less evident as defervescence progresses(7) and usually lasts for 3-4 weeks(6). Incidence of hepatomegaly is believed to be 2-3 times more common in typhoid fever than para typhoid fever(6) and has been reported between 23-90% in children with typhoid fever(1-6,11-14). A higher incidence of hepatomegaly has been reported in children suffering from multidrug resistant typhoid fever(1-3,11). Hepatomegaly was observed in 51.6% of our cases which is consistent with these results. The enlargement of liver in typhoid fever is caused by hypertrophy and hyperplasia of Kupffer's cells. Tender hepatomegaly observed in 2 of our cases,

suggested a more severe hepatocellular involvement as both of these cases presented with jaundice. Even though majority of cases with jaundice had hepatomegaly, liver was not enlarged in 1 case suggesting that significant hepatic dysfunction can occur in typhoid fever without hepatomegaly(6).

Jaundice associated with typhoid fever tends to occur at the peak of fever which differentiates it from viral hepatitis in which case fever usually comes down after the appearance of jaundice(10). Jaundice in most of these cases is due to typhoid hepatitis(2,3,15). However; hemolysis resulting in jaundice is a recognized complication of typhoid fever in patients with G-6-PD deficiency or thalassemia(14). Other causes of jaundice include ascending cholangitis, Salmonella liver abscess, suppurative pyelophlebitis and cholecystitis(16,17). Jaundice has been reported in 1-10% children with typhoid fever(2,3,12-14) and in the present

study it was observed in as many as 16.1% of cases. The higher incidence of jaundice in the present study may be because of MDRST which is believed to cause more severe disease and is frequently associated with complications(2).

Typhoid hepatitis is often of mild to moderate nature with abnormal liver function tests. Biochemical alterations of hepatic enzymes suggestive of hepatic damage have been reported in 24-87% of cases in various adult series(6,8,9). In the recent outbreak of MDRST elevated SGOT and SGPT have been described in 4-51% cases(2,10). Hepatic enzymes were elevated in more than 60% of our cases. Prolonged PT (>3 seconds from the controls) was observed in 9.7% of cases of typhoid hepatitis but none of them presented with bleeding from any site. Fourteen children (45.2%) had increased levels of liver enzymes without jaundice. SGOT was increased in 62.5% in patients with hepatomegaly and it is interesting to note that almost the same percentage of cases without hepatomegaly also had increased levels of SGOT. Similar observations were made with SGPT, AP and SA. No correlation was found between the occurrence and degree of hepatic enlargement or hyperbilirubinemia with abnormalities in liver function tests. Other workers(4,6,9) also had similar observations. These findings suggest that there may be more than one mechanism responsible for hepatic injury in typhoid fever. Salmonella endotoxin induced consumptive coagulopathy, damage to hepatocytes, arteritis(16), direct invasion of the hepatocytes by the organisms(5), immune complexes and consumption of complement(18) are believed to contribute to hepatic insult. The clinical presentation and extent of hepatic dysfunction in typhoid fever would, therefore, depend upon these

contributory factors and may or may not be associated with hepatomegaly.

It is concluded that presence of high fever, jaundice and tender hepatomegaly should arouse suspicion of typhoid hepatitis. Hepatic dysfunction in these cases, despite its high incidence and serious nature, is transient and responds favorably to appropriate antibiotic therapy.

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