
ORIGINAL ARTICLE**Profile of liver function test in patients with dengue infection**

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ABSTRACT

Background: Atypical manifestations of dengue infection with liver involvement have frequently been reported, ranging from mild elevations of aminotransferase levels to fulminant hepatitis.

Materials and Methods: An analysis of 27 serologically confirmed cases of dengue infection at our tertiary care hospital was made. Patients with normal aminotransferase levels were categorized into Grade A, those with at least one of the enzymes raised to less than 3 times the reference range as Grade B, those with at least one of the enzymes elevated more than 3 times but less than 10 times as Grade C and those with elevations more than 10 times as Grade D.

Results: 89% of the cases had alterations in the aminotransferase levels, with 37% categorized into Grade B, 30% into Grade

C, and 22% as Grade D or acute hepatitis ($P < 0.001$). Aspartate aminotransferase (AST) levels were higher compared to the levels of alanine aminotransferase (ALT) (mean: 390.7 U/l and 296.9 U/l, respectively).

Conclusion: Liver damage with alteration of aminotransferases is a common complication of dengue infection and valuable marker for monitoring these patients.

Key words: Aminotransferase, dengue fever, hepatic injury.

Introduction

Dengue, one of the most rapidly spreading mosquito-borne viral diseases in the world, is an acute infection caused by an arbovirus in the Flavivirus genus, and the mosquito *Aedes aegypti* is the vector. Epidemic dengue is a major public health problem in South East Asia, especially in India where there is a reported case fatality ratio of 3–

5%.^[1] The classical form has an incubation period of 4–8 days followed by onset of fever, generalized body ache, myalgia, arthralgia, and headache.^[1] Over the past few years, atypical manifestations of dengue have been reported with multiple organ involvement.^[2] Hepatic involvement is characterized by right hypochondrium pain, hepatomegaly, jaundice, and elevated aminotransferase levels peaking at ninth day and gradually returning to normal within 4 weeks. Although liver is not the main target for this disease, histopathology findings include centrilobular necrosis, fatty alteration, hyperplasia of Kupffer cells, acidophil bodies, and monocyte infiltration of portal tract.^[3]

We studied the profile and degree of liver involvement in patients affected during a recent outbreak of dengue fever.

Materials and Methods

A total of 53 patients, attending department of Medicine, between August 2013 and October 2013 were included in the study. Dengue was suspected when two or more of the following symptoms were present: fever, retro-orbital pain, myalgia, arthralgia, skin rash, nausea/vomiting, and hemorrhagic manifestations. Complete blood counts and liver function tests were carried out.

Tests for detection of anti-dengue antibodies

and/or NS1 antigen test were carried out in all patients. These samples were subjected to immunoenzymatic assay (Panbio dengue IgM-Capture ELISA). When results of either of these tests were positive, patients were considered to be currently infected with dengue virus, while cases in which the results were negative were considered unconfirmed.

The degree to which liver was involved was classified according into four groups based on aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. The reference value of AST and ALT was 40 U/l. Patients with normal aminotransferase levels were assigned Grade A. Those with the level of at least one of the aminotransferases elevated but less than 3 times the reference range were assigned Grade B. Patients with the level of at least one of the aminotransferases more than 3 times the reference range but less than 10 times the reference value were graded as C, and those with an increase in the level of one or both the enzymes more than 10 times were classified as Grade D, thereby defining the presence of hepatitis. In these patients, other causes of hepatitis, mainly hepatitis A, B, and C were ruled out using appropriate test. Descriptive statistics were calculated. Numbers and percentages were enumerated

for all categorical variables such as biochemical tests parameters.

Results

Twenty-seven of the 53 patients (51%) had a positive serological test, with 17 (63%) males and 10 (37%) females. Data has been summarized in Table 1.

No cases of encephalopathy or fulminant hepatitis were observed. One patient had coagulopathy (elevated prothrombin time); however, there was no clinically relevant bleeding manifestation. No deaths due to the disease occurred.

The albumin level was significantly lower in confirmed cases ($P = 0.03$). Twenty-three (85%) of the patients had elevation of at least one of the liver enzymes ($P < 0.001$) with alterations in AST seen in 23 (85%) and ALT seen in 21 (77.8%) of the patients. AST elevations were much higher than those of ALT (390.7 U/l vs. 296.9 U/l). Both enzymes were normal in 3 (11%) of the 27 confirmed cases (Grade A), 10 (37%) had altered level of at least one of the enzymes (Grade B), 8 (30%) had at least one enzyme increased to 3 times its reference value (Grade C), and 6 (22%) cases had acute hepatitis (Grade D) [Table 2].

The mean AST was higher in males, while the mean ALT was higher in females. Seventeen (89%) of the subjects with a

platelet count less than 100,000 cells/mm³ had elevated liver enzymes, although there was no statistical significance between the severity of thrombocytopenia and alterations in aminotransferases. Four patients had liver enzymes above 1000 U/l, with the total bilirubin elevated above the reference level.

Discussion

Our data showed that liver involvement was almost universal in patients with dengue infection, which is comparable to previous reports from other developing countries.^[4] Majority of these patients had mild to moderate liver dysfunction, although one-fifth of the patients had acute hepatitis without significant complications.

In the present study, most of the patients had elevated AST levels. In patients with grade B, C, or D hepatic involvement, elevation of AST occurred in most cases either together with ALT elevation or as a lone alteration. ALT levels were normal in 22% of the patients compared to normal AST levels in 15% patients. Similar trend has been reported in other studies.^[3,5] This general pattern with AST increasing more quickly and peaking at higher level is unusual and differs from those during acute hepatitis caused by hepatitis viruses,^[6] but has been described in dengue infection.^[7,8] Given the

prominence of musculoskeletal symptoms in dengue, skeletal muscle injury could explain the higher AST levels.

De Souza et al. classified 42.5% of patients as Grade B, 17.5% as Grade C, and only 1.8% as Grade D, according to aminotransferases' levels. ^[9] On the contrary, 22% of our patients had Grade D liver involvement. AST and ALT were elevated more than 10 times the reference value in 18.5% and 15% of the confirmed cases, respectively.

Kuo et al. reported that most severely ill patients had higher levels of aminotransferases and lower level of globulin, whereas increases in albumin, alkaline phosphatase (ALP), bilirubin, and prothrombin were unrelated to the severity of the disease. ^[10] Similarly, in the present study, globulin levels were significantly lower in confirmed cases. The reduction in serum globulin is an important factor in fluid loss in the third space, which is indicative of severity of dengue due to reduction in gradient of intra- and extravascular pressure. Thus, AST, ALT, and globulin are valuable parameters for evaluation of severity of infection. ^[6,9]

However, the study has its limitations. Because of the small sample size, the exact association of the aminotransferases with

different grades of dengue fever could not be ascertained. A larger study is required to truly establish whether the aminotransferases could be used as a prognostic marker. Secondly, due to financial constraints, second convalescent sera for confirmation of dengue infection could not be done.

In conclusion, among the 27 serologically confirmed dengue infection patients, liver involvement in the form of elevation of transaminases levels occurred in almost all patients. However, association with the severity of the disease could not be ascertained due to the small sample size. Jaundice and acute hepatitis developed in significant proportion of the patients. In most patients, the effect was mild and full recovery was usual with supportive treatment. Care must be taken not to make a mistaken diagnosis of viral hepatitis.

Ethical approval: The study was approved by the institutional ethics committee

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Conflict of Interest: None declared

Table 1: Biochemical profile of patients in the study

Parameters	Subjects with positive Serological result (n = 27)	Subjects with negative Serological result (n = 26)	P value
	Mean (\pm SD)	Mean (\pm SD)	
Age (years)	34.30 (\pm 15.0)	37.38 (\pm 14.5)	P = 0.348
Platelets (cells/mm ³)	81,926 (\pm 63,315)	150,817 (\pm 73,290)	P < 0.0001
Total bilirubin (mg/dl)	1.2 (\pm 1.4)	0.786 (\pm 0.46)	P = 0.21
Direct bilirubin (mg/dl)	0.65 (\pm 1.07)	0.27 (\pm 0.46)	P = 0.25
Total protein (g/dl)	6.69 (\pm 0.48)	7.25 (\pm 0.59)	P = 0.001
Albumin (g/dl)	3.85 (\pm 0.38)	4.25 (\pm 0.45)	P = 0.0321
Globulin (g/dl)	2.83 (\pm 0.37)	3.0 (\pm 0.28)	P = 0.039
AST (U/l)	390.69 (\pm 730.68)	47.22 (\pm 6.08)	P = 0.03
ALT (U/l)	296.9 (\pm 562.0)	42.15 (\pm 23.69)	P = 0.029
ALP (U/l)	98.78 (\pm 51.01)	107.82 (\pm 71.11)	P = 0.76

Table 2: Classification of study subjects according to aminotransferase levels

Classification	Mean	A (%)	B (%)	C (%)	D (%)	Total (N = 53)
Sex P = 0.9920						
Male		12 (34.3)	13 (37.1)	6 (17.1)	4 (11.5)	35
Female		5 (27.8)	7 (38.9)	4 (22.2)	2 (11.1)	18
Serology						
Positive (P = 0.709)		3 (11)	10 (37)	8 (30)	6 (22)	27 (51)
AST (U/l)	390.7 (\pm 730.6)	4 (15)	10 (36.5)	8 (30)	5 (18.5)	
ALT (U/l)	296.9 (\pm 562.08)	6 (22)	12 (44.5)	5 (18)	4 (15)	
Negative P < 0.001		14 (54)	10 (38)	2 (8)	0 (0)	26 (49)

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