Original Article

The Magnitude of Hepatic Transaminase Rise and Its Correlation with the Severity of Dengue Fever

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Abstract

Background and Objective: *Biochemical evidence of hepatic enzyme rise is very common in dengue fever. This study was designed to see the levels of elevated hepatic enzymes and their correlation with severity of dengue fever (DF).*

Materials and Methods: *It was an observational study conducted in the Department of Internal Medicine of BIRDEM Hospital, Dhaka, over a period of six months (July to December, 2010). Fifty serologically confirmed (IgM/IgM and IgG) dengue fever patients were included in the study.*

Results: *Of the 50 patients, 32 (64%) were male and 18 (36%) were female. The mean age was 44.2 (21-54) years. Out of 50 cases, 23 (46%) cases had classical dengue fever, 20 (40%) had dengue haemorrhagic fever (DHF) Grade I, 6 (12%) had DHF Grade II and 1 (2%) had DHF Grade III. Hepatic enzymes were raised in 47 (94%) cases. Mean aspartate aminotransferase (AST) was 98.77 U/L, mean alanine aminotransferase (ALT) was 88.09 U/L. In 46 (92%) cases AST was more than ALT. Enzyme rise was more in DHF (Grade III- mean AST 298 U/L, mean ALT 232 U/L, Grade II- mean AST 212.6 U/L, mean ALT 198.7 U/L, Grade I- mean AST 97.3 U/L, mean ALT 86.2 U/L) than classical dengue fever (mean AST 61.7 U/L, mean ALT 54.9 U/L). Mean bilirubin was 1.82 mg/dl. No difference was observed between classical dengue fever and DHF regarding serum bilirubin level.*

Conclusion: *The above results suggest that hepatic involvement in dengue fever is common and the amplitude of transaminase rise indicates the severity of the disease.*

Key words: *Alanine aminotransferase; aspartate aminotransferase; dengue fever; dengue hemorrhagic fever; hepatic transaminase.*

(Birdem Med J 2015; 5(2): 74-77.)

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Received: October 10, 2014 **Accepted:** July 30, 2015

Introduction

Dengue fever (DF) is the most prevalent mosquito-borne viral disease and each year over 390 million infections occur through-out the world.[1] It may present with a wide range of clinical manifestations; from mild febrile illness to life threatening shock syndrome as well as unusual manifestations such as hepatitis, encephalitis, myocarditis, Reye's syndrome, hemolytic uremic syndrome and thrombocytopenic purpura.[2] Analysis of the dengue patients done in few studies in different countries of the world revealed that in addition to these features there were other features such as liver dysfunction including a preferential rise of the liver enzymes.[3] Not only that, the severity of hepatic transaminase rise is associated with the severity of

dengue hemorrhagic fever.[4] Our study was done to see the frequency of hepatic involvement and aminotransferase level change in dengue fever. The study also intended to find out the relation of transaminase level change with the disease severity and to see the outcome of hepatitis in dengue fever.

Materials and Methods

This cross-sectional observational study was done in the Department of Internal Medicine of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh. The study period was July-December, 2010. Fifty hospitalized adult patients with the clinical diagnosis of dengue fever and who were serologically positive for dengue antibody (IgM with or without IgG) were purposively and consecutively included in this study. Patients with fever for more than 7 days or with definite evidence of etiology of fever other than dengue or serologically negative for dengue antibody (IgM) were excluded from the study. Classification of dengue fever was done according to The National Guideline 2010.[5]

Results

A total of 50 patients were included in this study with a male predominance (male 32 and female 18). Among them 17 were diabetic and 33 were non-diabetic. Mean age of the study population was 44.2 (range 21-54) years. Considering the severity of dengue syndromes patients were classified into four groups; 23 (46%) had classical DF, 20 (40%) had dengue haemorrhagic fever (DHF) DHF-I, 6 (12%) had DHF-II, 1 (2%) had DHF-III and no one had DHF-IV. Hepatic enzymes were raised in 47(94%) cases. Mean aspartate aminotransferase (AST) was 98.77 U/L, mean alanine aminotransferase (ALT) was 88.09 U/L. In 46 (92%) cases AST was more than ALT. Enzyme rise was more in DHF (Grade III- mean AST 298 U/L, mean ALT 232 U/L, Grade II- mean AST 212.6 U/L, mean ALT 198.7 U/L, Grade I- mean AST 97.3 U/L, mean ALT 86.2 U/L) than classical dengue fever (mean AST 61.7 U/L, mean ALT 54.9 U/L). There was no significant rise of serum bilirubin as well as alkaline phosphatase which were 1.82 mg/dl and 125U/L respectively. Hepatic enzymes returned to normal level within 3 weeks in 92% cases. Mean lowest total count of WBC and mean lowest platelet counts were more marked in DHF-III than other classes of dengue fever (Table I). Both AST and ALT were higher in DHF-III and their value increased with the increase in severity of dengue (Table I). Evidence of serositis and mean duration of hospital stay were also more in higher grades of dengue syndrome (Table I).

Discussion

In this study we primarily focused on the serum transaminase level change in different grades of dengue fever and the relation of transaminase level change with the disease severity. The limitations of the study were also addressed.

Among our patients, 94% had hepatic involvement as evidenced by raised AST and ALT levels. Similar results were found by Shukla and Chandra, where 97% had hepatic involvement with raised liver enzymes.[6] In our study population, patients with DHF-I had twice the upper limit of normal AST level reaching up to 5 to 7

Table I

Features of the study subjects (N=50)

Type of DF	Frequency (%)	Mean lowest WBC Count /mm^3	Mean lowest platelet count /mm^3	Mean AST (U/L)	Mean ALT (U/L)	Ascites Frequency (%)	Pleural effusion Frequency (%)	Mean hospital stay (days)
Classical DF	23 (46)	4400	1,05,000	61.7	54.9	0 (0)	0 (0)	4
DHF Grade-I	20 (40)	3720	48,000	97.3	86.2	4 (20)	2 (10)	6
DHF Grade-II	6 (12)	3680	42,000	212.6	198.7	3 (50)	2 (33.3)	6
DHF Grade-III	1 (2)	3760	22,000	298	232	1 (100)	1 (100)	10
DHF Grade-IV	0 (0)	—	—	—	—	—	—	—

times higher value than normal upper limit (40 U/L) corresponding with ascending grades of severity, whereas DF had AST level raised only up to 1.5–2 times of upper limit. In regard of ALT, it was 1.5 times higher than upper limit of normal in DF whereas 2 to 4 times higher in DHF. So, it showed that higher the level of AST and ALT, the greater is the tendency to be DHF. Mean AST levels were greater than ALT in both DF and DHF. Louiz J de S et al. had studied aminotransferase changes and acute hepatitis in 1,585 dengue patients.[7] Their average AST level was greater than that of ALT in both DF and DHF. They also found higher average AST and ALT value in DHF than DF that corresponds with our findings. Almost all the patients with alterations of hepatic enzymes during the period of our study returned to normal within 3 weeks. The above findings were also compatible with the findings of Kuo et al. where 270 dengue patients were evaluated and had raised AST and ALT in 93.2% and 82.2% cases respectively with greater elevation of AST than ALT which returned to normal after 3 weeks.[8]

The lack of acute liver failure in our study was not unusual, as the incidence of acute liver failure in dengue patients was 1.1% in studies done by Trung and Kuo.[9] In contrast to these adult studies, it is noteworthy that in dengue endemic countries, dengue may be an important cause of acute liver failure in children.[10,11] The mechanism of liver involvement in dengue infection is not clear and may explain a direct injury to liver cells or an immunological response.[12]AST is expressed in the heart, skeletal muscle, red blood cells, kidneys, brain and liver, while ALT is secreted primarily by the liver cells.[13] Because dengue infection can cause acute damage to these non-hepatic tissue types that express AST, raised aminotransferase levels may not be entirely due to severe liver involvement. There was no significant rise of serum bilirubin as well as alkaline phosphatase in our study. Lawn SD et al. also published similar observations in their case report.[14] A study involving 240 dengue patients was also conducted in the Department of Gastroenterology, BIRDEM in 2006 that published almost similar findings with our ones.[4] Sixty percent of our patients had leucopenia with mean lowest total WBC count of 3,680/mm^3 and mean lowest platelet count of 22,000/mm^3 in DHF-III. Duration of hospital stay increased proportionately with the increase in severity of the syndromes.

Our study had some limitations. These patients with elevated AST or ALT were not comprehensively evaluated for other etiologies of viral and non-viral hepatitis although we did exclude those with known liver co-morbidities. Tang et al. showed that dengue and hepatitis B co-infected patients have an aberrant cytokine secretion profile compared with those with dengue alone.[15]

Conclusion

Dengue is now a common febrile illness in our country and serum transaminase level in dengue has been shown to be associated with disease severity. So, from this transaminase level change physicians can be alert and ready to face and manage the complications of the disease. Large scale, multi-centered study may be carried out in future to achieve our goal.

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