



AMINOTRANSFERASES AND TOTAL SERUM BILIRUBIN LEVEL DERANGEMENT IN PATIENTS WITH DENGUE INFECTION

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ABSTRACT **Background:** Dengue infection can affect the liver with a wide spectrum of manifestations. The aim of this study was to evaluate the impact of dengue virus infection on liver function by measuring aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total serum bilirubin levels in patients serologically diagnosed with NS1 ELISA.

Methods: NS1 ELISA positive patients were included in the study and all the patients underwent aminotransferase and bilirubin analysed.

Results: AST was elevated more as compared to ALT and hyperbilirubinemia was observed in 9.2% of cases.

Conclusion: Transaminase level analysis in dengue patients are crucial markers for severe acute liver cell injury.

KEYWORDS : ALT, AST, Dengue Fever, Hyperbilirubinemia

INTRODUCTION

Dengue is the most common arboviral disease in India which has emerged as a notable public health problem in recent decades in terms of morbidity and mortality associated with it^{1,2}. World Health Organization (WHO) has categorized Dengue as the quickest spreading arboviral disease in the World and about 50% the World's population is at jeopardy of getting affected by this deadly viral infection^{3,4,5}. Dengue is a daunting global disease and economic burden⁶. One recent estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease)⁷. Dengue can affect multiple organs like nervous system, heart and liver causing encephalitis, myocarditis and hepatitis. It can affect the liver with a wide spectrum of manifestations. Usually the hepatic involvement is asymptomatic and clinical manifestations like jaundice, increased liver size, elevated transaminase levels and acute liver failure (ALF) may occasionally complicate the clinical picture. Hyperbilirubinemia and low albumin levels may also be observed. In endemic countries like India, Dengue is recognized as an important cause of acute liver failure. The aim of the study was to analyse derangement in transaminases (ALT, AST) and total bilirubin levels among NS1 antigen positive Dengue cases.

METHODS

This was a retrospective observational analysis conducted in the Department of Microbiology and Department of Biochemistry, Narinder Mohan Hospital, Ghaziabad, India on 87 NS1 antigen positive cases from August 2019 to November 2019. Inclusion criteria included patients of both sexes and all age groups. Patients with malaria, typhoid, scrub typhus or any pre existing liver disease were excluded from the study. All the patients underwent transaminase and total bilirubin levels done. Total Serum Bilirubin levels were tested by Diazo Method using Beckman Coulter AU 480 Autoanalyzer. Alanine aminotransferase [ALT] and Aspartate aminotransferase [AST] were tested by methods based on IFCC (International Federation for Clinical Chemistry). Dengue NS1 antigen testing was done using Panbio® Dengue Early ELISA Kit. Index value was calculated using the standard formula Sample Absorbance / Cut-off value. Index value of more than 1.1 was considered as a positive result.

RESULTS

Of the total 87 Dengue NS1 positive patients, 8 patients (9.2%) had total serum bilirubin values consistent with Hyperbilirubinemia (Total serum bilirubin > 1.2 mg/dL) [Figure 1], 8 patients had normal aspartate aminotransferase (AST) levels, 21 patients (24.1%) had less than 2 fold increase in AST levels, 29 (33.3%) had 2-4 fold increase, 20 (23%) had 4-10 fold increase, 9 (10.3%) had more than 10 fold increase

[Figure 2], 22 (25.2%) patients had normal alanine aminotransferase [ALT] levels, 31 (35.6%) patients had less than 2 fold increase in ALT levels, 18 (20.6%) had 2-4 fold increase, 13 (14.9%) had 4-10 fold increase, 3 (3.4%) had more than 10 fold increase [Figure 3], AST/ALT ratio was observed to be less than 1 in 8 (9.2%) patients, more than 1 and less than 2 in 51 (58.6%) and more than 2 in 28 (32.1%) patients [Figure 4].

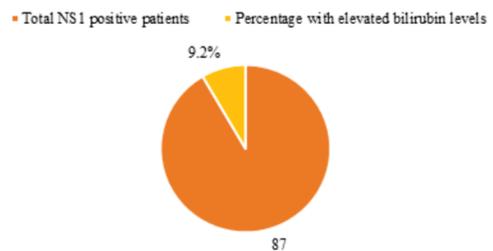


Figure 1. Percentage of NS1 Positive Patients with Elevated Total Serum Bilirubin Levels

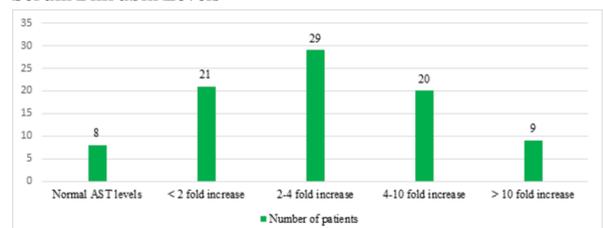


Figure 2. Derangement of Aspartate Aminotransferase (AST) Levels in NS1 Positive Patients

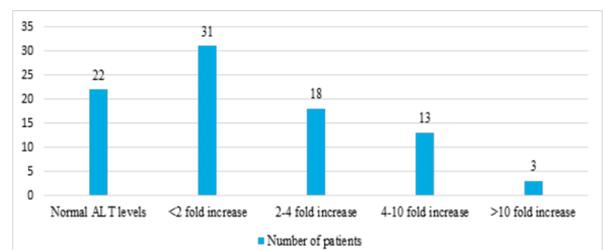


Figure 3. Derangement of Alanine Aminotransferase (ALT) Levels in NS1 Positive Patients

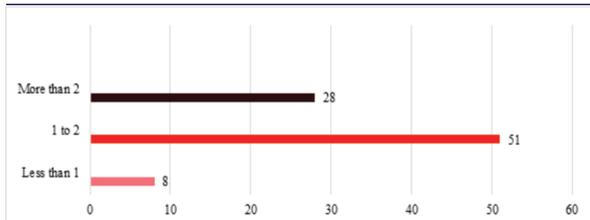


Figure 4. AST/ALT Ratios in NS1 Positive Patients

DISCUSSION

Atypical manifestations of dengue have been reported with multiple organ involvement over the past few years⁸. In the severe form of Dengue, high level of viremia is associated with involvement of different organs like liver, brain⁷. The virus seems to have hepatotoxic effects with hepatocytes and kupffer cells being the prime targets^{10,11,12} as confirmed in biopsies and autopsies¹³, this is reflected in the form of elevation of alanine aminotransferase [ALT] and aspartate aminotransferase [AST], hyperbilirubinemia and serum albumin derangements. AST and ALT elevation is common in acute dengue illness, occurring in 65–97%^{14,15,16,17} of dengue patients. It was further observed that, secreted NS1 antigen protein of dengue virus has the ability to attach to the liver cells via interactions with heparan sulfate and chondroitin sulfate E and thus modulate the functions¹⁸. Another important study has described that, the secreted form of dengue virus NS1 protein is engulfed by hepatocytes, that further accumulate in the endosomes showing an important mechanism for the development of dengue associated pathophysiology¹⁹. World Health Organization (WHO) in the year 2009 revised its guidelines for dengue and proposed severe organ impairment as one category of severe dengue. In addition, there is severe plasma leakage and severe bleeding. Severe liver involvement was defined as AST or ALT more than or equal to 1000 units/liter (U/L). Our study reports 9.2% cases of bilirubinemia which was comparable to the study by Narasimhan D et al²⁰ where Hyperbilirubinemia was observed in 5% of cases. Similar study done by Parkash et al¹⁴ reported 3.1% of patients having bilirubinemia. Hyperbilirubinemia in 3.1% of cases was also reported by Larreal Y et al²¹ where they reported elevated bilirubin levels in 2 of 63 patients (3.1%). In our study, AST was observed to be elevated more as compared to ALT which was similar to study done by Amit Soni et al²² and Narasimhan et al²⁰. 9.2% of patients had AST/ALT levels to be more than 2. The increased AST/ALT ratio is useful for differential diagnosis from acute hepatitis caused by the hepatitis A, B or C viruses where it is rarely observed²³.

CONCLUSION

Dengue virus being hepatotoxic may provoke varying degrees of damage to the hepatic parenchyma, ranging from mild increase in the aminotransferase levels to increase of more than 10 folds the reference values. This alteration of aminotransferases is a common complication of dengue infection and valuable marker for monitoring these patients. Hyperbilirubinemia may also be observed. Therefore, the use of liver tests to evaluate the degree of liver damage is of great importance, and markers such as AST and ALT may be used as parameters to evaluate the severity. Also the increased AST/ALT ratios can be used to differentiate dengue infection from viral hepatitis where it is infrequently seen²³.

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