Journal of Islamabad Medical & Dental College (JIMDC); 2016:5(1):10-13

Original Article

Liver Biochemistry: Difference between Dengue Fever and Non Dengue Febrile illnesses

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Abstract

Objectives: To assess the degree of liver involvement in patients of dengue fever and to compare it with the patients having other non specific febrile illnesses.

Materials and Methods: In this cross-sectional study patients with febrile illness admitted in District Headquarter Hospital Rawalpindi and Social Security Hospital, Islamabad were included consecutively. Dengue serology was done in all patients and patients were divided into two groups on the basis of dengue serology. At the same time liver biochemistry was done in all the patients. The data was entered and statistically analyzed in SPSS version 20 for further analysis.

Results: A total of 152 patients were included in our study. Among them 99 (65%) were males and 53 (35%) were females. The mean age of patients was 30.36 ± 13.8 years. Dengue viral serology was positive in 98 (64%) patients and negative in 54 (36%) patients. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST), were normal only in 21 out of 98 (21%) confirmed cases of dengue fever compared with 33 out of 54 (61%) patients having other febrile illnesses. Median and interquartile range of ALT in dengue fever patients was much higher 109.0 and 141.25 IU/L as compared to the patients with other febrile illnesses 38.0 ± 44.75 IU/L.

Conclusion: Liver injury is more common in patients with dengue infection as compared to those having other febrile illnesses.

Key Words: ALT, AST, Dengue fever, Febrile illness.

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Received: Dec 3rd, 2015; Accepted: April 1st 2016

Introduction

Dengue fever has emerged as one of the important causes of febrile illness in tropical and subtropical region.[1] It is a mosquito borne disease and is transmitted to humans by Aedes mosquitoes, mainly Aedes aegypti, with an estimated 50 million infections occurring each year.[2] It has become a major health problem in Southeast Asia with 2-3 epidemics per year and fatality rate of 1 to 5%. Dengue virus has four serotypes but all of them cause similar illness ranging from asymptomatic infection to severe dengue.[3] This disease has been found to have profound effect on multiple organ systems, the commonest being the liver.[4,5] Dengue virus is non-hepatotropic, however, hepatomegaly is commonly found along with raised serum aminotransferases. Liver dysfunction in dengue virus infection may be due to direct effect of virus on hepatocytes or as a result of abnormal host immune responses.[6] When infection occurs, certain cytokines are released.[7,8] High levels of TNFα, IL-2, IL-6 and INF-α have been detected in serum in first three days of Dengue fever whereas IL-10, 1L-5 and IL-4 are seen in later phase of infection (4 days after fever).[9] Elevated levels of TNF-α have been strongly linked to the severity of disease. Moreover, significant it has been reported that circulating levels of IL-2 and TNF-a with changes in liver enzyme
es at an early stage of the clinical disease is predictive of severe forms of DENV infections.[10]

Clinical manifestations of dengue fever vary from mild self-limiting infection to more severe form of Dengue hemorrhagic fever. It has been observed in different studies that both innate and adaptive or cell mediated immune response are known to contribute to the progression of dengue virus infection. The liver dysfunction in dengue

fever varies from mild elevation of aminotransferases to even fulminant hepatic failure.[5] Early laboratory diagnosis of dengue fever is important to provide appropriate treatment to the patients and to prevent potential complications. The most commonly used techniques in the laboratory include virus isolation, detection of viral nucleic acid by RT-PCR, detection of dengue-specific IgG or IgM by MAC-ELISA and rapid kit test to detect dengue virus non-structural protein 1 (NS1) antigen.[11] Liver biochemistry is also deranged commonly in dengue fever; especially AST and ALT are raised. This study was conducted to assess the degree of liver involvement in patients of dengue fever and to compare it with the patients having febrile illnesses other than Dengue fever in two tertiary care hospitals of Rawalpindi and Islamabad to see whether this can help in differentiating between dengue fever and other febrile illnesses.

Materials and Methods

This cross-sectional study was done at District Headquarter Hospital Rawalpindi and Social Security Hospital, Islamabad from 1st July 2015 to 30th October 2015. The patients admitted with febrile illness, both male and female, of all age groups were included in the study. Patients with known chronic liver disease due to any cause or taken hepatotoxic drugs for any other illness in previous three months were excluded. Informed consent was taken, Ethical approval was obtained and data was collected. The diagnosis of dengue fever was confirmed by detection of dengue-specific IgG or IgM antibodies by MAC-ELISA, or by positive NS1 ELISA based antigen and patients were categorized in two groups: Group-A included patients with positive dengue viral markers (confirmed cases of dengue fever) and Group-B included patients with negative viral markers (having febrile illness other than Dengue fever).

At the same time, Liver function tests were also performed for all the patients. Patients were categorized into four groups on the basis of severity of liver involvement. Group-I included patients with normal liver enzymes, Group-II included patients who had up to two-fold increase in liver enzymes, Group-III included patients with two to four-fold increase in liver enzymes and Group-IV included patients with liver enzymes of more than four folds of normal. The normal upper limits for ALT and AST were taken as 32 IU/L and 40 IU/L respectively. [12]

The data was entered and statistically analysed in SPSS version 20. Mean and standard deviations were calculated for age, duration of fever at the time of presentation, median and interquartile range was calculated for ALT and AST levels. Frequency was used to calculate percentage for qualitative data like gender, severity of liver involvement and result of viral markers. Pearson Chi-square test was used to compare the liver function tests between group-A, including confirmed cases of dengue fever, and Group-B having patients with febrile illness other than dengue fever. P-value less than 0.05 were considered as significant.

Results

A total of 152 patients having febrile illness were included in our study. Among them 99 (65%) were males and 53 (35%) were females. The mean age of patients was 30.36 $\pm$ 13.8 SD years (range 7–65 years). All the patients presented with fever for a mean duration of 5.13$\pm$1.3 days (range 2–9 days). Dengue fever was confirmed by viral serology which was positive in 98 (64%) patients, NS1 ELISA based antigen was positive in 98 (100%) patients while dengue-specific IgG or IgM antibodies were positive in 79 (81%) patients. Dengue viral serology was negative in 54 (36%) patients who were classified as having other febrile illnesses. Among the liver function test, Bilirubin and alkaline phosphates levels fell within the normal range for almost all the patients in both the groups. Liver enzymes, including ALT and AST, were normal only in 21 out of 98 (21%) confirmed cases of dengue fever compared with 33 out of 54 (61%) patients having other febrile illnesses. About 77 (78%) patients with Dengue fever had raised transaminase levels as compared to 21 (39%) patients with other febrile illnesses. Median and interquartile range of ALT in dengue fever patients was much higher (109.0 and 141.25 IU/L) as compared to the patients with other febrile illnesses (38.0 and 44.75 IU/L). Similarly, median AST and interquartile range in dengue fever patients was higher (124.0 and 155.5 IU/L) as compared to patients having other febrile illnesses (46.0 and 47.25 IU/L). There was highly significant association between raised liver enzymes and confirmed cases of dengue fever as compared to other febrile illnesses.

Table I: Liver enzymes in Dengue fever patients compared with those having other febrile illnesses

	Liver Enzymes (ALT &AST)				Total	Pearson Chi-square test (p-value)
	Normal	< 2 fold increase	2 to 4 fold increase	> 4 fold increase		
Confirmed cases of Dengue fever	21	21	31	25	98	**0.000**
Other febrile illnesses	33	19	02	00	54	
Total	54	40	33	25	152	

p value less than 0.05 was considered as significant.

Discussion

Dengue has emerged as an important arboviral disease with significant impact on the disease burden in population residing in tropical countries. The virus seems to have some hepatotoxic effects. Involvement of liver in form of derangements in the liver function tests is common and may include mild elevations in serum bilirubin, elevated transaminases and derangements in serum albumin. This disease has been found to have profound effect on multiple organ systems, the commonest being the liver. The disease may be asymptomatic with elevated transaminase levels to acute liver failure (ALF). Although asymptomatic in most cases, clinical manifestations like jaundice, and acute liver failure (ALF) may occasionally complicate the clinical picture and has been implicated as an important cause of ALF in endemic countries. ALT and AST were significantly higher in patients having dengue fever as compared to those who were having febrile illness other than dengue in our study. More than two-fold rise was more significant in this regards. Bilirubin and alkaline phosphatase level were not raised in both groups.[14] Raised transaminases level is a common finding in dengue fever, different studies show different results in this regard. The reported hepatic enzyme levels in dengue infection vary from 36.4% to 96% (as shown in different studies).[13,14] In our study, 78% of patients with dengue fever were found to have raised ALT and AST levels and these results are consistent with the previous study conducted in Brazil reporting that 65% confirmed cases of dengue infection had abnormal aminotransferase levels.[15] In another study conducted in Pakistan by Ahmed SI et al raised ALT levels were noted in 62% patients and raised AST levels were noted in 51% dengue fever patients;[16] both the studies supporting our results.

Elevation of AST was more compared with ALT in the present study similar to other observations and this may be due to involvement of myocytes in dengue fever.[17,18]

This differs from the pattern seen in viral hepatitis, in which ALT levels are usually higher than or equal to AST levels.[19] A study conducted in India showed that mean ALT level was much higher in patients of dengue fever as compared to those patients having febrile illnesses with negative dengue serology i.e.296.9 (±562.0) vs 42.15 (±23.69) and these are comparable with our results.[12] Mean AST levels were also significantly higher in dengue fever as compared to non-dengue febrile illnesses in our study. Mean AST levels 390.69 (±730.68) were found in Dengue fever patient's vs 47.22 (±6.08) in non-Dengue febrile illnesses in a study conducted at Kasturba Medical College Hospital, Karnataka.[20] In combination with other simple laboratory tests, raised levels of transaminases can be used as a marker to differentiate dengue fever from other febrile illnesses.

Study limitation: Our study has some limitations; as it only included indoor patients and did not include outdoor patients, hepatitis viral serology was also not done which may also affect the results. Further studies should be conducted to find out the association between raised aminotransferase levels in dengue fever and other febrile illnesses.

Conclusion

Liver injury is more common in patients with dengue infection as compared to those having other febrile illnesses. Dengue infection must be ruled out in patient presenting with febrile illnesses and raised transaminase levels.

Conflict of Interest

This study has no conflict of interest as declared by any author.

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