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Original Article

ALT; An Indicator of Hepatic Involvement in Dengue Infection

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Abstract

Background: Dengue infection, a major public health problem, affects all body systems including hepatobiliary system that can be assessed by measuring serum alanine aminotransferase (ALT) levels. The objective of this study was to compare the extent of hepatic involvement in the patients of dengue fever (DF) with that of the patients of dengue haemorrhagic fever (DHF) by comparing mean ALT levels and degree of rise in serum ALT levels in patients of both groups, DF and DHF.

Methods: A comparative analytical study was carried out at Department of Infectious Diseases, Holy Family Hospital from September 2016 to December 2016. A total of 184 seropositive dengue patients were taken using non-randomized consecutive sampling technique; 92 patients having DF and 92 patients having DHF. Blood samples for ALT levels were taken within 24 hours of diagnosis of DF and DHF. SPSS version 22 was used to analyse the data. Mann-Whitney U test was used to compare the mean ALT levels and Chi-Square test at 5% significance level was applied to compare the degree of rise in serum ALT levels in both groups.

Results: In this comparative analytical study, 184(42 females and 142males) seropositive dengue patients were included. The mean serum ALT level in patients of DF was 85.43(±58.685) while mean ALT levels in patients of DHF was 167.76(±155.656), (p=0.00).The degree of serum ALT rise in DHF patients was significantly higher than that of DF patients (p=0.00).

Conclusion: The extent of hepatic damage is more in dengue haemorrhagic fever as compared to uncomplicated dengue fever.

Keywords: dengue fever, dengue haemorrhagic fever, alanine aminotransferase

Introduction

Dengue fever also known as break bone fever, is a major public health problem in Pakistan.[1,2] It is an arthropod borne viral disease transmitted by mosquitoes mainly of the species Aedes aegypti.[3]

Dengue fever has very wide clinical spectrum including asymptomatic dengue fever, acute febrile illness, dengue fever, DF, (seropositive patients with fever and had other constitutional symptoms) , dengue haemorrhagic fever, DHF, (Haemorrhagic manifestation, thrombocytopenia and plasma leakage or hemoconcentration) and dengue shock syndrome, DSS (symptoms of DHF, narrow pulse pressure of less than 20 mm Hg and cold extremities).[4,5,6]

Dengue virus has four serotypes namely DEN-1, DEN-2, DEN-3 and DEN-4.[7] The patients acquires lifelong immunity against the causative serotype but if the same patient is affected by another serotype of dengue virus, chances to develop complicated disease increases i.e. DHF and DSS.[8]

Dengue infection affects the function of multiple organs including liver, so it is necessary to assess the integrity of liver parenchyma in dengue patients for appropriate and timely interventions.[7] Serum alanine aminotransferase (ALT) levels is an indicator of liver parenchyma function. Studies suggest that serum ALT levels rise in proportionate to liver injury.[9] A patient with hepatic involvement in dengue infection may develop jaundice (hyperbilirubinemia), hepatomegaly, GI hemorrhage and biochemical changes i.e., increase in serum aminotransferases.

The purpose of this study was to compare the extent of hepatic involvement in patients of DF with that of the patients of DHF by comparing mean ALT levels and degree of rise in serum ALT levels in patients of both groups, DF and DHF.

Materials and Methods

This comparative analytical study was conducted at department of infectious diseases, Holy Family Hospital, Rawalpindi from September 2016 to December 2016. The Hospital is a tertiary care affiliated with Rawalpindi Medical College, Rawalpindi, Pakistan.

A total of 184 seropositive dengue patients were studied using non-randomized consecutive technique; 92 patients having dengue fever and 92 having dengue haemorrhagic fever.

Patients were divided according to the WHO criteria, DF, DHF which includes dengue shock syndrome as well. The patients were divided according to their ALT levels into Grade A (normal serum ALT level), Grade B (mildly raised serum ALT), Grade C (moderately raised serum ALT) and Grade D (severely raised serum ALT).

ELISA technique for IgM, IgG and NS-1 was used to confirm the infectious status of the patients. Patients having any co-morbidity involving liver parenchyma were excluded. 2 ml blood was drawn from median cubital vein after cleansing the area with spirit swab using a 5 cc 21 gauge syringe, within 24hrs of diagnosis of DF and DHF. Blood samples were then sent to laboratory for estimation of serum ALT levels using Beckman counter AU 480.

Statistical Package for Social Sciences (SPSS) version 22 was used to enter and analyse the data. Mann Whitney U test was used to compare mean serum ALT levels and Chi Square Test at 5% significance level and keeping confidence interval at 95% was applied to compare the degree of rise in serum ALT levels in both groups. P value less than 0.05 was considered significant.

The ethical approval was granted by the institutional research forum of Rawalpindi Medical College, Rawalpindi.

Results

Out of 184 patients included in our study, 142 (77.2%) were males and 42 (22.8%) were females.

The disease was more prevalent among males with male to female ratio of 3.4: 1.

The mean age of affected population was 32.74±14.74 years.

The mean serum ALT level was significantly higher in the patients having dengue haemorrhagic fever as compared to the patients having dengue fever. Mean serum ALT levels in most of the patients with dengue fever lies in category of mildly raised ALT levels and that of dengue haemorrhagic fever lies in category of moderately raised ALT levels. (Table I)

When these levels were compared using Mann Whitney U test, very highly significant (p=0.000) results were obtained.

After a dengue viral infection, mildly raised serum ALT levels is seen in majority of the patients, it is seconded by moderately raised serum ALT levels which is more commonly found among patients of DHF. Severely raised serum ALT levels were, however, found only among patients of dengue haemorrhagic fever. (Table II)

TABLE I: Mean Serum ALT levels in DF and DHF

Diagnosis	Mean Serum ALT Level (U/l)
Dengue Fever	85.43 ± 58.685
Dengue Hemorrhagic Fever	167.76 ± 155.656

TABLE II: Distribution of Patients in DF and DHF in relation to serum ALT levels

ALT Level	GRADE	Serum ALT Level	Dengue Fever N=92(100%)	Dengue Hemorrhagic Fever N=92(100%)
Normal ALT Level	Grade A	< 43U/1	30(32.6%)	8(8.7%)
Mildly raised ALT level	Grade B	44-129 U/1	40(43.5%)	44(47.8%)
Moderately raised ALT level	Grade C	130-430 U/1	22(23.9%)	32(34.8)
Severely raised ALT level	Grade D	> 430 U/1	-	8(8.7%)

When these levels were compared using Pearson Chi-Square test, very highly significant (x^2 =22.779, p=0.000) results were obtained.

Degree of serum ALT rise was higher in DHF patients as compared to that of DF patients. (Figure I)

Difference was observed (p=0.00).

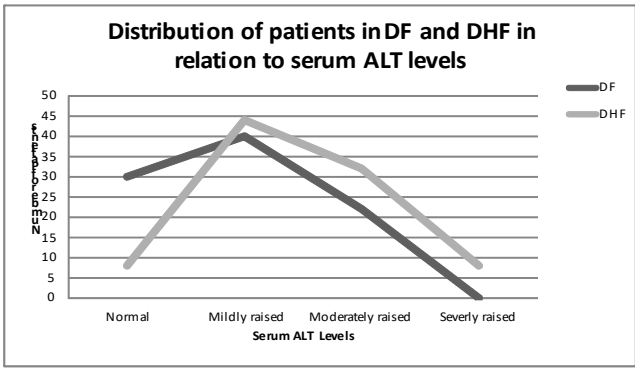

FIGURE I: Relation between number of patients and degree of rise in serum ALT

Severity of the disease is more among male population as compared to females. Severely raised ALT levels were only found among the male patients while there was a considerable difference in other categories with

raised serum ALT levels being more common among male patients. (Figure II)

When ALT level ranges in patients of DF and DHF were compared, statistically highly significant

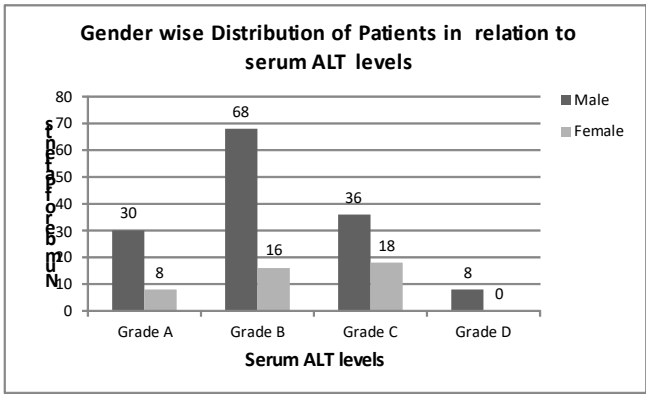

FIGURE II: Gender distribution and degree of serum ALT changes

Discussion

Dengue Fever is endemic in 125 countries of the world.[10,11] It is the most common viral infection affecting humans in this point of time.[12] The disease is more prevalent in tropics and subtropics especially in south East Asia.[13,14] In Pakistan first major outbreak of dengue infection was reported in 1994, followed by large number of cases reporting every year.[15] WHO has set a criteria and categorized the infection in three subgroups namely dengue fever, dengue haemorrhagic fever and dengue shock syndrome.

The involvement of liver in dengue viral infection is not uncommon.[16] The severity of the dengue infection is proportional to liver damage and hence a positive predictor of progression of DF to DHF.[17] It is widely accepted that liver damage and rise in serum ALT levels is significantly higher among patients of DHF and DSS as compared to patients with DF.[18,19] While these studies and our study show a significant difference in serum ALT level of patients having DF and DHF some studies show that there is no significant difference.[20,21]

It is proposed that an increase in serum ALT levels in dengue infection is because of the underlying hepatic inflammation and direct attack of virus on the hepatocytes, this inflammation releases the hepatic enzymes in blood.[22,23]

Hepatic involvement in dengue fever prolongs the disease process and leads to the complications of the disease.[19] Hepatic involvement in dengue fever is of significant importance because it can lead to fulminant hepatitis, hepatic encephalopathy, renal failure and gastrointestinal bleeding. All these combined may be fatal and may lead to death of the patient.[17,21,24]

The mean age of patients was 32.74±14.74.There was a greater incidence of dengue infection among male gender with a male to female ratio of 3.4:1, age and gender distribution were in accordance to the previously conducted studies. The probable reason of high incidence among male population is more exposure to outdoor environment, hence more exposure to mosquitoes.[25] Similar results have not been seen in studies conducted in India, Sri Lanka and Thailand.[26,27,28]

In our study the mean serum ALT levels in patients of dengue haemorrhagic fever was significantly higher as compared to patients having uncomplicated dengue fever. The mean serum ALT levels in patients of dengue fever and dengue haemorrhagic fever including dengue shock syndrome is 85.43 ± 58.685 and 167.76 ± 155.656 respectively. These results are in accordance with study done by Chhina RS.[30]

It was seen that indeed majority of patients with dengue infection have either mildly raised or moderately raised serum ALT levels while other patients have normal or severely raised ALT levels, this is in accordance to the studies already conducted.[29] It was seen that only the patients with DHF had severely raised serum ALT levels but the distribution in mildly raised serum ALTs was comparable in both groups. Moderately raised serum ALT levels were found to be more among the DHF group.

Hence, it is proposed that sero-positive dengue patients having raised serum ALT levels dealt with more care at the time of admission to hospital, so that complications of disease could be reduced.

Conclusion

This study concluded that extent of hepatic damage is more in dengue haemorrhagic fever as compared to uncomplicated dengue fever.

Our study suggests that

1) Serum ALT levels of seropositive dengue patients may serve as an indicator of disease progression in dengue infection during hospital stay.

2) Serum ALT levels at time of admission to hospital may serve as an indicator of disease severity in dengue infection.

Our study was based on serum alanine aminotransferase but other liver function tests such as serum aspartate aminotransferase, serum alkaline phosphatase and serum bilirubin may also be used to broaden the scope of the study.

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