Section: General Medicine

Original Research Article

A STUDY OF SERUM AMINOTRANSFERASE LEVELS IN DENGUE FEVER AT TERTIARY CARE HOSPITAL, HYDERABAD TELANGANA STATE

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Abstract

Background: To correlate the levels of enzymes with the severity of dengue infection. **Materials and Methods:** A total number of 100 cases were carried out in Tertiary Care Hospital, Telangana State during the period of July 2018 to June 2020. **Results:** The main presenting symptoms were fever which was present in all patients (100%), headache in 73 pt's (73%), Myalgia in 33 pt's (33%), arthralgia in 40 pt's (40%), hemorrhagic manifestations in 40 pt's (40%), vomiting in 43 pt's (43%) and abdominal pain in 40 pt's (40%). The results were compared with other studies in literature and discussed. **Conclusion:** Clinical and experimental observations suggest that liver involvement occurs during dengue infections. Clinical evidence includes hepatomegaly and increased serum liver enzymes, with liver involvement being more pronounced in the more severe forms of infection. Dengue viral antigens have been found within hepatocytes, and the virus appears to be able to replicate in both hepatocytes and Kupffer cells, and dysregulated host immune responses may play an important causative role in liver damage. Modulating these immune responses may have a therapeutic potential.

INTRODUCTION

Dengue infection, anarthro pod-borne viral hemorrhagic fever, continues to be a major challenge to public health, especially in South-East Asia.[1] It has a wide geographical distribution and can present with a diverse clinical spectrum.[2] Although dengue virus is a non hepatotropic virus, liver injury due to dengue infection is not uncommon and has been described since the 1960s.

Hepatic involvement can be characterized by manifestations of acute hepatitis, with pain in the right hypochondrium, hepatomegaly, jaundice, and raised amino transferase levels. In hepatitis, the levels of these enzymes reach a maximum on the ninth day after the onset of symptoms, and they gradually return to normal levels within three weeks. Although the liver is not the main target organ for this disease, histopathological findings, including centri lobular necrosis, fatty alterations, hyperplasia of the Kupffer cells, acidophil bodies and mono cyte infiltration of the portal tract have been detected in patients with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The liver dysfunction could be a direct viral effect or an adverse consequence of dysregulated host immune response against the virus.[2] Several out breaks of dengue infection have been reported from India. However, large clinical studies documenting hepatic involvement in dengue infection, especially in adults, are scarce.

Aim of the Study

The aim of this study is to measure the levels of serum amino transferase levels in patients with dengue fever and to correlate the levels of enzymes with the severity of dengue infection.

MATERIALS AND METHODS

A total number of 100 cases were carried out in Tertiary Care Hospital, Telangana State. After duly obtaining an informed consent, detailed history of all patients was taken. These patients will be evaluated with reference to clinical symptomotology, biochemical profile for Dengue Fever will be assessed, which includes a Complete Blood Count, Dengue Serology, Liver Function Tests, Widal Test, Smear for Malaria Parasite, Blood and Urine cultures, Anti-HAV Antibody, HBsAg, Anti-HCV Antibody, USG Abdomen and Renal Function tests.

All patients were evaluated with detailed history including age, sex, presenting symptoms, history of co morbid illness, alcohol consumption and use of

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hepato toxic drugs were noted. The World Health Organization (WHO) grading system was used to classify patient as having classic dengue fever (DF) and dengue hemorrhagic fever (DHF) (WHO, 1997).

Inclusion Criteria

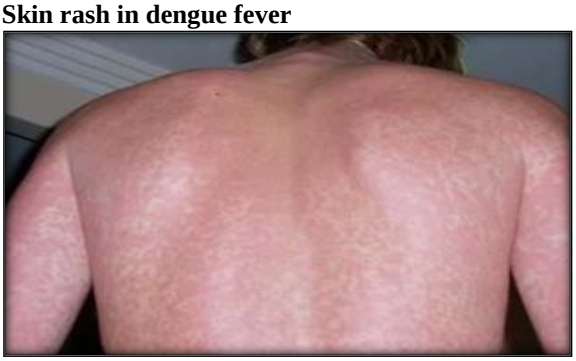
1. Patients with typical clinical features of Dengue Fever with NS1 Antigen or IgM Antibody Positive.
2. Patients over the age of 12 years are included in this study.

Exclusion Criteria

1. Chronic liver disease
2. Viral Hepatitis (Hepatitis A,B,C)
3. Malaria
4. Typhoid
5. Hepatotoxic Drugs
6. History of alcohol abuse
7. Age <12 years.

Ae. Aegypti mosquito

Skin rash in dengue fever



RESULTS

Table 1: Diagnosis of Dengue Infection

Diagnosis	Number of patients IgM Positive	%	Number of patients IgG Positive	%
Dengue fever (DF)	85	85%	50	58%
Dengue Hemorrhagic Fever (DHF)	8	8%	2	25%
Dengue Shock Syndrome (DSS)	7	7%	1	14%
Total	100	100%	53	53%

Table 2: Symptomatology

Symptoms	Number of patients (n=100)	%
Fever	100	100
Headache	73	73
Retro-orbital pain	13	13
Arthralgia	40	40
Myalgia	33	33
Vomiting	43	43
Pain abdomen	40	40
Hemorrhagic manifestation	40	40
Jaundice	49	49

Table 3: Haemorrhagic Manifestations

Hemorrhagic manifestation	Number of patients (n=100)	%
Absent	60	60
Present	40	40
· Bleeding gums	10	10
· Petechiae / Rash	24	24
· Erythematous rash	4	4
· Ecchymosis	3	3
· Menstrual bleeding	2	2
· Epistaxis	1	1

Table 4: Symptomology in Dengue Sub groups

Variables	Diagnosis			'p' value
	DF (n=85)	DHF (n=8)	DSS (n=7)	
1) Fever	100(100%)	8(100%)	7(100%)	1.000

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2) Headache	63(81%)	5(70%)	6(100%)	0.075+
3)Retro-orbital pain	10(12.4%)	1(45%)	2(22.2%)	0.004**
4) Arthralgia	34(46%)	4(80%)	2(100%)	<0.001**
5) Myalgia	28(48.2%)	3(75%)	2(100%)	<0.001**
6) Vomiting	35(33.6%)	5(80%)	3(55.6%)	<0.001**
7) Pain abdomen	34(18.2%)	4(70%)	2(66.7%)	<0.001**
8)Hemorrhagic manifestation	19(35%)	8(100%)	7(100%)	<0.001**

Table 5: Comparison of liver enzymes in dengue subgroups

Variables	Diagnosis			'p' value
	DF (n=85)	DHF (n=8)	DSS (n=7)	
Aspartate amino transferase (AST) (0 - 42 U/L)				
• <1ULN	2(2%)	0 (0%)	0 (0%)	<0.001**
• 1-3ULN	38 (44.7%)	0 (0%)	0 (0%)	
• 3-10ULN	45 (52.2%)	8 (100%)	0 (0%)	
• >10ULN	0(0%)	0 (0%)	7 (100%)	
Alanine amino transferase (ALT) (0 - 48 U/L)				
• <1ULN	7 (8%)	0 (0%)	0 (0%)	<0.001**
• 1-3ULN	23 (27%)	0 (0%)	0 (0%)	
• 3-10ULN	55 (64.7%)	8 (100%)	0 (0%)	
• >10ULN	0 (0%)	0 (0%)	7 (100%)	
Alkaline phosphatase (ALP) 20 - 125 U/L				
• <1ULN	50(58.8%)	2(25%)	0(0%)	<0.001**
• 1-2ULN	32(37.6%)	5(62.5%)	4(57%)	
• >2ULN	3(3.5%)	1(12.5%)	3(43%)	

Table 6: Comparison of LFT levels with hemorrhagic manifestations

Liver functiontest (LFT)	Hemorrhagic Manifestations		'p' value
	No	Yes	
Total bilirubin	0.83±0.40	1.98±1.3	<0.001**
AST	206.11±68.78	365.95±310.5	<0.001**
ALT	115.38±52.57	278.4±278.2	0.001**
ALP	110.34±82.42	168.7±86.4	0.202
Total protein	6.72±0.45	5.56±0.92	<0.001**
S Albumin	3.35±0.34	3.10±0.78	0.002**

Table 7: Comparison of clinical signs in DF and DHF

Variables	DF (n=137)	DHF (n=20)	'p' value
Age in years	36.23±13.78	32.9 ± 7.54	0.530
Temperature (ºF)	98.02 ± 7.70	98.6 ± 0.00	0.938
Pulse (beats/min)	79.97 ± 9.71	86.2 ± 11.70	0.026*
SBP (mm of Hg)	117.46 ± 9.42	119.4 ± 13.61	0.693
DBP (mm of Hg)	74.96 ± 6.54	76±9.40	0.803
RR (breath/min)	18.20 ± 2.30	18.95±1.43	0.321

Table 8: Comparison of clinical signs in DF and DSS

Variables	DF (n=137)	DSS (n=9)	'p' value
Age in years	36.23±13.78	34.00±6.63	0.870
Temperature(ºF)	98.02±7.70	99.73±0.98	0.761
Pulse (beats/min)	79.97±9.71	108.44±9.32	<0.001**
SBP (mm of Hg)	117.46±9.42	82.50±7.07	<0.001**
DBP (mm of Hg)	74.96±6.54	62.22±4.41	<0.001**
RR (breath /min)	18.20±2.30	20.67±1.41	0.003**

DISCUSSION

Dengue fever is a common viral illness throughout the world. Classical Dengue fever carries less mortality and less rate of complications as compared to dengue fever and dengue shock syndrome which are more severe forms of illness.

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Studies have shown that dengue fever affects the reticulo-endothelial cells, thus liver involvement is a well-known feature of dengue virus infection.

In this study, we have determined the changes in liver enzymes in the course of acute dengue infection and also the relationship of liver involvement with the degree of viraemia, onset and extent of fluid leakage and levels of cytokines.

AST and ALT are considered as indicators of liver cell injury as they are released into the circulation following infection.

In this study, DHF and DSS were present in 8% (8/100) and 7% (7/100) patients respectively. This is as with the results of a recent study from Punjab done by Rajoo et al,[3] (DHF and DSS in 13.6% and 5.1% respectively) and from Delhi done by Makroo et al,[4] (DHF and DSS in 9.3% and 2.2% respectively). However a few other studies had reported a higher percentage of DHF.

The mean age of patients in our study was 29.3 ± 13.7 years, with male to female ratio being near equal. In a recent study done by Rajoo et al mean age was 31.6 years with a range of 15 to 80 years, with predominant male patients (male: female ratio = 3.3:1).

Jaundice in dengue infection has been associated with fulminant liver failure and by itself is a poor prognostic factor. In our study hyperbilirubinemia was significantly morecommon in patients with DSS and DHF when compared to DF patients with or without hemorrhage. Rajooetal. found Hyperbilirubinemia to be significantly more common in patients with DSS, DF patients with hemorrhage and in non- survivors. Thus, observations support the fact that high bilirubin may act as a bad prognostic marker in patients with dengue infection.

Hepatomegaly was observed in 13% patients in this study, compared to 12.1% in Rajoo et al. and 17.6% - 20.4% in other Indian studies. The relative higher incidence of hepatomegaly reported by Sharma et al,[5] could be attributed to the fact that all their patients belonged to the DHF group. Although liver size does not correlate with disease severity, an enlarged liver is observed more frequently in shock than in non-shock cases. In our study, too, hepatomegaly was more frequent in the DSS group as compared to DF group (71.4 %; 5/7 v/s 25%; 2/8).

Biochemical liver dysfunction, in the form of increased transaminases, was found in most of the patients in our study 89-98%, similar to the results of Rajoo et al. (93.9%–97.7%) and other studies. However, in a study by Souza et al.[6]

AST and ALT were deranged only in 63.4% and 45% patients respectively. In our study, increased levels of ALP and serum bilirubin were noted in a smaller proportion of patients, as with the results of Rajoo et al. and Itha et al.[7]

The aspartate amino transferase (AST) levels in dengue infection tend to be greater than alanine aminotransferase (ALT) levels. In our study too, aspartate amino transferase (AST) levels (269 ± 228.5 U/L) tend to be greater than alanine amino transferase (ALT) levels (187±196.5U/L). This pattern is similar to that we see in alcoholic hepatitis but differs from that seen in other viral hepatitis. The exact cause of this is uncertain, but it has been suggested that it may be due to excess release of AST from damaged myocytes during dengue infection. This preferential elevation of liver enzymes, with AST being significantly higher than ALT was also noted in study done by Rajoo et al. This abnormality may act as an early indicator of dengue infection. Comparing the three subgroups of dengue infection (DF, DHF and DSS), it was observed that the frequency of liver dysfunction (raised AST, ALT and ALP) was equally common in all the groups Similar results were noted in Itha et al.

However, Wahid et al,[8] found liver dysfunction to be more common in DHF than in DF patients. The severity of hepatic dysfunction in dengue infection has been associated with disease severity. Indeed, liver injury has been proposed to be a good positive predictive factor for the development of DHF.

We noted a greater degree of hepatic injury in the DHF & DSS group (significantly deranged liver parameters) as compared to the DF group, suggesting that the degree of liver injury may be related to the severity of dengue infection. Similar data have been suggested by Souza et al. However, in two other studies, the degree of elevation of liver enzymes in the DF and DHF groups was not significantly different.

In our study, the mean bilirubin, AST, ALT, total protein, albumin and coagulation profile values were significantly deranged in patients with hemorrhage as compared to those without. Rajoo et al. observed that the mean bilirubin, ALT and ALP values were significantly higher in patients with hemorrhage as compared to those without hemorrhage, and were even higher in those with GI hemorrhage. Wahid et al, also observed that the ALT and ALP levels were significantly higher in DHF patients with spontaneous bleeding than those without bleeding ($p<0.05$), while Nguyen et al,[9] noted significantly higher elevation of AST and ALT in DHF patients with gastrointestinal hemorrhage. A possible reason for this could be an ischemic injury to the liver due to hypotension.

In the present study, AST and ALT levels was significantly higher in patients with sequential dengue infection as compared to those with primary infection. Rajoo et al., observed that the mean bilirubin, ALT and ALP values were significantly higher in patients with sequential dengue infection as compared to those with primary infection, while the mean AST value in the two groups was similar. Nguyen et al, observed that the results of transaminases did not differ significantly between the two groups, while Souza et al. noted that transaminases were significantly higher in cases with sequential infection.

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Serum amino transferase elevation is seen in all patients with dengue infection, directly correlating with severity of infection.

Limitation of the study is Ns1Ag (non-structural protein) test could not be done due to non-availability of kit during the study period.

CONCLUSION

1. Serum amino transferase levels are significantly raised in all forms of dengue infection and it directly correlates with severity of infection.
2. Serum as part ate amino transferase was significantly raised compared to alanine amino transferase levels in all forms of dengue infection.

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