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Original Research Article

Correlation of severity of dengue with serum aminotransferase levels

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ABSTRACT

Background: In dengue, association of fever (most common presenting symptom) with hepatic involvement can be relatively more serious. Such patients may have raised serum aminotransferase levels as well as can be more prone to bleeding due to deranged liver functions. Thus, the present study was conducted with an objective to correlate these enzyme levels with the severity of dengue fever.
Methods: This prospective, observational study was carried out for 1.5 years at a tertiary care teaching hospital in southern Rajasthan after ethics committee approval. Those patients diagnosed with dengue, admitted at this tertiary centre, aged 18 years and above and willing to give consent for participation, were included in the study. Patients were assessed for clinical features of dengue along with both laboratory and radiological investigations. Severity of dengue was correlated with aminotransferase levels. Data analysis was carried out using appropriate statistical tests.
Results: Total 200 patients were analysed. Mean age was 36.92±14 years while male: female ratio was 1.23:1 in the study population. All patients (100%) had fever whereas shock and bleeding tendency were noted in 16 (8%) and 4 (2%) patients respectively. Majority 130 (65%) patients had moderate dengue. Raised aminotransferase levels were noted in approximately 65% study patients out of which nearly 40% patients had moderate dengue. Correlation of raised aminotransferase levels with thrombocytopenia, shock, bleeding tendency were not statistically significant.
Conclusions: Serum aminotransferase levels were elevated in moderate dengue patients. However, there was no significant correlation of raised enzyme levels with thrombocytopenia, presence of shock and bleeding tendency or as the severity of dengue increases. Thus, it is quite subjective whether to predict severity of dengue from raised enzyme levels or not.

Keywords: Bleeding tendency, Dengue, Liver function test, Serum aminotransferase, Shock

INTRODUCTION

Dengue is an acute, mosquito-borne viral infection, characterized by a wide spectrum of clinical features such as fever, headache, retro-orbital pain, bleeding tendencies, shock etc. Its incidence has reached upto100-400 million infections per year over the last decade, leading to an increased global burden.[1] For Asian-Pacific population, the risk of dengue infection is nearly 70%.[1]

Dengue patients may present either with mild/asymptomatic infection or atypical manifestations such as central nervous system involvement/cardiac alterations/ elevated aminotransferase (also known as transaminase) levels which are relatively more severe.[2] The laboratory finding of elevated aminotransferases [serum glutamic oxaloacetic transaminase (SGOT)-also known as aspartate transaminase (AST); serum glutamic pyruvic transaminase (SGPT)-also known as alanine transaminase (ALT)] is mainly due to reactive hepatitis and hepatic parenchymal damage by the virus itself.[3] These levels usually peak between day 7-10 after onset of symptoms and normalize within three weeks. The hepatic histopathological findings of centrilobular necrosis, fatty alterations, hyperplasia of Kupffer cells and monocyte infiltration of portal tract have also been noted in patients

with dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4] They are prone to an increased risk of bleeding tendency due to deranged liver function. Thus, severe dengue can be potentially life-threatening.

The inclusion of liver function test as a standard of care for the management of dengue fever thus improves patient's prognosis. There is paucity of related data from southern Rajasthan and such a study has never been conducted at this tertiary care teaching hospital. Hence, the present study was envisaged with an objective to measure serum aminotransferase levels in dengue patients as well as to correlate these levels with the severity of dengue fever.

METHODS

After obtaining institutional ethics committee approval, this prospective, observational study was conducted from January 2019 to June 2020 at a tertiary care teaching hospital of southern Rajasthan, India.

Those patients diagnosed with dengue infection (clinically and serologically-ELISA positive), admitted in intensive care unit (I.C.U.) or medicine ward of this tertiary centre, aged 18 years and above as well as willing to give written informed consent for participation were included in the study whereas those with chronic liver disease, viral hepatitis (Hepatitis A, B and C), malaria, scrub typhus, leptospirosis, typhoid, history of alcohol abuse and use of acute or chronic hepatotoxic drugs were excluded.

After a detailed history taking and thorough clinical examination, patients were assessed for duration of fever, bleeding tendency if any, history of hepatitis or alcohol abuse at the time of admission. Laboratory and radiological investigations such as complete blood count, plasma glucose, liver and renal function test, fever profile, antibodies for viral hepatitis, serology for dengue, scrub typhus and leptospira, chest X-ray, and abdominal sonography were also carried out.

For assessment of severity, dengue was classified into mild, moderate and severe categories.[5] Here, presence of warning clinical features among dengue patients such as recurrent vomiting, abdominal pain, minor bleeding, pleural effusion, ascites, hepatomegaly was considered to be indicators of severity and few of these were also correlated with aminotransferase levels.

After entering the data into Microsoft excel 365, statistical analysis was done using IBM statistical package for social sciences (SPSS) v27. Descriptive analysis was done using mean, standard deviation (S.D.), ratio and proportion with percentage (%). The quantitative data was analysed using independent student's t-test, Pearson correlation coefficient and ANOVA test. P value<0.05 was considered as statistically significant.

RESULTS

A total of 200 patients were analysed. Mean age was 36.92±14 years while male: female ratio was 1.23:1 in the study population. Majority patients (34%) were young adults aged 31-40 years whereas 5% patients belonged to 51-60 and 61 and above age groups each (Figure 1).

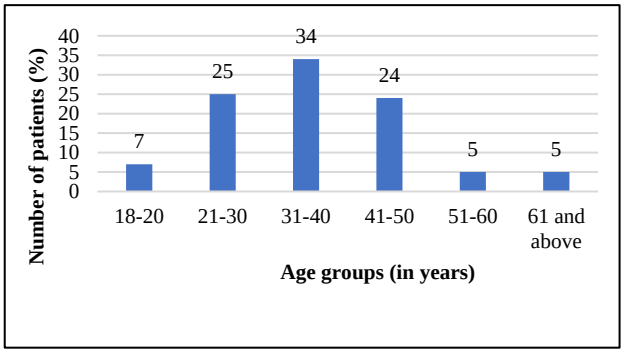

Figure 1: Age distribution of patients (n=200).

Fever was noted in 100% of the patients. Out of 200 patients; 30% and 15.5% had vomiting and hepatomegaly while 8% were in shock and 2% had bleeding tendencies (Table 1).

Table 1: Clinical features among all the dengue patients (n=200).

Clinical features	Total number of patients n (%)
Fever	200 (100)
Headache	146 (73)
Myalgia	123 (61.5)
Vomiting	60 (30)
Abdominal pain	50 (25)
Hepatomegaly	31 (15.5)
Pallor	31 (15.5)
Icterus	24 (12)
Rash	22 (11)
Pleural effusion	20 (10)
Ascites	16 (8)
Shock	16 (8)
Raised haematocrit	14 (7)
Multi-organ dysfunction syndrome	5 (2.5)
Bleeding	4 (2)

27, 65 and 8% patients out of 200 had mild, moderate and severe dengue respectively. Raised SGOT and SGPT levels were noted in 67.5 and 66% patients respectively. Mean SGOT levels were 152.02±254.83, 189.12±303.31 and 238.69±382.40 IU/l respectively while mean SGPT levels were 122.09±149.65, 149.73±216.22 and 141.88±148.90 IU/l in mild, moderate and severe dengue patients respectively. The p value was not statistically significant.

Among 200 dengue patients, maximum 44 and 42.5% patients with moderate dengue had raised SGOT and SGPT levels respectively whereas only 5% patients with severe dengue had raised SGOT and SGPT levels each (Table 2).

Out of 200 dengue patients, 46% had thrombocytopenia.

Among these 46% patients, 17% had raised SGOT levels and 16% had raised SGPT levels. Similarly, out 54% dengue patients with normal platelet count, 39% and 38.5% patients had raised SGOT and SGPT levels respectively (Table 3).

Table 2: Severity of dengue and aminotransferase levels among dengue patients.

Severity of dengue	Total number of dengue patients (N=200) (%)							
	For SGOT[#] levels (IU/l)				For SGPT[#] levels (IU/l)			
	Normal[$]	Less than 3 times (35-120)	3-10 times (121-400)	More than 10 times (>400)	Normal[$]	Less than 3 times (45-120)	3-10 times (121-400)	More than 10 times (>400)
Mild	8.5	10	7.5	1	8.5	10	7.5	1
Moderate	21	23.5	16	4.5	22.5	22	15	5.5
Severe	3	1.5	3	0.5	3	1.5	3	0.5
P value*	0.80				0.68			

*Note: *P value-statistically nonsignificant; [#]SGOT=serum glutamic oxaloacetic transaminase; [#]SGPT=serum glutamic pyruvic transaminase; [$]Normal range of SGOT=0 to 35 IU/l and SGPT=0 to 45 IU/l.[6]*

Table 3: Platelet count and aminotransferase levels among dengue patients.

Range of platelet count (cells/mm^3)	Total number of dengue patients (N=200) (%)							
	For SGOT[#] levels (IU/l)				For SGPT[#] levels (IU/l)			
	Normal[$]	Less than 3 times (35-120)	3-10 times (121-400)	More than 10 times (>400)	Normal[$]	Less than 3 times (45-120)	3-10 times (121-400)	More than 10 times (>400)
Less than 20,000	4.5	2.5	3.5	0	4.5	2.5	3.5	0
21,000 to 40,000	2.5	3	1.5	1	2.5	3	1.5	1
41,000 to 1,50,000	10.5	9	5.5	2.5	11.5	8	5	3
More than 1,50,000	15	20.5	16	2.5	15.5	20	15.5	3
P value*	0.52				0.40			

*Note: *P value-statistically nonsignificant; [#]SGOT=serum glutamic oxaloacetic transaminase; [#]SGPT=serum glutamic pyruvic transaminase; [$]Normal range of SGOT=0 to 35 IU/l and SGPT=0 to 45 IU/l.[6]*

Table 4: Shock, MODS and bleeding tendency with aminotransferase levels among dengue patients.

Warning clinical features among dengue patients		Total number of dengue patients (N=200) (%)							
		For SGOT[#] levels (IU/l)				For SGPT[#] levels (IU/l)			
		Normal[$]	Less than 3 times (35-120)	3-10 times (121-400)	More than 10 times (>400)	Normal[$]	Less than 3 times (45-120)	3-10 times (121-400)	More than 10 times (>400)
Shock	Present	4	2	1.5	0.5	4	2	1.5	0.5
	Absent	28.5	33	25	5.5	30	31.5	24	6.5
	P*	0.47				0.57			
MODS[@]	Present	1	0.5	1	0	1	0.5	1	0
	Absent	31.5	34.5	25.5	6	33	33	24.5	7
	P*	0.78				0.77			
Bleeding tendency	Present	1.5	0	0	0.5	1.5	0	0	0.5
	Absent	31	35	26.5	5.5	32.5	33.5	25.5	6.5
	P*	0.06				0.09			

*Note: *p value-statistically nonsignificant; [#]SGOT=serum glutamic oxaloacetic transaminase; [#]SGPT=serum glutamic pyruvic transaminase; [@]MODS=multi-organ dysfunction syndrome; [$]Normal range of SGOT=0 to 35 IU/l and SGPT=0 to 45 IU/l.[6]*

Out of 8, 2.5 and 2% dengue patients presenting with warning clinical features (shock, MODS and bleeding tendency respectively); 4, 1.5 and 0.5% patients had raised enzyme levels respectively (Table 4). Mean SGOT levels in patients with shock, MODS and bleeding were 183.07±297.47, 134.4±140.77 and 212.25±384.5 respectively. Similarly mean SGPT levels in those patients were 141.64±195.16, 138.8±128.77 and 223±395.36 respectively.

DISCUSSION

Dengue infection is a global public health concern, especially for the developing nations. In India, round the year transmission is noted in the south and from April to November in the north.[7] It consists of a wide spectrum of clinical features as mentioned above. Those having hepatic involvement (a warning clinical feature) may present with hepatomegaly (clinically) or raised liver enzyme levels (biochemically).[8] Since the data on similar background is scarce from southern Rajasthan, the present study was planned and conducted to correlate the severity of dengue with aminotransferase levels at our tertiary centre.

The present study in dengue patients showed a male predominance. Studies by Pandey and Ayaz et al also showed that dengue infection was higher in males than in females.[9-10] Among 200 dengue patients of present study, majority were young adults (31-40 years and 21-30 years) with a mean age of 36.92±14 years. Similarly, a study by Jnaneshwari et al showed that mean age of 166 dengue patients was 35.71±12.9 years with maximum patients in 21-30- and 31-40-years age groups.[4] This can be attributed to the biological and gender-related factors which can change over human life-span and also differ across countries.[11]

In the present study, fever was the most common presenting symptom among dengue patients at the time of hospital admission. It was also associated with warning clinical features such as vomiting, abdominal pain, hepatomegaly, ascites, shock, MODS and bleeding in less than 30% of the study population. Studies by Verma and Pandey et al also showed a similar pattern of clinical features where 100% patients had presented with fever.[8-9] This indicates that in spite of its wide range, clinical features may or may not vary greatly among dengue patients but will always be associated with fever in a majority (~100% patients). When classified as per Indian national guidelines for clinical management of dengue fever, majority patients had moderate severity of dengue infection.[5] These guidelines are currently being used for clinical management of dengue cases in our country.

Approximately 15% dengue patients in our study had hepatic involvement. However, laboratory investigations showed raised serum aminotransferase (SGOT and SGPT) levels in nearly 65% of the study patients. The mean SGOT and SGPT levels were raised up to 3-10 times (121-400 IU/l) the normal range in these 65% dengue patients. Similarly, 80% of 50 dengue patients in Balakumar et al study and nearly 60% of 1585 dengue patients in Souza et al study had elevated SGOT and SGPT levels.[12-13] The findings from Verma et al study slightly differed, where mean SGOT and SGPT levels were 396±746 IU/l and 285±460 IU/l respectively (up to >10 times higher the normal range).[8] These abnormal laboratory findings in dengue are probably due to the aggression of the virus or hepatotoxicity of the drugs.[13]

With respect to correlation of severity of dengue with raised serum aminotransferase levels, approximately 40% dengue patients with moderate severity had raised enzyme levels. Nearly 20% of these had raised SGOT and SGPT levels up to less than 3 times the normal range (upper limit of normal range to 120 IU/l). Only one patient with severe dengue had raised enzyme levels up to more than 10 times (>400 IU/l) the normal range. These results indicated that the severity of dengue was associated with raised serum aminotransferase levels. However, the results were statistically not significant. Jnaneshwari et al has also mentioned that aminotransferase levels appear to have a directly proportional correlation with grading of dengue infection.[4] One of many such studies also indicated that the presence of severity of dengue in most of their study patients was evidenced by increased level of serum transaminases.[12]

Few clinical features (that indicate the severity of dengue) such as platelet count, presence of shock (DSS) and bleeding tendency (DHF); were also analysed and correlated with serum aminotransferase levels. Thrombocytopenia was found in nearly half of the study patients out of which ~15% had raised aminotransferase levels. Contrary to this, 40% from remaining half of the study patients with normal platelet count had raised SGOT and SGPT levels. However, it was not found significant. Few studies showed thrombocytopenia in a greater number of patients as compared to our study, but the trend of decrease in platelet count was similar.[9,14]

Nearly half of the dengue patients that had presented with shock and bleeding tendency also had elevated enzyme levels. The mean SGOT and SGPT levels in-patients with shock and bleeding tendency were slightly more as compared to mean values among all dengue patients of the present study. However, there was no significant correlation. These findings were in accordance to results from Wahid et al study where elevated enzyme levels were observed more frequently in DHF compared to dengue fever.[15] It was observed with Chhina et al study that number of patients with raised SGOT and SGPT levels in DHF and DSS were lower as similar however, mean enzyme levels were significantly different which could be due to patients with hepatitis and other liver pathology not getting excluded.[16] In a study by Chaudhuri et al, it was also observed that patients with 10 folds increase in SGOT and SGPT levels were more prone for dengue shock syndrome and bleeding manifestations.[17] Thus, the results are quite varied in different studies.

This study has few limitations; type of dengue virus among study patients was not analysed. Data on number of days to peak in SGOT and SGPT levels among mild, moderate and severe dengue patients was not analysed.

It has been noted that the dengue fever has distinct epidemiological patterns. Thus, such studies exploring the profile of dengue fever patients should be planned and conducted frequently at regular intervals. Data from those studies can add more accuracy to the Indian data. The extent of global burden can be estimated as well.

CONCLUSION

In the southern Rajasthan region, male population and young adults were more prone to dengue fever. Fever was the most common presenting feature with a majority having moderate dengue infection. Raised serum aminotransferase levels in dengue patients with thrombocytopenia, presence of shock or bleeding tendency was found, however not significantly correlated with severity of dengue. So, whether to use serum aminotransferase levels to predict the severity of disease is subjective and dependent upon epidemiology as well as profile of dengue fever which is quite varied.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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