ORIGINAL RESEARCH PAPER

General Medicine

A CROSS- SECTIONAL STUDY REGARDING ASSESSMENT OF SERUM AMINOTRANSFERASE LEVEL IN SEVERITY OF DENGUE FEVER IN ONE OF THE TERTIARY CARE HOSPITALS OF NORTHERN INDIA

KEY WORDS:
Aminotransferase, Dengue Fever, Dengue Hemorrhagic Fever, Dengue Shock Syndrome

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ABSTRACT

Background: Dengue fever (DF) is the most common arbovirus-related infection worldwide. Most of the dengue infections are asymptomatic. The clinical presentation of DF varies from mild febrile illness to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Both DHF and DSS are severe forms of illness and carry higher rates of mortality. Various clinical parameters are associated with severe DF. The objective of this study was to determine any relation between elevated alanine aminotransferase (ALT) levels at presentation and development of severe DF. **Material and Methods:** This cross-sectional study was carried out at a tertiary care hospital in Lucknow from January 2021 to July 2022. Total 100 dengue patients having age >18 years were enrolled and their ALT levels were recorded at presentation after receiving consents from them. All the patients were managed as per guidelines in a similar way, and clinical course was followed for the development of severe forms of DF, such as DHF and DSS. Results: Fever, Headache, Myalgia, Vomiting, Abdominal Pain were some of the most presenting features among the study participants. The mean value of ALT level was 100.3±102.1. Patients having DHF and DSS were having higher levels of ALT as compared to DF patients, which was also statistically associated with p Value < 0.05 using Chi square test. **Conclusion:** Higher serum levels of ALT at presentation can give a clue about possibility of progression to severe forms of DF (DHF and DSS). Therefore, patients with higher ALT at presentation should be prioritized and monitored more rigorously.

Introduction:

Dengue fever (DF) is the most common arbovirus borne infection worldwide, and its incidence is increasing continuously throughout the globe.[1] Approximately, 50-100 million cases occur annually with around 10,000 dengue deaths per annum.[2]

Most of the dengue infections are asymptomatic. The clinical presentation of DF varies from mild febrile illness to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[3] The classical DF is mild, febrile illness, while on the other hand DHF is characterized by high-grade fever, increased vascular permeability, plasma leakage, and hemorrhagic manifestations which if accompanied by shock is termed as DSS. Both DHF and DSS are severe forms of illness and carry higher rates of mortality. [4] Various clinical parameters and laboratory investigations, such as leukocyte count, prothrombin time, activated partial thromboplastin time, alanine aminotransferase (ALT) levels, aspartate aminotransferase levels, and hematocrit levels, have been studied internationally to forecast severity of infection.[3,5]Liver is not the major target organ of dengue virus, but hepatic involvement can occur due to a direct viral effect on hepatic cells or due to dysregulated immune response of the body.[6,7]
In past, many national and international studies have been done to evaluate the role of liver function tests in forecasting the severity of DF. However, there was a paucity of data, pertaining specifically to relationship between elevated ALT levels and development of DHF and DSS. Early identification of DHF and DSS patients can be very crucial in resource-limited setups as these patients can be saved by strict monitoring and early aggressive management. ALT levels being widely available and inexpensive can be very useful in such less resourceful setups. Therefore, this study was designed with an objective to assess the utility of ALT as a marker of severe DF.

Materials and Methodology:

This cross-sectional study at Department of Medicine, Career Institute of medical sciences. After approval from ethical committee and obtaining written and informed consent from all patients, the study was done over a period of 18 months from January 2021 to July 2022. A total of 100 patients patients diagnosed with dengue infection of either sex between the age group of 18-60 years were included in this study.

Method of collection of data:

Those patients diagnosed with dengue infection (clinically and serologically-ELISA positive), admitted in intensive care unit (I.C.U.) or medicine ward of Career Institute of Medical Sciences, 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 fever, duration of fever, frontal headache, retro-orbital pain, back pain along with Severe myalgia's, Weakness, bleeding tendency if any, transient macular rash & petechial such as duration of disease, medication, personal history and history pertaining to the other comorbid conditions like history of hepatitis or alcohol abuse at the time of admission were recorded. Laboratory and radiological investigations such as complete blood count, plasma glucose, liver and renal function test, fever profile, antibodies for viral hepatitis, GBP for malaria, Widal or typhi dot, HBsAg, HCV, 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. 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.

Ethical clearance

The research procedure followed was in accordance with the approved ethical standards of Career Institute of Medical Sciences, Lucknow, UP, India Ethics Committee (Human).

Statistical analysis

Data was analyzed and evaluated using Statistical Package for Social Sciences, version 23 (SPSS Inc., Chicago, IL). Results for continuous variables are shown as mean ± standard deviation (SD), whereas results for categorical variables are shown as number (percentage). For comparison of nominal data, chi-square (2) test was used. The level P < 0.05 was considered as the cut-off value or significance.

Observation/Results:

Majority 36 (36.0%) patients were belonged to 31-40 age group followed by 32 (32.0%), 16 (16.0%), 10 (10.0%) and 6 (6.0%) patients were belonged to ≤30, 41-50, 51-60 and >60 age group respectively. Total 54 (54.0%) patients were male and 46 (46.0%) patients were female. In presenting symptoms, all 100 (100.0%) patients had fever followed by 73 (73.0%), 62 (62.0%), 33 (33.0%), 26 (26.0%), 16 (16.0%), 15 (15.0%), 13 (13.0%), 11 (11.0%), 9 (9.0%), 9 (9.0%), 7 (7.0%), 6 (6.0%), 3 (3.0%) and 2 (2.0%) patients had Headache, Myalgia, Vomiting, Abdominal Pain, Pallor, Hepatomegaly, Rash, Icterus, Pleural effusion, Shock, Ascites, Raised haematocrit, Multi organ dysfunction syndrome and Bleeding respectively.

Majority 67 (67.0%) patients had moderate dengue followed by 26 (26.0%) and 7 (7.0%) patients had mild and severe dengue respectively. The mean value of studied patients based on blood parameters TLC, ALT, AST, PT & APTT was 4.7±2.2, 100.3±102.1, 234.2±136.1, 16.8±3.6 and 34.4±1.7 respectively. That in SGOT normal level majority 18 patients had moderate dengue followed by 14 and 1 patients had mild and severe dengue respectively. In SGOT 35-120 IU/l majority 23 patients had moderate dengue followed by 8 and 1 patients had mild and severe dengue respectively.

The association between SGPT level and Severity of dengue of the studied patients was found to be statistically non-significant (p>0.05). It was observed that association between clinical profile and severity of dengue of the studied patients was found to be statistically significant (p<0.05) except fever, pleural effusion and raised haematocrit clinical profile. The association of complications with severity of dengue was found to be statistically significant (p<0.001). The association between Platelets count and Severity of dengue of the studied patients was found to be statistically significant (p<0.05).

Table 1: Distribution of the studied patients based on the association of clinical profile with the severity of dengue

Clinical Profile	Severity of Dengue			p-value
	Mild (n=26)	Moderate (n=67)	Severe (n=7)	
Fever	26	67	7	1.00
Headache	6	60	7	<0.001
Myalgia	2	56	6	<0.001
Vomiting	1	25	7	<0.001
Abdominal Pain	0	19	7	<0.001
Hepatomegaly	0	9	6	<0.001
Pallor	0	10	6	<0.001
Icterus	0	5	6	<0.001
Rash	2	6	5	<0.001
Pleural effusion	0	7	2	0.049
Ascites	0	4	3	<0.001
Shock	1	4	4	<0.001
Raised haematocrit	1	3	2	0.033
Multi-organ dysfunction syndrome	0	0	3	<0.001
Bleeding	0	1	1	0.049

Graph 1: Distribution of the studied patients based on the association of complications with mild dengue

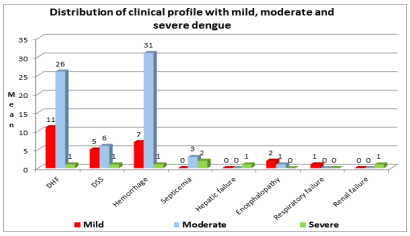

Table 2: Comparison of ALT in dengue subgroups

Variables	Diagnosis			p-value
	DF (n=83)	DHF (n=12)	DSS (n=5)	
ALT (0-48 U/L)				
<1 ULN	2 (2.4)	0 (0.0)	0 (0.0)	<0.001
1-3 ULN	17 (20.5)	0 (0.0)	0 (0.0)	
4-10 ULN	64 (77.1)	11 (91.7)	0 (0.0)	
>10 ULN	0 (0.0)	1 (8.3)	9 (100.0)	

Discussion:

In the present study the majority of the studied patients were in the age group ranging from 31-40 years (36.0%) followed by less than 30 years (32.0%) with mean age 37.82±1.9 years and male predominance (54.0%). This can be attributed to the biological and gender-related factors which can change over human life-span and also differ across countries. Our findings were in accordance with the findings of Moolrajani K and Jain A who reported that in their study males (61.0%) to female (39.0%) ratio was 1.56:1 and the mean age of patients was 38 ± 6.2 years. There was no patient in the present study who aged less than 15 years of age.[8]

In our study the distribution of the cases was don on the basis of clinical features and it was found that all the studied cases were having fever (100.0%) followed by headache (73.0%), myalgia (62.0%), vomiting (33.0%) and abdominal pain (26.0%), pallor (16.0%), hepatomegaly (15.0%), rashes (13.0%) and bleeding in 2.0%. Our findings were consistent with the findings of Balakumar J et al who reported that all the patient had fever as a presenting complaint. Most of them had myalgia at the time of presentation.[9] According to Javed S et al fever was noted in 100.0% of the patients. Of 200 patients; 30.0% and 15.5% had vomiting and hepatomegaly while 8.0% were in shock and 2.0% had bleeding tendencies.[10]

In this study the cases were divided on the basis of severity of dengue and it was found that the majority of the studied cases were having moderate dengue (67.0%) followed by mild dengue (26.0%) and severe dengue in 7.0% cases. Our findings were comparable to the findings of Javed S et alwho reported that 27.0%, 65.0% and 8.0% patients out of 200 had mild, moderate and severe dengue respectively.[10] Moolrajani K and Jain A found that out of total study participants 27% patients had mild symptoms, 60% patients had moderate symptoms and 13% had severe dengue fever.[8]

Shivkar RR et al in their study concluded that transaminase levels increase in almost all dengue patients.[11] The rise in AST and ALT level increases with increase in dengue severity which is indicated by fall in platelet count as they are negatively correlated with each other. In our study also 32 patients had reduced platelet count (less than one lakh) and all the 32 patients had elevated serum aminotransferase level which indicates the increase in severity. Kulkarni V et al reported that the aspartate aminotransferase levels were found to be greater than alanine aminotransferase levels and hepatic dysfunction in the form of raised transaminase levels was severe in secondary dengue cases with only 2.0% of them having normal transaminase levels and 40% having transaminases raised >3 times and around 14.5% having

transaminases raised more than 10 times the normal as compared to 7.0% in primary dengue cases.[12]

Recommendations of the study

Liver function tests should be used as routine initial part of the investigative studies in a patient with suspected dengue fever. Serial monitoring of liver function tests, especially alanine transaminase (ALT), should be done to identify high-risk cases.

Conclusion:

Hepatic involvement is common in dengue fever. It is characterized by elevated liver enzymes, AST more than ALT levels. Elevated liver enzymes are associated with complications like bleeding, shock and organ impairment. In addition to thrombocytopenia, hepatic involvement plays a significant role in bleeding. Elevated live enzymes have got prognostic value in this study. Hence, liver enzymes are mandatory in dengue fever to look for complications and it is of prognostic value. Those patients with elevated liver enzymes should be monitored carefully than those patients with normal liver enzymes.

REFERENCES:

1. The global burden of dengue: an analysis from the Global Burden of Disease study 2013. Stanaway JD, Shepard DS, Undurraga EA, et al. Lancet Infect Dis. 2016;16:712–723. [PMC free article] [PubMed] [Google Scholar]
2. Estimating dengue transmission intensity from sero-prevalence surveys in multiple countries. Imai N, Dorigatti I, Cauchemez S, Ferguson NM. PLoS Negl Trop Dis. 2015;9:0. [PMC free article] [PubMed] [Google Scholar]
3. Prognostic indicators for dengue infection severity. Pongpan S, Wisitwong A, Tawichasri C, Patumanond J. Int J Clin Pediatr. 2013;2:12–18. [Google Scholar]
4. Factors predicting severe dengue in patients with dengue fever. Khan MIH, Anwar E, Agha A, Hassanien NSM, Ullah E, Syed IA, Raja A. Mediterr J Hematol Infect Dis. 2013;5:0. [PMC free article] [PubMed] [Google Scholar]
5. Assessment of dengue fever severity through liver function tests. Ahmed A, Alvi AH, Butt A, Nawaz AA, Hanif A. https://pubmed.ncbi.nlm.nih.gov/25233967/ J Coll Physicians Surg Pak. 2014;24:640–644. [PubMed] [Google Scholar]
6. Biochemical alterations as markers of dengue haemorrhagic fever. Villar-Centeno LA, Diaz-Quijano FA, Martinez-Vega RA. Am J Trop Med Hyg. 2008;78:370–374. [PubMed] [Google Scholar]
7. Liver histopathology and biological correlates in five cases of fatal dengue fever in Vietnamese children. Huerre MR, Lan NT, Marianneau P, et al. Virchows Archive. 2001;438:107–115. [PubMed] [Google Scholar]
8. Moolrajani K, Jain A. Assessment of serum aminotransferase levels and its correlation with severity of dengue fever at tertiary care hospital. Int.J.Med.Sci.Educ 2020;7(1):84-89
9. Balakumar J, Balasubramaniyan S, Paari N. Study of serum Aminotransfersase levels in dengue fever and its correlation. JMSCR. 2019;7 (11):Page 36-41.
10. Javed S, Singh P, Paliwal SK. Correlation of severity of dengue with serum aminotransferase levels. Int J Adv Med 2021;8:415-9.
11. Shivkar RR, Padwal MK, Vaidya A. Correlation of Liver Transaminases with Platelet count in Dengue patients from Tertiary Care Hospital in Western India; Int J Cur Res. 2018;10(5):
12. Kulkarni V, Koppad B, Shetty MU. Profile of serum transaminases in patients with dengue infection in a tertiary care hospital. Int J Contemp Pediatr 2018;5:23-6