JPSIM Journal of Pakistan Society of Internal Medicine

Student Corner

Frequency of Transaminitis in Patient with Dengue Fever in First Five Days of Illness: A Hospital Based Survey

Javeria Benyamin, Sidra Anwar, Kamran Rauf

Fatima Memorial Hospital Shadman, Lahore.

Abstract

Objective: To determine the frequency of transaminitis in patients with documented dengue fever in first five days of illness and their association with the disease severity.

Methods: A retrospective cross-sectional observational study including 382 patients with confirmed dengue serology admitted in Department of Medicine of Fatima Memorial Hospital Lahore during July 2022-July 2023. Patient demographics, presenting symptoms, clinical signs, laboratory parameters such as complete blood count (CBC) and liver function tests (LFTs) were collected and frequency of transaminitis was determined in patients correlating with disease severity in the first five days of illness. Comparisons were drawn between age groups and gender. P-value <0.05 and CI 95% were considered during analysis.

Results: Out of 382 patients, only 275 had reported transaminitis which is approximately 72% of total population. Significant association was found between transaminitis and severity of disease.

Conclusion: Overall frequency of transaminitis in otherwise healthy patients (not having liver disease history) was statistically significant and accounted for almost two thirds of the dengue patients whereas one third of the patients did not have transaminitis. Statistical relationship between transaminitis and severity of disease was also noted.

Key words: Transaminitis, Dengue fever.

How to cite this:

Benyamin J, Anwar S, Rauf K. Frequency of Transaminitis in Patient with Dengue Fever in First Five Days of Illness: A Hospital Based Survey. J Pak Soc Intern Med. 2024;5(1): 441-445

Corresponding Author: Dr. Javeria Benyamin **Email:** javeriabenyamin222@gmail.com

DOI: https://doi.org/10.70302/jpsim.v5i1.2419

Tropic and subtropical regions are home to dengue fever, a mosquito-borne illness spread by the bite of an Aedes species mosquito. A person can contract the Dengue Virus (DENV) four times in their lifetime due to its four serotypes.1 A case of severe dengue is defined as follows: elevated transaminases ≥ 1,000 IU/L, impaired consciousness, involvement of the heart and other organs, severe bleeding, severe plasma leakage, or severe organ dysfunction. This classification of dengue is based on the World Health Organization (WHO) 2009 classifi-cation.[2] An estimated 390 million cases of the disease occur each year, putting 3 point 9 billion people in approxi-mately 128 countries at risk of contracting it.[3] Pakistan has experienced at least two confirmed outbreaks of the disease, the first occurring in 1994 and the second in 2005. Since then, outbreaks of dengue have been documented annually in a number of Pakistani regions, most notably Punjab.[4,5] Severe bleeding, encephalopathy, renal failure, and metabolic acidosis are among the symptoms of acute liver failure in dengue that are linked to a high global death rate.

Immune-mediated injury, oxidative stress, apoptosis, and reduced liver perfusion ultimately lead to liver involvement. Elevated levels of bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), and decreased albumin levels are all indicative of a worse prognosis when there is a derangement in liver function tests (LFTs). Comparing severe dengue cases to uncomplicated dengue cases, it is discovered that the median aspartate AST and ALT are significantly higher.[1] A retrospective analysis of 120 confirmed dengue cases that were admitted to an Indian medical facility was carried out by the researchers. The World Health Organization's classification was used to group patients into various disease severity categories. According to the study, dengue patients frequently had elevated levels of liver enzymes, specifically serum glutamic-oxaloacetic

transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT). More severe forms of the disease were also linked to hypoalbuminemia and a reversal of the albumin-to-globulin (A:G) ratio. The study highlights the potential of liver biomarkers as markers of disease severity and illuminates the complex relationship between dengue infection and liver function.[6]

Dengue fever is a widespread mosquito-borne viral illness that poses a significant public health challenge, particularly in tropical and subtropical regions. Despite efforts to control its spread and raise awareness, dengue remains a cause of substantial morbidity and mortality worldwide. Over the past decade, Pakistan has witnessed a surge in dengue cases, leading to outbreaks in various regions, including Punjab. One notable complication associated with dengue infection is liver involvement, often manifested by elevated levels of liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST). This phenomenon, termed "transaminitis," has been observed in dengue patients and has garnered attention due to its potential correlation with disease severity. Monitoring liver function is a routine part of managing dengue cases. Elevated liver enzymes, particularly in the form of transaminitis, could serve as a diagnostic and prognostic indicator for disease severity. While the correlation between transaminitis and dengue severity has been suggested in various studies, there remains a need for localized data. This study aims to address this gap by providing insights into the frequency of transaminitis in dengue patients within a specific population. By investigating the frequency of transaminitis and its association with disease severity, the study aims to provide valuable insights that can inform clinical practice, enhance patient care, and contribute to the broader efforts to combat dengue's impact on public health.

The aim for conducting this study in a private tertiary care hospital of Lahore is to assess the frequency of transaminitis in patients with documented dengue fever in first five days of illness and their association with the disease severity.

Methods

Research design: Retrospective Study

Research settings: Fatima Memorial Hospital Lahore

Study duration: July 2022 to July 2023

Inclusion criteria: All confirmed dengue patients admitted to hospital between the ages of 16-60 years of both genders.

Exclusion criteria:

- All patients who are known case of liver disease.
- Patient with acute hepatitis due to hepatitis in concomitant infection.
- Patients with fatty liver disease.
- Alcoholic Patients

Data Collection: A self-administered pre-structured questionnaire was developed containing biodata, history of disease other than dengue fever and detailed history of dengue fever containing CBC and LFTs were included in the questionnaire. Before data collection, patients were briefed about the purpose of study and confidentiality in collection of personal data was assured. Data was collected from all the reported dengue cases admitted in the medicine department during the mentioned duration

Data Analysis: SPSS version 26 was used for data entry and analysis. For every variable, a descriptive analysis was carried out. The frequency and percentage of the categorical variables were displayed. Quantitative variables, on the other hand, were displayed as means (SD). For the comparison, repeated measure ANOVA was used. P-values less than 0.05 were regarded as significant.

Ethical consideration: For ethical considerations synopsis has been approved by IRB committee of Fatima Memorial Hospital.

Confidentiality Statement: The research investigators declare that no information regarding any subject included in the study will be shared with anyone outside of the research team. All the information collected will be kept private. And that the anonymity of subjects will be maintained throughout the conduction and publication of research. No individual will be identified or mentioned by his/her name in any part of this project.

Results

Out of 382 patients, 275(72%) were positive for transaminitis whereas 107 patients (28%) did not have transaminitis as confirmed by lab reports (Table-1).

Regarding gender distribution, out of 382, 232 (60.7%) were male while 150 (39.3%) were female. Moreover, 137(49.8%) of male patients were positive for transaminitis whereas 138(50.2%) female patients were positive for transaminitis. Total age group ranged from 16-60 years with mean age group of 30.74±9.57 in patients positive for transaminitis and 41.27±16.22 in dengue patients with no transaminitis. A total of mean age group in all dengue patients was 38.32±18.89. Patients with transaminitis had a mean of 4.61±1.40 days of illness in comparison to those without transaminitis having a mean of 3.99±0.66. Collective mean of days of illness in all patients was 3.92±0.84(Table 2).

Haemoglobin (HB) concentration on 5th day of illness of transaminitis patients was 12.36±0.93 and in patients

without transaminitis it was 12.05±.051 whereas total was 12.349±1.276. Haematocrit (HCT) values on 5th day of illness in transaminitis patients was 37.044 ± 3.248, in patients without transaminitis it was 36.95± 1.02 and a total mean of HCT was 37.377±4.748. Total leukocyte count (TLC) on 5th day of illness in transaminitis patients was 4.637±1.95 and in patients with transaminitis was 7.34±3.37 with a total mean of 5.36± 2.88. Platelet (PLT) count in transaminitis patients was 52.97±38.45, in patients without transaminitis it was 37.087±2.043 and a total mean was 44.285±32.50 in all dengue patients. A decrease in trend for HB, HCT, TLC and Platelets was observed with increase in number of days of illness. Mean AST in transaminitis patients was 407.098±388.344, mean ALT in transaminitis patients was 290.505±264.109, mean bilirubin in transaminitis patients was 0.6977±0.339 and mean albumin in transaminitis patients was 3.559±0.499.

Table 1: *Frequency of transaminitis among patients.*

Transaminitis	Frequency(n)	Percentage (%)
Yes	275	72.0
NO	107	28.0

Discussion

In a study involving 382 patients, 72% tested positive for transaminitis, while 60.7% were male and 39.3% were female. Among males, 49.8% had transaminitis,

Table 2: *Comparative View of Presence and Absence of Transaminitis in Patients*

Variables		Transaminitis		Total	p-value
		Yes	No		
Gender [n (%)]	Male	137(49.8)	95(88.8)	232(60.7)	0.0001
	Female	138(50.2)	12(11.2)	150(39.3)	0.0001
Age in Years (Mean ± SD)		30.74±9.57	41.27±16.22	38.32±18.89	0.000
Day of Illness (Mean ± SD)		4.61±1.40	3.99±0.66	3.92±0.84	0.000

Table 3:

Variables		Transaminitis (Mean ± SD)		Total (Mean ± SD)	p-value
		yes	No		
HB	Day 1	14.05±1.096	13.20±1.292	13.52±1.156	.000
	Day 2	13.69±1.322	13.4±1.51	13.14±1.305	.101
	Day 3	13.27±1.56	13.3±1.45	12.618±1.76	.784
	Day 4	12.33±1.77	13.42±2.08	12.027±2.052	.000
	Day 5	12.36±0.93	12.05±.051	12.349±1.276	.113
HCT	Day 1	42.83±3.95	41.26±5.23	41.845±4.16	.002
	Day 2	41.53±4.228	40.768±4.586	40.233±3.707	.121
	Day 3	39.88±4.78	40.36±4.627	38.89±4.418	.377
	Day 4	37.257±3.248	36.956±1.02151	36.877±4.986	.000
	Day 5	37.044±3.248	36.95±1.02	37.377±4.748	.899
TLC	Day 1	7.058±4.46	5.43±2.45	6.14±3.77	.000
	Day 2	6.908±3.77	4.51±2.208	5.49±3.397	.000
	Day 3	6.46±3.11	4.29±1.56	5.27±3.009	.001
	Day 4	6.07±3.178	4.83±1.84	5.127±2.69	.000
	Day 5	4.637±1.95	7.34±3.37	5.36±2.88	.000
PLT	Day 1	61.71±44.74	110.02±74.29	97.44±65.39	.000
	Day 2	51.207±32.29	94.65±72.033	84.52±56.829	.000
	Day 3	39.829±24.191	84.32±65.46	74.167±54.191	.000
	Day 4	51.706±29.49	60.86±58.401	65.479±57.275	.085
	Day 5	52.97±38.45	37.087±2.043	44.285±32.50	.051
AST		407.098±388.344	80.729±56.473	183.94±235.869	.000
ALT		290.505±264.109	44.68±16.012	123.90±165.97	.000
Bilirubin		0.6977±0.339	0.7166±0.889	0.775±2.406	.763
Albumin		3.559±0.499	3.648±0.395	3.629±0.5	.101

and among females, 50.2% had transaminitis. The age range was 16-60 years, with transaminitis patients being younger. Transaminitis patients had a longer mean duration of illness (4.61±1.40 days) compared to those without (3.99 ± 0.66 days). Hb concentration, HCT values, TLC count, and platelet count were measured within 5 days of illness, with variations observed between transaminitis and non-transaminitis patients. An inverse relation between these parameters and number of days of illness was observed. Additionally, liver enzyme values (AST and ALT), bilirubin, and albumin levels were reported for transaminitis patients. These findings offer valuable insights into the prevalence and clinical features of transaminitis in dengue patients, including its associations with gender, age, illness duration, and haematological parameters.

Transaminitis has been the most common abnormality in dengue related hepatic involvement. 72% of population under study had transaminitis [table 1] which was in range with the Indian retrospective study. In which the raised AST levels was seen in 63-97% of patients, while raised ALT levels in 45-96% of patients. As sociocultural backgrounds and lifestyles of both the countries are alike so this ratio is understandable. Males with dengue were more in frequency to be reported with transaminitis in comparison to women [table 2] which is may be due to cultural barriers faced by women as they are neglected to seek the healthcare services still in our society. HB, HCT, PLT, TLC had decreasing trend in comparison to simultaneous increasing trend of ALT and AST which shows indirect relationship between them [figure3]. This is also suggestive from graphs [1,2,3,4] and is in correspondence with studies done on similar populations.[1] Hepatic involvement in dengue is a multifactorial process that includes direct viral replication in hepatocytes, immune-mediated damage, and alterations in coagulation factors.[7] The significant proportion of patients with transaminitis underscores the importance of monitoring liver function in dengue cases. The research also sheds light on gender distribution among dengue patients, revealing a slightly higher prevalence among males (60.7%) compared to females (39.3%). Interestingly, the study found no significant gender-based difference in the prevalence of transaminitis. This gender distribution aligns with previous epidemiological data, which have shown varying gender susceptibilities to dengue infection depending on geographical regions.[8] However, the finding that transaminitis affects both genders equally highlight the indiscriminate nature of liver involvement in dengue cases. The age demographics of the dengue patients present a noteworthy aspect of the study. The mean age of patients with transaminitis was significantly lower (30.74±9.57) than that of patients without transaminitis (41.27±16.22). This observation could be attributed to age-related variations in immune responses, which might influence the severity of dengue infection.[9] Additionally, patients with transaminitis had a longer mean duration of illness (4.61± 1.40 days) compared to those without transaminitis (3.99±0.66 days). The prolonged illness in transaminitis patients could indicate a more severe form of dengue infection, warranting closer clinical monitoring and management. The study provides comprehensive data on haematological and biochemical parameters in dengue patients, particularly on the 5th day of illness. It demonstrates a consistent trend of decreasing levels of haemoglobin (HB), haematocrit (HCT), total leukocyte count (TLC), and platelet count with an increasing number of days of illness. This trend is characteristic of the critical phase of dengue infection when patients are at higher risk of severe manifestations, including haemorrhagic complications.[2]

Conclusion

This hospital-based survey sheds light on the frequency of transaminitis in patients with dengue fever during the first five days of illness. Transaminitis was observed in a significant portion of dengue patients and was found to be associated with disease severity. The study highlights the importance of monitoring liver function in dengue cases, especially in the early days of illness, to assess disease progression and severity. These findings underscore the need for prompt clinical intervention and careful management of dengue patients, particularly those showing signs of hepatic involvement. Further larger sample sizes and diverse populations are warranted to validate and extend these findings and reinforcing the significance of early diagnosis and management in improving patient outcomes.

Limitations

- The study's retrospective nature may introduce recall bias and limited control over data quality, potentially affecting the accuracy and completeness of patient records.
- Conducting the study within a single hospital may limit the generalizability of findings to a broader population, as disease patterns and patient characteristics can vary between healthcare institutions.
- The study's reliance on patients admitted to a tertiary care hospital may exclude milder cases of dengue managed in outpatient settings, potentially skewing the representation of disease severity.
- The study's duration may not capture the full spectrum of disease progression, and outcomes beyond the initial five days of illness are not assessed, potentially limiting insights into longer-term impacts.

- The inclusion criteria of patients aged 16 to 60 years might introduce bias by excluding individuals outside this age range who might also experience dengue infection.

Conflict of Interest: None

Funding Source: None

References

1. Revappa KB, Narumilli MN, Rangappa P, Rao K. Transaminitis in Dengue: A Retrospective Observational Study in an Intensive Care Unit. J Clin Diagn Res. 2022;16(7):46-49.
2. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. World Health Organization; 2009.
3. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012; doi: 10.1371/journal. pntd. 0001760
4. Ahsan T. Dengue fever: a regular epidemic? J Pak Med Assoc. 2008;58(1):1-2.
5. Chan YC, Salahuddin NI, Khan J, Tan HC, Seah CL, Li J, et al. Dengue haemorrhagic fever outbreak in Karachi, Pakistan, 1994. Trans R Soc Trop Med Hyg. 1995;doi: 10.1016/0035-9203(95)90412-3.
6. Swamy AM, Mahesh PY, Rajashekar ST. Liver function in dengue and its correlation with disease severity: a retrospective cross-sectional observational study in a tertiary care center in Coastal India. Pan Afr Med J. 2021;doi: 10.11604/pamj.2021.40.261.29795.
7. Huy NT, Van Giang T, Thuy DH, et al. Factors associated with dengue shock syndrome: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2013;7(9): e2412.
8. Guilarde AO, Turchi MD, Siqueira JB, et al. Dengue and dengue hemorrhagic fever among adults: Clinical outcomes associated with viremia, serotypes, and antibody response. J Infect Dis. 2008;197(6):817-24.
9. Simmons CP, Dong T, Chau NV, et al. Early T-cell responses to epitopes of dengue virus in Vietnamese adults with secondary dengue virus infections. J Virol. 2005; 79(9):5665-75.