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# Association of Liver Function Test with Severity of Dengue Fever in Suburbs of Islamabad

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## Abstract

*Aim*: **This study aimed to identify the key parameters to assist the early diagnosis of Dengue Infection to prevent severe outcomes.**

*Methodology*: **A cross-sectional study was conducted from June 2022 to December 2022 at a tertiary care hospital. 149 patients who presented with dengue symptoms for less than 5 days were enrolled in the study. Hepatic functioning was assessed by monitoring Serum Alanine Transaminase (ALT) (normal = 7−56 IU/L), and serum Aspartate Transaminase (AST) (normal = 10−40 IU/L) levels. Abdominal ultrasound and chest X-Ray were performed, and findings were recorded. Statistical analysis was done using SPSS Version 24.**

*Results*: **81 patients (54.36%) were found to have Classical DF, while 46 patients (45.64%) were diagnosed with DHF or DSS. Dengue fever is more common in males than in females, and it disproportionately affects those under the age of 30. Only 81 (54.63%) of the total 149 individuals developed DF, but of those, 79 (74.4%) had normal ALT levels and 2 (4.26%) had elevated ALT levels. Among the 68 patients with DHF (45.64%), 41 (87.23%) had elevated ALT, while only 23 (22.55%) had normal ALT and all 4 (8.51%) with DSS did as well. The p-value for the correlation between platelet count and elevated ALT levels is 0.007, which is statistically significant.**

*Conclusion*: **Management of dengue disease requires close monitoring of hepatic enzyme levels, particularly ALT and AST, along with the platelet count. It will aid in reducing the severity of the dengue virus. In addition, there should be particular outdoor exposure guidelines, particularly during dengue season evenings, i.e., monsoon.**

*Keywords:* Dengue fever, LFT, Liver function tests, ALT, DHF, Ascities, Liver failure, Haemorrhage, Severity

## 1. Introduction

The Aedes Aegypti mosquito is responsible for spreading the flavivirus that causes dengue fever. It's a mosquito-borne virus that's spreading at an alarming rate.[1] According to current research,[2] Dengue fever has been spreading fast over the world in recent decades. Dengue fever is endemic in many countries throughout the tropical and subtropical belt, with about 100 million illnesses and 24,000 deaths worldwide each year. Each year, between 100 and 400 million people become infected. The real number of cases recorded is likely lower since[2] most patients are asymptomatic or have minor diseases and do not seek medical care and are typically handled at home with supportive treatment. Due to the similarity between the symptoms of this and other febrile infections,[3] a misdiagnosis is common. In some areas, this may reduce the number of reported cases.[4]

One study estimates that there are 390 million annual cases of dengue virus (95% credible interval: 284−528 million).[3] Of these, 96 million (67−136 million) presented with clinical symptoms, the

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severity of which can vary greatly. A total of 48,906 cases of Dengue had been documented in Pakistan as of November 25 of that year, with 183 fatalities (Pakistan: Dengue Response Operation Update Report n 1, DREF Operation n MDRPK022).

Dengue virus infection is a potential health problem for the world's 3.9 billion population, according to yet another study on the disease's prevalence. 70% of the global burden of Dengue infection is in Asia,[2] but with climate change and other conditions, the spread of the disease to other parts of the world, such as Europe and the Americas, is possible.[4] The majorities of people who are infected with the dengue virus do not exhibit any symptoms and recover without incident. Some, however, will fall ill after 4–7 days, with a high temperature, nausea, vomiting, and muscular and/or joint difficulties. The majority of these symptomatic patients recover without symptoms, whereas a few develop severe disease marked by severe plasma leakage, excessive bleeding, or serious organ failure.[3]

However, dengue infection can also manifest as a clinical spectrum including dengue fever, dengue hemorrhagic fever, and dengue shock syndrome, or it might be asymptomatic or present as an undifferentiated febrile illness.[5,6]

Hepatocyte apoptosis by the virus itself, impaired perfusion due to fluid leak, oxidative stress, or immune mediation, and varying degrees of liver involvement at different stages of dengue fever are all causes of liver dysfunction, which can lead to encephalopathy, severe bleeding, renal failure, and metabolic abnormalities.[7]

Liver injury due to Dengue can happen with or without shock, although the extent of liver damage caused by different stages of Dengue has not been explored in depth.

Ascites can be caused by an intra-abdominal source, such as a tumour or a viral aetiology, or it can be an indication of a systemic condition, such as cardiac or hepatic failure. Ascites on US and an initial assessment of the nature of the fluid should therefore prompt a more focused questioning of the peritoneal cavity, with every attempt made to provide a clinical explanation. The US also triages patients who may benefit from additional cross-sectional imaging with CT or X-rays, as well as magnetic resonance imaging (MRI), and most commonly, the diagnosis requires correlation of the radiological data. US can give a non-invasive, qualitative evaluation of the fluid's composition. US can be used to carefully target the relevant fluid component using an aseptic method, reducing the danger of visceral harm from the usual ward 'blind' procedure. A decision on whether to proceed with percutaneous drain implantation can also be made confidently based on both quantitative and qualitative assessment.[8] Ascites patients are difficult to manage, necessitating the formation of an interprofessional team to guarantee that the patient receives the appropriate therapy, including a liver transplant.

A number of studies have identified risk factors for severe dengue, such as older age, female sex, and the presence of comorbidities. Race, hemoglobinopathies, diabetes, pre-existing liver injury, and the use of hepatotoxic medications are also variables.[9] Admission to a hospital is necessary for close monitoring as well as therapeutic management of life-threatening disorders. There is no specific treatment to treat dengue fever, and medications are mostly used to reduce symptoms in dengue patients. Despite intensive monitoring and treatment in hospitals, dengue-related deaths continue to occur, particularly with complications like hepatitis, myocarditis, and encephalitis.[10]

The purpose of this research is to determine how liver damage progresses during dengue fever, specifically whether or not patients whose liver enzymes are abnormal at the onset of the disease go on to develop DHF or another dengue-related consequence.

## 2. Material and methods

This cross-sectional study was conducted at a tertiary care hospital from June 2022 to December 2022. A sample size of 149 was calculated using Rao soft sample size, keeping a 95% confidence interval and 5% margin of error. A nonprobability consecutive sampling technique was used.

149 patients presented to OPD during dengue season with fever were screened according to WHO Guidelines from July 2021 to December 2021 cases which were confirmed by NS1Ag and, Dengue Virus IgG, and IgM Serology were included in our study. We took a detailed history of all the patients and did detailed clinical examinations along with baseline investigations Serum Alanine Transaminase (ALT) (normal = 7–56 IU/L), serum Aspartate Transaminase (AST) (normal = 10–40 IU/L), ultra-sound abdomen and chest X-ray was performed to check for any liver pathology.

Patients who were previously diagnosed with other liver diseases like Chronic Liver disease, Alcoholic Hepatitis, Drug-Induced Hepatitis, or Chronic renal disease, pregnant ladies, those on

steroid doses of >40 mg/dl for one week, and those patients who have been given NSAIDs for the treatment of fever before diagnosis were excluded from the study.

Patients with a duration of illness <5 days from the onset of symptoms were included in the study. The day on which the Patient developed fever was considered the first day of the illness patients were given the recommended dose of paracetamol only as the main aim of the study was to determine the correlation between the development of dengue hemorrhagic fever with deranged liver enzymes the clinical features along with vital signs and CBC and LFTs were done daily at 10 am along with USG Abdomen and chest for the detection of fluid leak. The severity of dengue infection was classified according to WHO Guidelines into mild-moderate and severe illness.

Statistical analysis was performed using SPSS Version 24. Descriptive statistics are applied to determine the prevalence of dengue fever (DF), and dengue hemorrhagic fever (DHF) among different age groups and gender. The Chi-square test and odds ratio was used to observe the relationship between ALT values and platelet count.

## 3. Results

Data represented that a major portion of the population was diagnosed with dengue fever 81(54.36%), followed by 64(42.95%) with Dengue hemorrhagic fever (DHF). Only four individuals (2.69%) from the sample suffered from DSS (Dengue Shock Syndrome). Ultrasound findings revealed that a lesser portion of patients had ascites. Chest X-Ray was found to be clear in most cases, and few presented with effusion.

Those with DHF (Dengue hemorrhagic fever) were found to have raised ALT levels at the time of admission as compared to Dengue Fever patients. 64 patients were diagnosed with DHF out of which 41 (64%) had high ALT levels. This shows a direct association of ALT (Alanine transaminase) levels with the severity of dengue disease, as shown below in Table 1.

A direct association was found between Platelets count and ALT value, shown in Table 1, with a Pearson chi-square value of 0.007.

The majority of Patients who have raised ALT levels on presentation are found to have a fluid leak either in the form of pleural effusion, ascites, or pericholecystic fluid as compared to patients who have a normal level of ALT on presentation. In our sample size of 149 Patients 64 patients had DHF, 26 (62%) were found to have ascites, 10 patients (24%) with GB thickness, whereas only 6 (14%) were found with pleural effusion, as shown in Fig. 1.

Sample cases were categorized into four age groups; as follows; Young (below 30 years of age), Middle age (31–60), and Old (61–90). It was observed that in all age groups, dengue fever was most prevalent than DHF and DSS. So no association was found between age and the severity of dengue disease. The Chi-square value turned out to be 0.85, which means no significant association between the two categorical variables, as tabulated below (Table 2). Similarly, no such relationship was found between gender and dengue disease.

The severity of Dengue among cases with various comorbidities was also determined. We found no significant association between dengue severities with other comorbidities. A significant value was obtained as 0.172 through the chi-square test. Results are presented in Table 3.

The variables such as age of patients, ultrasound, and range of platelet count were determined. The range of platelet showed high level mean value 1.102–5.427 with high ALT Levels as shown in Table 4.

## 4. Discussion

Our results match the national report published previously; it says that Dengue infection commonly occurs in August, September, and October as they are the most humid season in Pakistan, and the breeding of mosquitos is more in this rainy season.[11,12]

In our study, we have observed that the most affected age group by Dengue is the young population, i.e., <30 years of age.[13] The reason could

*Table 1. ALT in association with different types of Dengue fever.*

| Range of ALT levels | Dengue fever (DF) | Dengue hemorrhagic fever (DHF) | Dengue shock syndrome (DSS) | Total cases |
|---|---|---|---|---|
| High | 2(4.26%) | 41(87.23%) | 4(8.51%) | 47 |
| Normal | 79(77.45%) | 23(22.55%) | 0 | 102 |
| **Range of ALT levels** | **Normal platelet count (<80,000)** | **High platelet count (>80,000)** | **Total** | **P-Value** |
| High | 88 | 28 | 116 | 0.007 |
| Normal | 1 | 32 | 33 | |

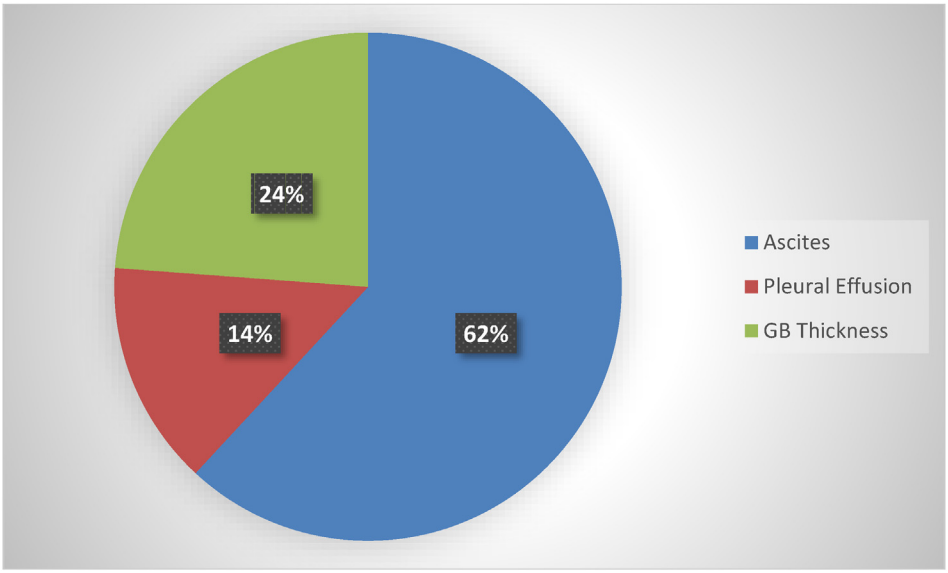


*Fig. 1. Complications of DF.*

probably be their greater exposure to an outdoor environment. Another interesting finding in our study was that dengue fever was more prevalent among male patients than females,[13] however gender is not related to the severity of Dengue. This is probably because females are usually confined inside the homes, and males take on outdoor responsibilities. Similar results were shown in another study.[14]

Liver involvement is widespread and seen in dengue infection, as the virus also targets the reticuloendothelial system.[15,16] This is because of hepatocyte apoptosis either directly by the virus or hypoxic damage due to impaired liver perfusion from the fluid leak, the immune reaction of Host Mediated injury, or oxidative stress.[7,17]

In our study, we have observed that most patients who present the deranged liver enzyme at the start of the febrile phase, most of them go into hemorrhagic manifestation. We observed that ALT (alanine aminotransferase) levels are raised in Dengue, which also accounts for the severity of the disease. Moreover, ALT levels are also directly related to platelet counts. So we can take ALT and AST as indicators to assess severity, and we should keenly follow those patients with deranged liver enzymes to develop hemorrhagic manifestations. It can help pick up serious patients from the start, and we can prevent many complications of the fluid leak through regular follow-up and early treatment.

*Table 3. Severity of Dengue among cases with various comorbidities.*

| Comorbidities | Low ALT levels | High ALT levels | Total | P-Value |
|---|---|---|---|---|
| Asthma | 1 | 0 | 1 | 0.172 |
| Diabetes | 3 | 8 | 11 | |
| Hypertension | 3 | 7 | 10 | |
| Ischemic heart disease | 0 | 3 | 3 | |
| Smoking | 0 | 3 | 3 | |
| Pregnancy | 1 | 0 | 1 | |
| None | 23 | 97 | 120 | |

*Table 4. Odds risk for patients with high ALT levels.*

| Variables | Value | 95% Confidence Interval |
|---|---|---|
| Age category = less than 40 | 1.183 | 0.754–4.359 |
| Ultrasound = ascites | 0.377 | 0.280–0.507 |
| Ranges of platelet count = high count | 7.733 | 1.102–5.427 |
| platelets count = >80,000 | 1.007 | 0.455–2.226 |

*Table 2. Age group stratification with different types of Dengue fever.*

| Age groups | DF (Dengue fever) | DHF (dengue hemorrhagic fever) | DSS (Dengue shock syndrome) | P-Value |
|---|---|---|---|---|
| Young (<30 years) | 55.4% | 40.5% | 4.1% | 0.85 |
| Middle age (31–60) | 52.9% | 45.7% | 1.4% | |
| Old (61–90) | 50% | 50% | 0% | |

## 5. Conclusion

Raised levels of Serum ALT at presentation give an indication of disease progression to severe forms like DHF and DSS, So the patients who have a higher level of ALT on presentation should be given priority, and they have to be keenly monitored for the development of complication so that any clinical deterioration can be picked early and managed appropriately.

In conclusion, dengue infection in adults is usually harmless and self-limiting. It is usual to see transient mild-to-moderate transaminase increase. Dengue haemorrhagic a high temperature, recurrent infection, thrombocytopaenia, elevated blood concentration, female sex, and children have all been recognized as risk factors for liver damage. Repeated liver function tests are therefore unnecessary, especially in individuals with suspicious clinical and laboratory characteristics. They should be taken between the third and eighth day of illness. They can be repeated at least 3 weeks following discharge if clinically indicated. Hepatitis serology can help individuals with suspected hepatitis or persistent liver function abnormalities. Routine hepatobiliary ultrasonography is not advised in cases with acute dengue infection. Sonographic abnormalities such as gallbladder wall thickening, splenomegaly, and ascites will disappear on their own.

**Limitations of the study**: 1) The study sample is small, which means it may be statistically less accurate than studies with a bigger population, and our investigation was conducted retrospectively. 2) The patients were chosen from a tertiary care center, which typically shows a clustering of more severe cases because less severe cases can be handled on an out-patient basis. As a result, the study's findings may not be an accurate reflection of the total population. 3) Due to economical and ethical constraints, a liver biopsy, which is a definite diagnostic test for dengue hepatitis, was not performed.

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## Data availability statement

Available on request to the corresponding author.

### Conflict of interest

No conflict of interests declared by the authors.

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## References

1. Stanaway JD, Shepard DS, Undurraga EA, et al. The global burden of dengue: an analysis from the global burden of disease study 2013. *Lancet Infect Dis*. 2016;16(6):712–723.
2. World Health Organizations. Dengue and severe dengue. [homepage on the Internet]. c2022 [updated 2022 Jan 10; cited 2022 Jan10]. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.
3. Khetarpal N, Khanna I. Dengue fever: causes, complications, and vaccine strategies. *J Immunol Res*. 2016:1–14.
4. Pongpan S, Wisitwong A, Tawichasri C, Patumanond J. Prognostic indicators for dengue infection severity. *Int J Clin Pediatr*. 2013 16;2(1):12–18.
5. Laoprasopwattana K, Jundee P, Pruekprasert P, Geater A. Outcome of severe dengue viral infection-caused acute liver failure in Thai children. *J Trop Pediatr*. 2016 Jun;62(3):200–205. https://doi.org/10.1093/tropej/fmv099. Epub 2016 Feb 6. PMID: 26851434.
6. Chia PY, Thein TL, Ong SWX, Lye DC, Leo YS. Severe Dengue and liver involvement: an overview and review of the literature. *Expert Rev Anti Infect Ther*. 2020 Mar;18(3):181–189. https://doi.org/10.1080/14787210.2020.1720652. Epub 2020 Feb 3. PMID: 31971031.
7. Verma R, Sharma P, Garg RK, Atam V, Singh MK, Mehrotra HS. Neurological complications of dengue fever: experience from a tertiary center of north India. *Ann Indian Acad Neurol*. 2011 Oct;14(4):272–278. https://doi.org/10.4103/0972-2327.91946. PMID: 22346016; PMCID: PMC3271466.
8. Rumack C, Wilson S, Charboneau J, et al. *Diagnostic ultrasound*. 4th ed. St Louis, MO: Mosby; 2011.
9. Lee IK, Hsieh CJ, Lee CT, et al. Diabetic patients suffering dengue are at risk for development of dengue shock syndrome/severe dengue: emphasizing the impacts of coexisting comorbidity(ies) and glycemic control on dengue severity. *J Microbiol Immunol Infect*. February 2020;53(1):69–78.
10. World Health Organization. *Handbook for clinical management of dengue*. Geneva: World Health Organization; 2012.
11. Jahan F. Dengue fever (DF) in Pakistan. *Asia Pac Fam Med*. 2011 Feb 24;10(1):1. https://doi.org/10.1186/1447-056X-10-1. PMID: 21349169; PMCID: PMC3050821.
12. Shabbir W, Pilz J, Naeem A. A spatial-temporal study for the spread of Dengue depending on climate factors in Pakistan (2006–2017). *BMC Publ Health*. 2020;20:995. https://doi.org/10.1186/s12889-020-08846-8.
13. Kumar M, Verma RK, Nirjhar S, Singh M. Dengue in children and young adults, a cross-sectional study from the western part of Uttar Pradesh. *J Fam Med Prim Care*. 2020 Jan 28;9(1):293–297. https://doi.org/10.4103/jfmpc.jfmpc_770_19. PMID: 32110607; PMCID: PMC7014909.
14. Anker M, Arima Y. Male-female differences in the number of reported incident dengue fever cases in six Asian countries. *Western Pac Surveill Response J*. 2011 Jun 30;2(2):17–23. https://doi.org/10.5365/WPSAR.2011.2.1.002. PMID: 23908884; PMCID: PMC3730962.
15. Ahmed SI. Dengue fever in Northern Pakistan: the hepatic implications. *J. Rawalpindi Med. Coll*. 2009;13(2):56–59.
16. Ayaz F, Furrukh M. Assessment of severity of dengue fever by deranged alanine aminotransferase levels. *Cureus*. September 19, 2020;12(9):e10539. https://doi.org/10.7759/cureus.10539.
17. Fernando S, Wijewickrama A, Gomes L, et al. Patterns and causes of liver involvement.