Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.779

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Assessment of Abnormal Liver Function Tests in Dengue Fever: Implications for Disease Severity and Outcome

Muhammad Jamil[1], Taimoor Ahmed[1], Muhammad Mohaymin Ali[1], Hafiz Junaid Javed[2], Ayesha Waheed[3], Adeel Ahmed[1], Muhammad Irfan Jamil[4]

[1]Nishtar Hospital, Multan, Punjab, Pakistan.
[2]Mukhtar A. Sheikh Hospital, Multan, Punjab, Pakistan.
[3]Bakhtwar Amin Hospital, Multan, Punjab, Pakistan.
[4]Lahore General Hospital, Lahore, Punjab, Pakistan.

ARTICLE INFO

Keywords

Dengue, Liver Function Tests, Hepatomegaly, Hemorrhagic Manifestations, Mortality.

Corresponding Author: Adeel Ahmed, Nishtar Hospital, Multan, Punjab, Pakistan. Email: mohammodadeel786@gmail.com

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History

Received: 15-11-2024, Revised: 04-02-2024
Accepted: 03-03-2025, Published: 13-04-2025

ABSTRACT

Background and Objective: Dengue fever, a significant tropical disease, often presents with liver dysfunction. This study evaluated the association between elevated liver function tests (AST, ALT, bilirubin) and clinical outcomes and mortality, to identify prognostic indicators. **Material & Methods:** This cross-sectional study was conducted in the department of Medicine, Nishtar Hospital, Multan, over a 15-month period from July 2024 to September 2024. Patients with confirmed dengue fever were enrolled using a non-probability consecutive sampling technique. Statistical analysis was performed using SPSS version 26.0. **Results:** A total of 146 patients were included, with a mean age of 48 ± 17 years; the most common age group was 31 to 45 years (32%). Males constituted 78 (53%) of the sample. Dengue fever (DF) was identified in 85 (58%), dengue hemorrhagic fever (DHF) in 37 (25%) and dengue shock syndrome (DSS) in 24 (16%). AST and ALT levels were significantly elevated in DSS (670.4 ± 701.5 U/L and 700.8 ± 750.3 U/L) compared to DHF (550.7 ± 660.3 U/L and 560.4 ± 720.8 U/L) and DF (482.8 ± 645.6 U/L and 496.1 ± 683.1 U/L) ($p < 0.001$). Mortality was 38% in DSS and 11% in DHF ($p<0.001$). AST, ALT, and bilirubin were significantly higher in non-survivors ($p<0.001$). Severe liver dysfunction (AST + ALT > 300 U/L) was associated with increased mortality. **Conclusion:** This study highlights the strong association of elevated LFTs with severe dengue outcomes, underscoring their prognostic value in assessing severity and guiding interventions.

INTRODUCTION

Dengue fever is a mosquito-borne viral illness caused by the dengue virus, a member of the Flaviviridae family, transmitted primarily by Aedes aegypti mosquitoes [1]. The disease pathogenesis involves a complex interaction of viral replication, immune activation, and endothelial dysfunction, leading to manifestations ranging from mild fever to severe complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [2]. The incidence of dengue has grown dramatically worldwide in recent decades. Over 2.5 billion people—more than 40% of the world's population—are now at risk of dengue. The World Health Organization currently estimates that there are an estimated 50–100 million dengue infections worldwide annually [3]. In Pakistan, dengue outbreaks have become increasingly frequent, with significant morbidity and mortality, particularly after the rainy season. Pakistan reported its first outbreak in 1994 [4]. Dengue virus has 4 distinct but related serotypes (DEN1-4). Immunity to one serotype increases the risk of severe dengue upon reinfection [5]. Many studies have identified risk factors such as old age, female gender, low socioeconomic status, and comorbid conditions like hemoglobinopathies, diabetes, pre-existing liver injury and hypertension are associated with severe disease outcomes [6].

Individuals diagnosed with dengue fever often exhibit a spectrum of findings such as fever, retro-orbital, joint pain, vomiting, fatigue, headache and diverse bleeding manifestations [7]. Liver involvement is common in dengue infection and dengue associated liver injury was first reported in 1967 [8]. The prevalence of liver dysfunction reported in patients with dengue fever is 67%. The existing literature highlights significant variability in LFT abnormalities and their correlation with dengue severity [9]. Saghir et al. (2023)

demonstrated that elevated ALT levels were strongly associated with severe dengue, with 64% of DHF cases and all DSS cases showing significant enzyme derangements [10]. Rejee et al. (2023) observed elevated AST and ALT in severe dengue, accompanied by increased bilirubin levels and gallbladder wall edema [11]. Similarly, Dhotre et al. (2022) reported significant liver dysfunction in DSS, with mean AST and ALT levels exceeding 1500 IU/L and 1000 IU/L, respectively [12].

Among the clinical features of dengue infection, thrombocytopenia—a reduction in platelet count—is a hallmark finding that plays a significant part in the pathophysiology and progression of the disease [13]. Dengue virus, specifically serotype 2, inhibits megakaryopoiesis, induces precursor apoptosis and accelerates peripheral platelet destruction, collectively leading to thrombocytopenia [14]. The enzyme-linked immunosorbent assay (ELISA) for detecting non-structural protein 1 (NS1) antigen and immunoglobulin M (IgM) antibody is the preferred diagnostic method in regions where dengue is endemic [15]. Current management strategies are supportive, focusing on hydration and symptomatic relief. However, severe cases necessitate close monitoring for complications like bleeding, shock, and organ dysfunction [16]. This study aims to investigate the relationship between LFT abnormalities and clinical outcomes in dengue patients, focusing on the association of elevated AST, ALT, and bilirubin levels with complications such as hepatomegaly, and mortality. By identifying reliable markers for severe disease, this study seeks to contribute to the development of evidence-based protocols for early intervention, ultimately lowering morbidity and mortality in dengue-endemic regions.

METHODS AND MATERIALS

It was a cross-sectional study conducted at the Department of Medicine, Nishtar Hospital, Multan, after obtaining ethical approval from the Ethical Review Committee (IRB: 8034), over duration of 15 months from July 2023 to September 2024. After explaining the purpose, risks and benefits of the study, informed consent was taken. The sample size of 146 was computed using the prevalence of liver dysfunction as 67%, with 95% confidence level and 7% margin of error [17]. A non-probability consecutive sampling technique was utilized for participant enrollment.

Inclusion & Exclusion Criteria

Patients of both genders, aged 15–80 years, who presented with clinical features indicative of dengue fever, such as fever, headache, myalgia, retro-orbital pain and abdominal pain, were included in the study. Eligibility was further confirmed by a laboratory diagnosis of dengue through positive NS1 antigen or IgM dengue antibodies using standard diagnostic assays. Patients with pre-existing chronic liver diseases, such as alcoholic or non-alcoholic fatty liver disease hepatitis B & C or cirrhosis, as well as those with concurrent infections such as malaria or enteric fever, were excluded. Individuals with a recent history of hepatotoxic medication use, such as acetaminophen overdose within the past four weeks or those undergoing chemotherapy or immunosuppressive therapy, were also not eligible.

Data Collection Procedure

After obtaining informed consent, demographic and clinical details of the participants were recorded, including age, gender and presenting symptoms. Dengue severity was assessed, along with the presence of hemorrhagic manifestations, including petechiae, purpura, gum bleeding, epistaxis, hematemesis, hemoptysis, hematuria and melena. Laboratory parameters such as platelet count, hematocrit (Hct), liver function tests (ALT, AST, ALP and total bilirubin) and serum albumin were documented. Patients were classified into three diagnostic groups—DF, DHF and DSS—based on the WHO-defined clinical and laboratory criteria. Further classification was performed based on liver function test results, specifically AST and ALT levels (measured in U/L). Patients were categorized into three groups: Group I comprised those with mild enzyme elevation (≤ 110 U/L), Group II comprised those with moderate enzyme elevation (≤ 300 U/L) and Group III comprised those with severe enzyme elevation (> 300 U/L). Chest X-rays and abdominal ultrasounds were performed to evaluate for pleural effusion and ascites, as well as to assess liver and spleen size. Mortality and the length of hospital stay were documented for all patients.

SPSS version 26.0 was used to analyze the data. Descriptive statistics were employed to compile baseline aspects, with categorical variables demonstrated as frequencies and percentages and continuous variables as medians with interquartile ranges (IQR) or means with standard deviations (SD), as appropriate. The Kruskal-Wallis test, a non-parametric test, was applied to compare continuous variables (e.g., platelet count, hematocrit, AST, ALT, total bilirubin, serum albumin, and length of hospital stay) across the three groups of dengue fever. To compare the categorical variables the Chi-Square test was applied. ANOVA was applied to assess the effect of mortality on continuous variables, including AST, ALT and total bilirubin levels. The results were acknowledged statistically significant at a p-value ≤ 0.05.

RESULTS

A total of 146 patients were included, with a mean age of 48 ± 17 years. Among these, the most common age group was 31 to 45 years, accounting for 47 (32%), followed by 46 to 60 years with 42 (29%), greater than 60 years with 35 (24%), and 17 to 30 years with 22

(15%). The male population constituted 78 (53%) of the sample, while females represented 68 (47%). Based on the clinical diagnosis, dengue fever was identified in 85 (58%) patients, dengue hemorrhagic fever in 37 (25%), and dengue shock syndrome in 24 (16%). Mortality was significantly higher in dengue shock syndrome (9, 38%) compared to dengue hemorrhagic fever (4, 11%), with no deaths reported in dengue fever ($p < 0.001$). Further clinical and demographic characteristics are detailed in Table 1.

Table 1

Baseline Characteristics, Clinical Features, and Outcomes in Patients with Dengue Spectrum

Characteristics	Dengue Fever (85)	Dengue Hemorrhagic Fever (37)	Dengue Shock Syndrome (24)	p-value
Age Group				
17 to 30 years	16 (19%)	5 (14%)	1 (4%)	0.216
31 to 45 years	30 (35%)	12 (32%)	5 (21%)	
46 to 60 years	23 (27%)	11 (30%)	8 (33%)	
>60 years	16 (19%)	9 (24%)	10 (42%)	
Gender				
Male	45 (53%)	21 (57%)	12 (50%)	0.867
Female	40 (47%)	16 (43%)	12 (50%)	
Fever	71 (84%)	30 (81%)	18 (75%)	0.635
Headache	69 (81%)	27 (73%)	18 (75%)	0.556
Retro-orbital Pain	23 (27%)	4 (11%)	10 (42%)	0.022*
Myalgia	66 (78%)	35 (95%)	21 (88%)	0.057
Abdominal Pain	57 (67%)	22 (59%)	17 (71%)	0.609
Hemorrhagic Manifestations	3 (4%)	17 (46%)	11 (46%)	<0.001*
Hepatomegaly	23 (27%)	12 (32%)	11 (46%)	0.215
Splenomegaly	20 (24%)	12 (32%)	12 (50%)	0.042*
Ascites	0 (0%)	17 (46%)	16 (67%)	<0.001*
Pleural Effusion	0 (0%)	24 (65%)	12 (50%)	<0.001*
Mortality	0 (0%)	4 (11%)	9 (38%)	<0.001*

Table 1: Pearson's chi-square test was applied to analyze associations between clinical characteristics and dengue spectrum. A p-value ≤ 0.05 was acknowledged statistically significant (*). Percentages represent proportions within the same group.

Median platelet count was lowest in DHF (35 × 10^3/µL, IQR: 12–74) and DSS (41 × 10^3/µL, IQR: 10–60) compared to DF (87 × 10^3/µL, IQR: 55–108). Hematocrit levels were highest in DSS (42%, IQR: 38–46). AST and ALT levels were markedly elevated in DSS (670.4 ± 701.5 U/L, 700.8 ± 750.3 U/L) and DHF (550.7 ± 660.3 U/L, 560.4 ± 720.8 U/L). Total bilirubin was significantly higher in DSS (3.6 ± 2.2 mg/dL). Serum albumin levels were lowest in DHF (3.05 ± 0.30 g/dL). Hospital stay was longest in DSS (8.5 ± 3.4 days), followed by DHF (6.9 ± 3.2 days) and DF (5.08 ± 2.54 days) (Table 2).

Table 2

Comparison of Laboratory and Clinical Parameters across Dengue Spectrum

Variable	Dengue Fever (n=85)	Dengue Hemorrhagic Fever (n=37)	Dengue Shock Syndrome (n=24)	p-value
Platelet Count (/µL)	87 (55–108)	35 (12–74)	41 (10–60)	<0.001
Hematocrit (%)	37 (33–41)	35 (30–40)	42 (38–46)	<0.001
AST (U/L)	150 (76–543)	92 (60–900)	129 (80–1,000)	<0.001
ALT (U/L)	155 (74–513)	93 (60–750)	129 (80–1,000)	<0.001
Total Bilirubin (mg/dL)	1.1 (0.6–2.1)	2.0 (1.1–3.5)	2.8 (1.5–4.0)	<0.001
Serum Albumin (g/dL)	3.4 (3.0–3.5)	3.0 (2.8–3.2)	3.2 (3.0–3.4)	<0.001
Length of Hospital Stay (days)	4 (3–6)	6 (4–8)	8 (6–10)	<0.001

Table 2: The Kruskal-Wallis test was used to compare the continuous variables across the three groups of dengue (Dengue Fever, Dengue Hemorrhagic Fever, Dengue Shock Syndrome). Statistical significance was set at $p \leq 0.05$.

The mean AST levels were significantly higher in patients who died compared to those who survived (1552.31 ± 293.18 U/L vs. 378.32 ± 571.40 U/L; $p < 0.001$). Similarly, ALT levels were elevated in non-survivors (1638.46 ± 400.06 U/L) compared to survivors (384.41 ± 597.50 U/L; $p < 0.001$). Total bilirubin was also markedly higher in non-survivors (5.12 ± 2.33 mg/dL) compared to survivors (1.54 ± 1.54 mg/dL; $p < 0.001$). The ANOVA results indicated a significant effect of mortality on AST ($F = 53.26$, $p < 0.001$, $\eta^2 = 0.270$), ALT ($F = 54.68$, $p < 0.001$, $\eta^2 = 0.275$), and total bilirubin levels ($F = 60.81$, $p < 0.001$, $\eta^2 = 0.297$).

Table 3
Association of Mortality and Liver Function Test (LFT) Levels across Dengue Spectrum

LFT Levels	Dengue Fever (n=85)	Dengue Hemorrhagic Fever (n=37)	Dengue Shock Syndrome (n=24)	p-value
Normal (≤ 55 U/L)	0 (0.0%)	0 (0.0%)	1 (100.0%)	<0.001
Mild High (≤ 110 U/L)	38 (100.0%)	1 (100.0%)	0 (0.0%)	-
Moderate High (≤ 300 U/L)	20 (100.0%)	15 (100.0%)	0 (0.0%)	-
Severe High (> 300 U/L)	0 (0.0%)	4 (21.1%)	8 (34.8%)	0.157

Table 3: The table presents the distribution of mortality across different levels of liver function tests (LFTs, combining AST and ALT values) and dengue diagnosis (Dengue Fever, Dengue Hemorrhagic Fever, Dengue Shock Syndrome). The Chi-Square test was applied. Percentages represent proportions within the same group.

Liver function test (LFT) abnormalities were significantly associated with mortality (p = 0.000). Normal LFT levels (AST + ALT ≤ 55 U/L) were linked to 100% survival in DF and DHF, while one death (100%) occurred in DSS. In the mild high LFT range (AST + ALT ≤ 110 U/L), survival remained 100% across all groups. For moderate high LFT levels (AST + ALT ≤ 300 U/L), survival was also 100%. However, in the severe high LFT group (AST + ALT > 300 U/L), 4 deaths (21.1%) occurred in DHF and 8 deaths (34.8%) in DSS, though the difference was not statistically significant (p = 0.157) (Table 3).

DISCUSSION

Dengue fever significantly impacts liver function, often causing elevated liver enzymes (AST, ALT) due to viral infection of hepatocytes. Severe cases may lead to liver inflammation, impaired function, and jaundice, necessitating monitoring through liver function tests (LFTs). In this study, patients had a mean age of 48 years, with the most affected age group being 31 to 45 years (32%). This trend aligns with Ahmad et al. (2024) and Kittitrakul et al. (2015), who reported mean ages of 37 and 26 years, respectively [17,18]. A male predominance (53%) was observed, consistent with Ahmed et al. (2014) and Ravilla et al. (2023), though Swamy et al. (2021) noted that severe cases, particularly DSS, were more common in females [19–21]. These variations in demographic distribution may be influenced by geographic and population differences.

Fever was the most common symptom in all diagnostic categories, consistent with prior studies where it was reported in nearly all cases [19,21]. Other frequent symptoms included headache, myalgia, and abdominal pain, with retro-orbital pain being significantly associated with DSS cases (42%, p=0.022). Hemorrhagic manifestations were notably more frequent in severe cases, present in 46% of both DHF and DSS cases, compared to only 4% in DF (p<0.001). This finding is in agreement with Swamy et al. (2021), who observed mucosal bleeding in 91.7% of severe dengue cases, and Ahmad et al. (2024), who reported bleeding in 55.9% of severe cases [17,20].

Hepatomegaly was present in 46% of DSS cases, similar to findings from Swamy et al. (77.8%) and Ravilla et al. (91.2%) [20,21]. Splenomegaly was noted in 50% of DSS cases (p=0.042), aligning with Ravilla et al. (2023) (41.2%) but differing from Dhotre et al. (2022) and Kittitrakul et al. (2015), where splenomegaly was rare [12,18]. Ascites and pleural effusion were significantly associated with severe disease, affecting 67% and 50% of DSS cases, respectively (p<0.001). These findings correlate with Ravilla et al. (2023), who reported ascites in 86.2% and pleural effusion in 82.4% of severe dengue cases, and Saghir et al. (2023), who found ascites in 62% of DHF cases [10,21].

The median platelet count decreased significantly with disease severity, with DSS patients having the lowest levels (41 × 10^3/µL, p<0.001). These findings are aligned with Ahmed et al. (2014), who reported platelet counts of 54.91 × 10^3/µL in severe cases, and Ravilla et al. (2023), who noted medians of 64 × 10^3/µL in severe dengue. AST and ALT levels were significantly elevated in DSS cases (670.4 ± 701.5 U/L and 700.8 ± 750.3 U/L, respectively, p<0.001) [19,21]. Similar elevations were displayed by Dhotre et al. (2022), with AST and ALT levels exceeding 1,500 U/L and 1,000 U/L, respectively, in DSS cases. Comparable trends were observed in Swamy et al. (2021) and Ahmed et al. (2014), highlighting the association between transaminase elevations and disease severity [12,20].

Total bilirubin levels were also markedly higher in DSS cases (3.6 ± 2.2 mg/dL, p<0.001), align with Ahmad et al. (1.737 ± 0.509 mg/dL in severe cases) and Dhotre et al. (2.83 ± 0.07 mg/dL in DSS). Rejee et al. similarly reported elevated bilirubin in severe dengue (1.4 mg/dL) compared to DF (0.78 mg/dL, p<0.05) [11,12,19]. Hypoalbuminemia was observed, with the lowest levels in DSS cases (3.1 ± 0.35 g/dL, p<0.001), consistent with Ravilla et al. (2023), who reported albumin levels of 2.7 ± 0.4 g/dL in severe dengue [21]. Mortality was highest in DSS (38%), significantly greater than in DHF (11%), with no deaths in DF (p<0.001). Elevated AST, ALT, and bilirubin levels were strongly associated with mortality. Non-survivors had AST levels of 1,552.31 ± 293.18 U/L and ALT levels of 1,638.46 ± 400.06 U/L (p<0.001). Similar findings were reported by Ahmed et al. (2014), where all

fatalities occurred in patients with severe liver dysfunction, and Ahmad et al. (2024), who observed significantly higher bilirubin levels in fatal cases. Swamy et al. (2021) documented two fatalities in severe dengue, associated with refractory hypotension and severe bleeding [17,19,20]. These findings reinforce the role of liver dysfunction as a predictor of dengue severity and poor outcomes.

This study's strengths include a comprehensive evaluation of clinical and laboratory parameters across the dengue spectrum, providing valuable insights into disease severity markers. The sample size was robust, enabling meaningful comparisons between diagnostic groups. Although, its single-center design, which may limit generalizability, and the absence of long-term follow-up to assess recovery patterns and sequelae are included in its limitations. Additionally, potential confounding factors, such as comorbidities, were not extensively analyzed. Future research should focus on multicenter studies with larger populations, including pediatric cohorts, to enhance generalizability and explore the prognostic value of liver function tests in guiding management and predicting outcomes.

CONCLUSION

This study highlights the significant association between elevated liver function test (LFT) parameters and severe complications in dengue patients. Elevated AST, ALT, and bilirubin levels were strongly associated to hepatomegaly, hemorrhagic manifestations, ascites, pleural effusion and higher mortality rates, particularly in dengue shock syndrome (DSS). The most severe clinical and laboratory abnormalities were presented in patients with DSS, reinforcing the prognostic utility of LFTs in identifying high-risk cases. These findings underscore the importance of early recognition and aggressive management of severe cases. Future studies should focus on validating these results across larger, multicenter cohorts to refine management strategies and improve outcomes.

REFERENCES

1. Li, H., Su, M. P., Wu, S., Tsou, H., Chang, M., Cheng, Y., Tsai, K., Wang, H., Chen, G., Tang, C., Chung, P., Tsai, W., Huang, L., Yueh, Y. A., Chen, H., Pan, C., Akbari, O. S., Chang, H., Yu, G., … Chen, C. (2023). Mechanical transmission of dengue virus by aedes aegypti may influence disease transmission dynamics during outbreaks. *eBioMedicine*, *94*, 104723. https://doi.org/10.1016/j.ebiom.2023.104723
2. Khanam, A., Gutiérrez-Barbosa, H., Lyke, K. E., & Chua, J. V. (2022). Immune-mediated pathogenesis in dengue virus infection. *Viruses*, *14*(11), 2575. https://doi.org/10.3390/v14112575
3. Khan, M. B., Yang, Z., Lin, C., Hsu, M., Urbina, A. N., Assavalapsakul, W., Wang, W., Chen, Y., & Wang, S. (2023). Dengue overview: An updated systemic review. *Journal of Infection and Public Health*, *16*(10), 1625-1642. https://doi.org/10.1016/j.jiph.2023.08.001
4. Zohra, T., Din, M., Ikram, A., Bashir, A., Jahangir, H., Baloch, I. S., Irshad, S., Waris, A., Salman, M., Iqtadar, S., & Ayaz, M. (2024). Demographic and clinical features of dengue fever infection in Pakistan: A cross-sectional epidemiological study. *Tropical Diseases, Travel Medicine and Vaccines*, *10*(1). https://doi.org/10.1186/s40794-024-00221-4
5. Shankar, R. B., Chakravarthy, B. S., Pilli, S., Raju, M. S., Naik, K. S., & Lagudu, R. N. (2024). LIVER ENZYMES AS AN EARLY PREDICTOR OF SEVERE DENGUE FEVER. *Int J Acad Med Pharm*, *6*(1), 333-336. https://academicmed.org/Uploads/Volume6Issue1/65.%20[2224.%20JAMP_Jafar]%20333-336.pdf
6. Weng, W., Chen, J., Peng, X., Huang, M., Zhang, J., Xiong, J., Cao, H., & Lin, B. (2022). Risk factors for underlying comorbidities and complications in patients with hepatitis B virus-related acute-on-chronic liver failure. *Epidemiology and Infection*, *150*. https://doi.org/10.1017/s0950268822001169
7. Nasir, M., Irfan, J., Asif, A. B., Khan, Q. U., & Anwar, H. (2024). Complexities of dengue fever: Pathogenesis, clinical features and management strategies. *Discoveries*, *12*(2), e189. https://doi.org/10.15190/d.2024.8
8. Leowattana, W., & Leowattana, T. (2021). Dengue hemorrhagic fever and the liver. *World Journal of Hepatology*, *13*(12), 1968-1976. https://doi.org/10.4254/wjh.v13.i12.1968
9. Campana, V., Inizan, C., Pommier, J., Menudier, L. Y., Vincent, M., Lecuit, M., Lamballerie, X. D., Dupont-Rouzeyrol, M., Murgue, B., & Cabié, A. (2024). Liver involvement in dengue: A systematic review. *Reviews in Medical Virology*, *34*(4). https://doi.org/10.1002/rmv.2564

10. Saghir, H., Tariq, M., Safdar, N., Zahoor, A., Rashid, F., Khan, S. E., Abid, S., & Mumtaz, H. (2023). Association of liver function test with severity of dengue fever in suburbs of Islamabad. *Journal of Community Hospital Internal Medicine Perspectives*, *13*(6). https://doi.org/10.55729/2000-9666.1250
11. Gupta, Dr. R. S. (2019). ASSESSMENT OF LIVER FUNCTION TESTS IN DENGUE FEVER. *International Journal of Medical and Biomedical Studies*, *3*(8). https://doi.org/10.32553/ijmbs.v3i8.437
12. Dhotre, P. S., Sanakal, D. B., Dhotre, S. V., Patil, R. S., & BS, N. (2022). Evaluation of alterations in liver function tests in dengue fever. *Res. Med. J*, *7*. https://www.resclinmed.eu/public/data_files/articles/153/article_153.pdf
13. Das, S., Abreu, C., Harris, M., Shrader, J., & Sarvepalli, S. (2022). Severe Thrombocytopenia associated with dengue fever: An evidence-based approach to management of Thrombocytopenia. *Case Reports in Hematology*, *2022*, 1-3. https://doi.org/10.1155/2022/3358325
14. Yang, M., Lin, C., Chen, Y., Lu, I., Su, B., Chen, Y., Liu, K., Wu, C., & Shiau, A. (2024). Prothymosin α accelerates dengue virus-induced thrombocytopenia. *iScience*, *27*(1), 108422. https://doi.org/10.1016/j.isci.2023.108422
15. Casenghi, M., Kosack, C., Li, R., Bastard, M., & Ford, N. (2018). NS1 antigen detecting assays for diagnosing acute dengue infection in people living in or returning from endemic countries. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd011155.pub2
16. Singh, R. K., Tiwari, A., Satone, P. D., Priya, T., & Meshram, R. J. (2023). Updates in the management of dengue shock syndrome: A comprehensive review. *Cureus*. https://doi.org/10.7759/cureus.46713
17. Ahmad, W., Younas, M., Kashif, M., Sajjad, M., Ali, M., & Ramzan, S. (2024). Elevated liver enzymes in dengue fever: implications for disease severity. *Gomal Journal of Medical Sciences*, *22*(1), 32-36. https://www.gjms.com.pk/index.php/journal/article/view/1454
18. Kittitrakul, C., Silachamroon, U., Phumratanaprapin, W., Krudsood, S., Wilairatana, P., & Treeprasertsuk, S. (2015). Liver function tests abnormality and clinical severity of dengue infection in adult patients. *J Med Assoc Thai*, *98*(Suppl 1), S1-8. https://www.thaiscience.info/Journals/Article/JMAT/10971027.pdf
19. Ahmed, A., Alvi, A. H., Butt, A., Nawaz, A. A., & Hanif, A. (2014). Assessment of dengue fever severity through liver function tests. *J Coll Physicians Surg Pak*, *24*(9), 640-644. https://www.jcpsp.pk/archive/2014/Sep2014/08.pdf
20. Swamy, A. M., Mahesh, P. Y., & Tumkur, S. R. (2021). Liver function in dengue and it's correlation with disease severity: An retrospective cross-sectional observational study in a tertiary care center in coastal India. *Pan African Medical Journal*, *40*. https://doi.org/10.11604/pamj.2021.40.261.29795
21. Ravilla, S., Padmaprakash, K. V., Arun, N., & Kanth, R. (2022). Liver function test abnormalities: Do they correlate with severity in dengue infection? An Indian perspective. *Journal of Marine Medical Society*, *25*(1), 48-52. https://doi.org/10.4103/jmms.jmms_88_22