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ORIGINAL RESEARCH

A Study on the Correlation between Disease Severity and Hepatic Dysfunction in Dengue Viral Infection

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ABSTRACT

Aim: To evaluate the correlation between disease severity and hepatic dysfunction in patients with dengue viral infection and identify key clinical and laboratory predictors of severity. **Material and Methods:** This observational, cross-sectional study was conducted over six months at a tertiary care center, involving 100 laboratory-confirmed dengue patients aged 18 years and above. Clinical data, laboratory investigations (including liver function tests, hematological parameters), and physical examinations were collected. Patients were classified based on the 2009 WHO Dengue Guidelines into three severity categories. Hepatic dysfunction was assessed using AST and ALT levels. **Results:** The majority of patients were aged 31–50 years, with a slight male predominance. Common clinical features included fever (100%), hepatomegaly (40%), and bleeding tendencies (35%). Elevated liver enzymes were present in most patients, with moderate elevation (42%) being most common. A statistically significant correlation was found between hepatic dysfunction and disease severity ($p = 0.004$). ALT, AST, platelet count, hematocrit, and hepatomegaly were significant predictors of severe dengue in regression analysis. **Conclusion:** Hepatic dysfunction is significantly associated with dengue severity. Elevated liver enzymes, low platelet count, and hepatomegaly serve as important indicators of severe disease. Timely assessment of these parameters can guide early intervention and improve patient outcomes.

Keywords: Dengue, Hepatic dysfunction, ALT, AST, Disease severity, Liver enzymes

INTRODUCTION

Dengue viral infection has emerged as one of the most significant mosquito-borne diseases affecting millions of people worldwide, particularly in tropical and subtropical regions. The clinical spectrum of dengue ranges from mild, self-limiting febrile illness to severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). In recent years, there has been increasing concern over the complex nature of the disease, its rising incidence, and the unpredictable clinical course it can take. Among the many complications associated with dengue infection, hepatic dysfunction is increasingly recognized as both a common and clinically significant feature.[1,2]

Liver involvement in dengue infection is not just a secondary phenomenon but a key component of the disease's pathophysiology. Patients with dengue, regardless of severity, often present with abnormal liver function tests, hepatomegaly, and in some cases, clinical signs of acute hepatitis. The extent of liver involvement varies widely, and it has been suggested that the degree of hepatic dysfunction may correlate with the overall severity of the disease. However, the precise nature of this correlation is not fully understood. Some individuals with relatively mild dengue fever exhibit significant liver enzyme elevation, while others with severe disease may show only modest hepatic impairment.[3]

The liver plays a central role in immune regulation, metabolism, and detoxification, and its dysfunction can have widespread consequences. In dengue, hepatic involvement may result from multiple mechanisms, including direct viral cytopathic effects, immune-mediated injury, ischemic hepatitis due to hypoperfusion in shock states, or as a consequence of systemic inflammation. These factors often coexist, making it challenging to distinguish the exact cause of hepatic injury in a given patient. Regardless of the mechanism, the clinical implication is clear: liver

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dysfunction in dengue patients is a potential marker of disease progression and severity.[4]

Dengue infection affects individuals of all ages, but children and young adults are particularly vulnerable to severe disease outcomes, including hepatic complications. Pediatric patients often present with more pronounced liver involvement, and they may experience a rapid progression from mild to severe forms, emphasizing the need for timely recognition and monitoring. In adults, pre-existing conditions such as non-alcoholic fatty liver disease or chronic viral hepatitis can exacerbate the impact of dengue on liver function, potentially leading to worse clinical outcomes. Thus, age, comorbidities, and individual immune responses are important variables that influence the pattern of hepatic dysfunction seen in dengue.[5,6]

A significant challenge in clinical practice is predicting which dengue patients are at risk of progressing to severe disease. Current diagnostic and prognostic tools largely rely on clinical signs and basic laboratory investigations. While parameters such as platelet count, hematocrit, and evidence of plasma leakage are commonly used to assess severity, liver function tests are increasingly being recognized as useful adjuncts in risk stratification. Elevated transaminase levels, particularly aspartate aminotransferase (AST) and alanine aminotransferase (ALT), along with elevated bilirubin and prolonged prothrombin time, may reflect not only hepatic involvement but also a higher risk of complications such as bleeding, encephalopathy, or multi-organ dysfunction.[6]

The correlation between disease severity and hepatic dysfunction is an area of active investigation, with implications for both clinical management and public health strategies. By understanding this relationship more clearly, healthcare providers may be able to identify high-risk patients earlier, initiate closer monitoring, and apply timely interventions to reduce morbidity and mortality. Furthermore, this understanding could help in guiding future research into therapeutic targets, vaccine development, and improved case definitions that include hepatic parameters as indicators of severity.[7,8]

Despite the increasing body of evidence linking liver dysfunction with severe dengue, variability in study designs, populations, and diagnostic criteria has made it difficult to draw definitive conclusions. Moreover, the dynamic nature of dengue, where laboratory values and clinical signs evolve rapidly over a short period, adds complexity to the assessment. It is therefore essential to conduct focused, systematic studies that examine the correlation between hepatic parameters and disease severity using consistent methodologies.[9,10]

This study aims to contribute to this growing area of research by exploring the extent and nature of hepatic dysfunction in patients diagnosed with dengue viral infection and analyzing its correlation with clinical severity. Through this investigation, the study seeks to determine whether hepatic parameters can serve as reliable indicators of disease progression and outcomes, thereby enhancing current diagnostic and prognostic frameworks. By identifying specific patterns and thresholds of liver involvement, the findings may help clinicians in making informed decisions regarding patient care, especially in resource-limited settings where early recognition of severe disease is crucial.

MATERIAL AND METHODS

This observational, cross-sectional study was conducted over a period of 6 months at, a tertiary care center. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study.A total of 100 patients diagnosed with dengue viral infection were included in the study. Patients were selected from those admitted to the medicine and infectious disease wards.

Inclusion Criteria

- Patients aged 18 years and above.
- Laboratory-confirmed dengue infection by either NS1 antigen, IgM ELISA, or RT-PCR.
- Patients admitted during the febrile or critical phase of the illness.

Exclusion Criteria

- Patients with pre-existing chronic liver diseases (e.g., hepatitis B, hepatitis C, alcoholic liver disease).
- Co-infections (e.g., malaria, typhoid).
- Patients on hepatotoxic drugs.
- Pregnant women.

Methodology

After obtaining informed consent from each participant, a comprehensive clinical history was taken and a thorough physical examination was performed. All information was recorded using a structured proforma. The collected data included demographic details such as age and gender, as well as clinical features including fever, bleeding tendencies, hepatomegaly, ascites, and other relevant symptoms. Laboratory investigations were conducted for each patient and comprised complete blood count (CBC), liver function tests (LFTs)—including serum bilirubin, SGOT (AST), SGPT (ALT), alkaline phosphatase, and serum albumin—coagulation profile (PT/INR), platelet count, and hematocrit levels.

Classification of Dengue Severity

Based on the 2009 World Health Organization (WHO) Dengue Guidelines, patients were classified into three categories to assess the severity of the infection: (1) Dengue without warning signs, (2) Dengue with warning signs, and (3) Severe dengue. This classification aided in stratifying the patient

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population and correlating clinical severity with hepatic involvement.

Assessment of Hepatic Dysfunction

Hepatic dysfunction was primarily evaluated through the measurement of liver enzymes, specifically aspartate transaminase (AST) and alanine transaminase (ALT). The levels of these enzymes were categorized to indicate the degree of liver involvement: mild elevation was defined as values 1–2 times the upper limit of normal (ULN), moderate elevation as 2–5 times ULN, and severe elevation as greater than 5 times ULN. This grading helped in assessing the extent of hepatic damage in relation to disease severity.

Statistical Analysis

All collected data were compiled and analyzed using SPSS version 26.0. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. The relationship between the severity of dengue infection and hepatic dysfunction was evaluated using the Chi-square test for categorical variables and Pearson's or Spearman's correlation coefficients for continuous variables, depending on the distribution of the data. A p-value of less than 0.05 was considered statistically significant in all analyses.

RESULTS

Table 1: Demographic Profile of Patients (n=100)

In the demographic profile, the study included 100 patients with dengue viral infection. The patients were divided into three age groups: 30% were aged between 18–30 years, 45% were in the 31–50 years age group, and 25% were older than 50 years. The data shows that the largest group of patients was in the 31–50 years range, indicating that dengue affects a significant proportion of adults in this age group.Regarding gender, 58% of the patients were male, while 42% were female. This suggests a slight male predominance among patients admitted with dengue at this tertiary care center. However, the p-value for both age group (0.21) and gender (0.18) were not statistically significant, indicating no strong gender or age-related difference in this cohort.

Table 2: Clinical Features Observed in Patients

As shown in Table 2, all 100 patients exhibited fever (100%), which is a hallmark feature of dengue viral infection. This aligns with the primary symptom of dengue and is expected in all cases.Other clinical features included bleeding tendency, which was observed in 35% of the patients, and hepatomegaly, found in 40%. Both of these features were statistically significant, with p-values of 0.042 and 0.017, respectively. This suggests that bleeding tendencies and hepatomegaly are common and clinically significant manifestations in dengue patients at this stage of infection.Ascites was observed in 20% of the patients, and vomiting in 60%. The p-values for ascites (0.031) and vomiting (0.065) suggest that ascites is statistically significant, whereas vomiting showed no significant association with disease presentation. Similarly, abdominal pain was noted in 48% of patients, but the p-value of 0.054 suggests it is not statistically significant. These findings highlight that ascites may indicate more severe forms of the disease, while vomiting and abdominal pain are more variable symptoms.

Table 3: Classification Based on Disease Severity

In terms of disease severity, 47% of the patients were classified as having Dengue with warning signs, which is the most common classification in this cohort. 28% were classified as having Dengue without warning signs, while 25% of the patients were categorized as having severe dengue. The distribution of disease severity suggests that a significant portion of the patients presented with moderate or severe forms of the disease, which is consistent with the clinical presentation of dengue in a tertiary care setting.

Table 4: Degree of Hepatic Dysfunction Based on ALT/AST Levels

The degree of hepatic dysfunction was assessed based on liver enzyme levels, specifically ALT (SGPT) and AST (SGOT). The majority of the patients (42%) exhibited moderate elevation in liver enzymes (2–5 times the upper limit of normal), followed by 38% with mild elevation (1–2 times ULN) and 20% with severe elevation (>5 times ULN). This suggests that a large proportion of dengue patients in this cohort experienced some level of hepatic dysfunction, with moderate elevations being the most common. These findings are consistent with the known liver involvement in dengue viral infection.

Table 5: Correlation Between Dengue Severity and Hepatic Dysfunction

This table illustrates the relationship between disease severity and the degree of hepatic dysfunction. The data reveals a significant correlation ($p = 0.004$) between disease severity and hepatic dysfunction, with a higher degree of hepatic dysfunction observed in patients with severe dengue. Specifically, patients with severe dengue had a higher prevalence of severe elevation in liver enzymes (8 out of 25 patients). Conversely, patients with dengue without warning signs had a lower frequency of severe hepatic dysfunction. These findings suggest that hepatic involvement increases with the severity of dengue, supporting the hypothesis that liver damage is more pronounced in severe forms of the disease.

Table 6: Multiple Linear Regression Analysis Predicting Disease Severity

The multiple linear regression analysis reveals several significant predictors of disease severity in dengue

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patients.ALT (SGPT) and AST (SGOT) were both significantly associated with increased disease severity, with p-values of 0.0003 and 0.0024, respectively. This indicates that higher levels of liver enzymes are strongly linked to more severe forms of the disease.Platelet count showed an inverse association with disease severity (β = -0.210, p = 0.0051), suggesting that lower platelet counts are predictive of more severe disease. This is consistent with the known pathophysiology of dengue, where platelet reduction is a hallmark of severe infection.Hematocrit percentage also showed a positive association (β = 0.145, p = 0.035), indicating that higher hematocrit levels may correlate with increased disease severity. This is often due to plasma leakage and hemoconcentration in severe dengue.Hepatomegaly was identified as a significant predictor of severe dengue (β = 0.180, p = 0.014), reinforcing its clinical relevance in identifying severe cases.Ascites and the constant (intercept) were not statistically significant (p = 0.104 and p = 0.067, respectively), indicating that while ascites is observed in severe cases, it does not appear to be a major independent predictor of severity in this analysis.The model explains 62% of the variance in disease severity (R^2 = 0.62), and the overall model was highly significant (p < 0.001), confirming the relevance of the included variables.

Table 1: Demographic Profile of Patients (n=100)

Variable	Number of Patients	Percentage (%)	p-value
Age Group			0.21 (NS)
18–30 years	30	30%	
31–50 years	45	45%	
>50 years	25	25%	
Gender			0.18 (NS)
Male	58	58%	
Female	42	42%	

NS = Not Significant

Table 2: Clinical Features Observed in Patients

Clinical Feature	Number of Patients	Percentage (%)	p-value
Fever	100	100%	—
Bleeding tendency	35	35%	0.042*
Hepatomegaly	40	40%	0.017*
Ascites	20	20%	0.031*
Vomiting	60	60%	0.065 (NS)
Abdominal pain	48	48%	0.054 (NS)

Table 3: Classification Based on Disease Severity

Dengue Classification	Number of Patients	Percentage (%)
Dengue without warning signs	28	28%
Dengue with warning signs	47	47%
Severe dengue	25	25%
Total	100	100%

Table 4: Degree of Hepatic Dysfunction Based on ALT/AST Levels

Liver Enzyme Elevation	Number of Patients	Percentage (%)
Mild (1–2× ULN)	38	38%
Moderate (2–5× ULN)	42	42%
Severe (>5× ULN)	20	20%
Total	100	100%

Table 5: Correlation Between Dengue Severity and Hepatic Dysfunction

Dengue Severity	Mild Elevation	Moderate Elevation	Severe Elevation	Total Patients	p-value
Dengue without warning signs	20	6	2	28	
Dengue with warning signs	12	25	10	47	
Severe dengue	6	11	8	25	**0.004***

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Table 6: Multiple Linear Regression Analysis Predicting Disease Severity

Independent Variable	β Coefficient (β)	Standard Error (SE)	t-value	p-value	Interpretation
ALT (SGPT)	0.312	0.082	3.80	0.0003***	Significantly associated
AST (SGOT)	0.275	0.089	3.09	0.0024**	Significantly associated
Platelet count	-0.210	0.073	-2.88	0.0051**	Inversely associated
Hematocrit (%)	0.145	0.068	2.13	0.035*	Mild positive association
Hepatomegaly (Yes=1, No=0)	0.180	0.072	2.50	0.014*	Significant predictor
Ascites (Yes=1, No=0)	0.125	0.076	1.64	0.104 (NS)	Not statistically significant
Constant (Intercept)	1.020	0.550	1.85	0.067 (NS)	—

$R^2 = 0.62$, **Adjusted $R^2 = 0.59$**, **$F(6, 93) = 12.7$**, **$p < 0.001$**

DISCUSSION

In the present study, the demographic characteristics of the 100 dengue patients revealed that the majority of the cases occurred in adults between the ages of 31–50 years, followed by the younger 18–30 years group. This finding is consistent with studies conducted in regions where dengue is endemic, which often show a higher incidence in the adult population (Chhina et al., 2008; Jagadishkumar et al., 2012).[11, 12]This age group may be more vulnerable to the complications of dengue due to higher exposure to risk factors such as mosquito bites and underlying comorbidities. The gender distribution showed a slight male predominance, with 58% of the patients being male, which is in line with previous studies (Nimmannitya et al., 1987). However, the lack of statistical significance in both age and gender groups ($p > 0.05$) suggests that these factors may not play a crucial role in dengue severity in this cohort.[13]

The hallmark feature of fever was present in all patients, as expected in dengue viral infections. Other clinical features observed included bleeding tendencies in 35%, hepatomegaly in 40%, and ascites in 20%, all of which are well-documented manifestations of severe dengue (Shivbalan et al., 2004).[14] The statistically significant correlation between hepatomegaly ($p = 0.017$) and bleeding tendency ($p = 0.042$) with the severity of the disease highlights the role of liver dysfunction in dengue. Hepatomegaly, a sign of liver involvement, is a common finding and has been reported in other studies as a significant clinical feature of severe dengue (Saha et al., 2013).[15] The observed ascites and vomiting were also prominent but with less significance. Ascites is often a sign of plasma leakage, which occurs in severe cases (Trung et al., 2010). The vomiting observed in 60% of the patients, although common, was not statistically significant in this study, which may indicate its more generalized nature in dengue.[16]

In line with the 2009 WHO Dengue Guidelines, the classification of patients into different severity categories revealed that the majority (47%) had Dengue with warning signs, followed by severe dengue (25%). This distribution supports the findings from Agarwal et al. (1999), which indicate that moderate to severe cases of dengue are more common in tertiary care settings. The percentage of patients with dengue without warning signs (28%) highlights the broader spectrum of the disease, from mild to severe, seen in this cohort. These findings also correlate with global trends where early detection and appropriate management are crucial for reducing severe disease progression.[17]

In assessing hepatic dysfunction, it was found that moderate elevation in ALT/AST was the most common (42%), followed by mild elevation (38%) and severe elevation (20%). Elevated liver enzymes, particularly AST and ALT, are known indicators of liver involvement in dengue infection (Chhina et al., 2008).[11] This finding is consistent with earlier studies, which have demonstrated that dengue virus can cause transient hepatocellular injury (Jagadishkumar et al., 2012; Trung et al., 2010).[12,16] Elevated ALT and AST levels reflect the extent of liver damage and are correlated with the disease's severity (Saha et al., 2013). While moderate elevations were more common in this cohort, the presence of severe elevations in some patients highlights the potential for severe liver damage in more critical cases.[15]

Table 5 shows a statistically significant correlation between disease severity and hepatic dysfunction ($p = 0.004$). Specifically, patients with severe dengue had a higher prevalence of severe liver enzyme elevation, which aligns with studies that report liver damage as a significant feature of severe dengue (Saha et al., 2013; Trung et al., 2010).[15,16] These findings support the hypothesis that hepatic dysfunction is more pronounced in severe forms of dengue. The association between elevated liver enzymes and severe dengue has been widely documented in the literature, including in studies by Wali et al. (1999) and Chhina et al. (2008), confirming that liver

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dysfunction is a marker of disease severity and a predictor of complications.[11,18]

The multiple linear regression analysis in Table 6 identified several significant predictors of disease severity. Both ALT and AST levels were strongly associated with increased disease severity ($p = 0.0003$ and $p = 0.0024$, respectively), suggesting that liver enzyme levels are critical biomarkers for predicting the severity of dengue infection. Previous studies have highlighted the role of liver enzymes as reliable indicators of severity, with higher AST/ALT levels linked to more severe cases (Jagadishkumar et al., 2012; Trung et al., 2010).[12,16] The inverse association with platelet count ($p = 0.0051$) is also consistent with known pathophysiology, where thrombocytopenia is a hallmark of severe dengue and contributes to the risk of hemorrhagic complications (Shivbalan et al., 2004).[14]

Additionally, the positive association with hematocrit ($p = 0.035$) supports the concept that hemoconcentration, due to plasma leakage, is indicative of more severe disease (Saha et al., 2013). Hepatomegaly was also found to be a significant predictor of severity ($p = 0.014$), which is consistent with findings from Chhina et al. (2008) that emphasize liver enlargement as a key clinical sign of severe dengue. The non-significance of ascites in the regression model ($p = 0.104$) suggests that while ascites is common in severe cases, it may not independently predict disease severity in this cohort.[11]

CONCLUSION

This study highlights the significant clinical and laboratory features associated with dengue severity, particularly the role of hepatic dysfunction. Elevated ALT and AST levels, low platelet count, and hepatomegaly were found to be strong predictors of severe disease. The correlation between liver enzyme elevation and dengue severity underscores the importance of monitoring hepatic parameters in clinical management. Fever was a universal symptom, while hepatomegaly and bleeding tendency were notable significant clinical indicators. Early identification of these factors can aid in prompt intervention and improved outcomes in dengue patients

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