The Effect of Dengue Infection Severity on Blood Parameters

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ABSTRACT

Objective: To evaluate the relationship between dengue infection severity, Alanine Aminotransferase levels, and platelet counts.

Study Design: Cross-Sectional study.

Place and Duration of Study: Akhtar Saeed Medical College-affiliated Farooq Hospital, Tehsil Murree, District Rawalpindi Pakistan, from Oct 2022 to Sep 2023.

Methodology: Data from the medical records of individuals admitted to the dengue ward and diagnosed with confirmed dengue fever were evaluated. Demographic data, platelet counts on days 3, 4, and 5, Alanine Aminotransferase levels, and reports of Dengue Shock Syndrome and Dengue Hemorrhagic Fever.

Results: Of the 69 participants, 76.8% were men, and most were aged 19–30 years. There was no significant difference in the mean Alanine Aminotransferase levels between the Dengue Hemorrhagic Fever positive and Dengue Hemorrhagic Fever negative patients (p=0.615). Patients with Dengue Shock Syndrome showed significantly different mean Alanine Aminotransferase levels (p=0.031). When comparing Dengue Shock Syndrome-positive individuals with Dengue Shock Syndrome -negative individuals, platelet counts were considerably lower (p=0.023).

Conclusion: Thrombocytopenia is an important marker for severe dengue fever outcomes, particularly in Dengue Shock Syndrome patients. Although there was no significant difference in Alanine Aminotransferase levels between Dengue Hemorrhagic Fever cases and Dengue Shock Syndrome-positive cases, there was a discernible increase in Dengue Shock Syndrome-positive cases, suggesting that liver function tests may be helpful in anticipating shock.

Keywords: Alanine Transaminase, Dengue, Dengue Shock Syndrome, Platelet Count, Thrombocytopenia.

INTRODUCTION

Dengue fever is a viral infection transmitted by vectors that is now endemic in over 100 countries, with the World Health Organization estimates showing that 2.5 billion individuals in 124 countries are at risk.[1,2] The dengue virus (DENV) has established year-round endemicity in Pakistan, particularly after the monsoon rainy season.[3] In Pakistan, various outbreaks have witnessed the presence of all four distinct dengue virus serotypes, DEN-I, DEN-II, DEN-III and DEN-IV.[4] Outbreaks in Pakistan have seen over 50,000 cases in Lahore in 2011 and approximately 8,546 cases with 33 deaths in Swat in 2013.[4] There are two types of dengue virus infections: primary and secondary. Primary infection causes acute febrile illness known as dengue fever, which typically resolves within seven days. Secondary infection, however, is more severe and can lead to Dengue shock syndrome (DSS) or Dengue hemorrhagic fever (DHF). DHF and DSS have the potential to be fatal.[5]

Thrombocytopenia, indicated by low platelet count, is a clinical manifestation of dengue fever and is common in patients with moderate or severe infection.[6] Platelet counts in many patients drop below the normal range of 150,000–450,000 platelets/µL during days 3–7 of fever and can even go as low as <20,000 platelets/µL.[7] Elevated liver enzymes, such as alanine aminotransferase (ALT), are also commonly seen in dengue patients, affecting 65–97% of cases and peaking between days 7–10. Increased ALT levels and thrombocytopenia may be early indicators of severity in dengue patients. Although the liver is not the primary organ targeted by the dengue virus, hepatic involvement can occur due to direct viral effects or an abnormal immune response.[8]This study was conducted to evaluate the relationship between dengue infection severity, alanine aminotransferase (ALT) levels, and platelet counts.

METHODOLOGY

The cross-sectional study was conducted at Farooq Hospital (Akhtar Saeed Medical College) in

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Tehsil Murree, District Rawalpindi Pakistan, from Oct 2022 to Sep 2023, after obtaining approval from the Institutional Ethical review Committee.

Inclusion Criteria: Patients of either gender aged 12 years and above with a confirmed diagnosis of dengue fever according to WHO[9] who had data on platelet counts within the initial three days of diagnosis and documented information regarding the severity of the disease were included.

Exclusion Criteria: Patients with missing or incomplete data, individuals with a history of chronic diseases known to impact platelet counts and those who had undergone specific medical interventions during the early stages of dengue infection were excluded.

The total number of patients admitted to the Dengue ward and diagnosed with dengue fever from 1st October 2022 to 30th September 2023 (1-year data) was 79. The primary data source was medical records of dengue fever patients at Farooq Hospital. Principal investigators and the other authors carefully examined the data and gathered relevant information from the medical records for each patient, including demographic details, clinical characteristics, laboratory results and other variables. This was then entered into MS Excel. The key variables included demographic information, confirmed dengue diagnosis, platelet counts on days 3rd, 4th, and 5th, ALT report on day 3rd, and documented disease severity.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 25. Shapiro-Wilk Test was used to check the normality of the data, which was found to be normally distributed. Quantitative variables were presented as Mean±SD, while qualitative variables as frequencies and percentages. Inferential statistics were explored using independent samples t-test. The p-value of ≤0.05 was considered statistically significant.

RESULTS

In the current study, out of 69 participants, 53(76.81%) were males and 16(23.18%) were females. Most patients were between 19 and 30 (n=20, 28.98%) years of age, followed by individuals aged 31 to 40 (n=14, 20.28%) (Table-I).

Mean Alanine Transaminase (ALT) levels among Dengue Hemorrhagic Fever (DHF) patients were 128.17±116.851, and in those without DHF were 105.86±88.117. However, the difference is insignificant (p=0.615). Mean ALT levels in patients reported with DSS were 202.25±120.702, and in patients without DSS

were 94.91±80.60. A significant difference has been observed (p=0.03) (Table-II).

Table-I: Demographic Characteristics of the Study Participants (n=69)

Variables	n(%)
Gender	
Female	16(23.2)
Male	53(76.8)
Age Groups	
upto 18	10(14.5)
19 to 30	20(29.0)
31 to 40	14(20.3)
41 to 50	8(11.6)
51 to 60	10(14.5)
above 60	7(10.1)

Table-II: Comparison of ALT Levels with Dengue Shock Syndrome and Dengue Hemorrhagic Fever (n=69)

Disease	ALT Levels		p-value
	Positive	Negative	
Dengue Shock Syndrome	202.25±120.70	94.91±80.60	0.030
Dengue Hemorrhagic Fever	128.17±116.85	105.86±88.11	0.61

Only on day four did platelet counts among patients diagnosed with DSS yield a mean value of 54,900±40,079, while DSS-negative patients exhibited a considerably higher mean platelet count (993,007±47,949). This difference was statistically significant (t= -2.320, p=0.023). Moreover, on day 4, the mean platelets count among DHF-positive patients was 57360±37492, which was much higher in DHF-negative patients (93260±48538). A significant difference has been observed (t= -2.320, p =0.023). No significant difference was observed on day 3rd and 4th. (Table-III)

Table-III: Comparison of Dengue Shock Syndrome and Dengue Hemorrhagic Fever with Platelet Count at Day 3,4 and 5 (n=69)

Day of Fever	Positive (Mean±SD)	Negative (Mean±SD)	p-value
Dengue Haemorhagic Fever (Platelet Count)			
3	76200±32830	10702±53960	0.08
4	54900±40070	93070±47940	0.02
5	72000±71640	102880±52330	0.10
Dengue Shock Syndrome (Platelet Count)			
3	75180±35949	108002±53638	0.05
4	57360±37492	93260±48538	0.02
5	68730±48210	104030±55950	0.05

No significant associations were observed between DHF and platelet fall from Day 3 to Day 4 (p=0.606) and Day 4 to Day 5 (p=0.616). No significant

associations were observed with DHF and fall of platelets from Day 3 to Day 4 (*p*=0.817) and from Day 4 to Day 5 (*p*=0.966). Platelet counts among patients diagnosed with DSS yielded a mean value of 54,900±40,079, while DSS-negative patients exhibited a higher mean platelet count of 93,007±47,949. This difference was statistically significant (t= -2.320, =0.023, *p*<0.05). The mean platelets count among DHF-positive patients was 57360±37492; in DHF-negative patients, the mean platelets were significantly higher, i.e. 93260±48538. A significant difference has been observed (t= -2.320, *p* =0.023), which can be seen in Table-IV.

Table-IV: Comparison of Dengue Haemorrhagic Fever and Dengue Shock Syndrome with Platelet Decline (n=69)

Days	Positive (Mean±SD)	Negative (Mean±SD)	*p*-value
Dengue Haemorrhagic Fever (Platelet Decline)			
3. 4	21300±28240	14220±41520	0.60
4. 5	-17100±42490	-9810±42210	0.61
Dengue Shock Syndrome (Platelet Decline)			
3. 4	17820±25325	14760±42119	0.81
4. 5	-11360±38854	-10780±42913	0.96

DISCUSSION

Our study population predominantly comprised males (76.8%), with the majority between 19 and 30. This demographic distribution coincides with existing literature that emphasizes a higher prevalence rate of dengue among young adults, possibly because of high exposure to mosquito vectors, increased outdoor activities, and lower socioeconomic conditions.[10] Adolescents spend a significant part of their day in school when arboviral disease vectors prefer feeding on blood. These feeding peaks in the early morning and late afternoon. Research conducted in Colombia revealed a significant prevalence and incidence of Ae. aegypti mosquitoes in schools, thus highlighting the need to include them in health education, monitoring, and infection control efforts.[11]

Hepatic involvement, characterized by increased ALT levels, has been associated with vascular leakage and capillary permeability, contributing to shock development in severe dengue.[12]

The liver damage observed in dengue infection is a complex process involving various mechanisms. Firstly, the virus directly impacts hepatocytes and Kupffer cells, resulting in liver damage. Secondly, an excessive immune response, characterized by T cell-mediated cytokine release, contributes to liver injury.

Additionally, in severe cases such as dengue shock syndrome, circulatory failure can reduce blood flow to the liver, further impairing its function.[13,14] These factors collectively give rise to a range of liver complications during acute dengue infection, ranging from mild increases in liver enzymes to severe acute liver failure. In severe cases, there is also the potential for multiorgan dysfunction and fatal outcomes.

The current study found a non-significant difference in ALT levels between DHF-positive and DHF-negative patients (*p*=0.615). This can be compared with a survey that reported that ALT levels are significantly high in DHF patients.[14] The lack of a significant difference in ALT levels between DHF-positive and DHF-negative patients aligns with a study by Lee *et al*.[15] This study suggested that although liver involvement is often seen in severe cases of dengue, ALT levels may not consistently correlate with the severity of hemorrhagic manifestations. A research conducted by Palmal *et al*. emphasized the correlation between increased ALT levels and the likelihood of DSS, thus emphasizing the significance of liver dysfunction as a predictor of severe outcomes in individuals with dengue fever.[16] Our study's findings on ALT levels have significance for clinical care and highlight the importance of using an individualized approach for determining the severity of a disease. Tracking ALT levels, particularly in the setting of Dengue Shock Syndrome, may assist in identifying individuals with an elevated likelihood of experiencing serious consequences. Medical practitioners should include liver function tests as part of the overall clinical evaluation to improve the accuracy of prognostic predictions.

In our study, the significantly lower mean platelet counts among patients diagnosed with DSS, compared to DSS-negative cases highlights the critical role of thrombocytopenia in identifying individuals at risk of developing shock in the course of severe dengue infection. The lower platelet counts found in cases positive for DHF are in accordance with guidelines set by the World Health Organization (WHO), which highlight the need to monitor platelet levels to identify people at risk of experiencing severe complications.[17]

Laboratory markers, such as thrombocytopenia or a low platelet count, have been linked to the severity of dengue infection, including DHF and DSS. However, our study results revealed no significant

association between DHF and DSS with platelet decline. This contradicts previous studies indicating a strong association between platelet decline and dengue manifestations like DSS and DHF.[18-19] The lack of a significant link between DHF and platelet drop from Day 3 to Day 4 and Day 4 to Day 5 diverges from studies suggesting platelet kinetics is essential for identifying DHF patients. The dynamic nature of platelet responses during dengue infection must be considered since different virus strains and host immunological heterogeneity may contribute to the observed variations.[20]

Moreover, the lack of a significant association between DSS and the decrease in platelet count contradicts established views that link a rapid decline in platelets to the development of severe dengue complications. Although thrombocytopenia is widely recognized as a hallmark of DSS, our findings indicate the need for a broader perspective. This emphasizes the importance of using more comprehensive criteria to accurately predict shock in patients with dengue fever. Research suggesting other indicators, such as the activation state of platelets or assessments of platelet function, may provide valuable insights into the fundamental processes contributing to DSS.[18-21]

CONCLUSION

Thrombocytopenia is an important marker for severe dengue fever outcomes, particularly in DSS patients. Although there was no significant difference in ALT levels between DHF cases and DSS-positive cases, there was a discernible increase in DSS-positive cases, suggesting that liver function tests may be helpful in anticipating shock.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MFB & TMS: Data acquisition, critical review, approval of the final version to be published.

MN & HN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

BGA & FN: Conception, data acquisition, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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