

## Significance of Hematological and Biochemical Parameters in Diagnosed Patients of Dengue infection

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### Abstract

**Objective:** The study aimed to assess the variation of Total leukocyte count (TLC), Hematocrit (HCT), platelets, serum albumin, and alanine transaminase (ALT) among patients with different severities of dengue infections.

**Materials & Method:** It was a cross-sectional study conducted during five months (1st June to 31st October) of the year 2023. Patients admitted to the dengue ward and diagnosed with dengue viral syndrome, dengue hemorrhagic fever, and dengue shock syndrome were included. About three to five milliliters of blood was collected for hematological and biochemical parameters like TLC, HCT, platelets, serum albumin, and ALT. The results were retrieved through an automated hematology and chemistry analyzer. The data was analyzed through SPSS version 25.0.

**Results:** Out of 134 patients, 52.2% were males and 47.8% were females. The mean age of patients was 44.22±17.87 years. There were 70.9%, 20.1%, and 9.0% of patients who presented with dengue viral syndrome, dengue hemorrhagic fever, and dengue shock syndrome respectively. Among total subjects, 69 (51.49%) patients had leukopenia, 68 (50.74%) patients had increased HCT level, 103 (76.86%) patients had thrombocytopenia, 09 (6.71%) patients had decreased level of serum albumin, and 122 (91.04%) patients have increased ALT levels. A statistically significant association was found between length hospital stay (days) with TLC (0.002) and dengue infections (DHF, DVS, and DSS) with platelets (0.012). All other parameters showed non-significant rise or fall.

**Conclusion:** Hematological parameters such as thrombocytopenia and leukopenia vary according to the severity of dengue infection. However, no statistically significant difference was found except TLC. Biochemical changes such as elevated ALT, and decreased serum albumin could serve as predictors of dengue complications but further studies are required to confirm the finding.

**Keywords:** Dengue viral syndrome (DVS), dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS), hematological changes, biochemical changes.

**How to cite:** Arshad A, Farooq O, Yousaf Z, Mumtaz A, Khan E, Fayyaz A. Significance of Hematological and Biochemical Parameters in Diagnosed Patients of Dengue infection. *Esculapio - JSIMS* 2024;20(02):233-238

**DOI:** <https://doi.org/10.51273/esc24.251320217>

### Introduction

Dengue is a mosquito-borne tropical disease caused by an arbovirus transmitted by the *Aedes aegypti*

mosquito and affects millions of people around the world. Most cases of dengue viral syndrome (DVS) are mild and self-limiting.<sup>1</sup> In some instances, the disease can progress to severe dengue as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).<sup>2</sup> Four serotypes of dengue virus are antigenically distinct namely “DENV-1, DENV-2, DENV-3, and DENV-4”. A fifth serotype (DENV-5) was detected through genetic sequence analysis in Sarawak state of Malaysia in October 2013.<sup>3</sup>

DVS tends to be more prevalent among adults and teenagers. Its manifestation can vary, ranging from a mild

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Submission Date:	21-02-2024
1st Revision Date:	15-05-2024
Acceptance Date:	14-06-2024

fever to a more debilitating illness. The severe form is marked by a sudden onset of high fever, intense headache, retro-orbital pain, muscle and joint aches along rash, mainly experienced during the initial phase of fever.<sup>2,4</sup> During the critical stage, the skin might display a flushed appearance accompanied by a petechial rash, usually appearing as the fever subsides, typically between days three to seven. This phase is linked to capillary leakage and bleeding. Some cases can develop into DSS, involving abnormalities in clotting, increased plasma leakage, and raised vascular fragility. An increase in capillary permeability results in fluid loss leading to hypovolemic shock and failure of multiple organs.<sup>5</sup>

For diagnosis of DVS, clinical presentation, laboratory tests, and patient's medical history are required. Accurate and timely diagnosis is crucial for providing appropriate medical care and managing DVS effectively.<sup>6</sup> Laboratory tests are essential to confirm the diagnosis and determine the severity of dengue infection. Currently, the serological test is used to confirm the diagnosis of dengue infection such as the detection of the dengue NS1 antigen (sensitivity 76% and specificity 98%) by the ELISA method.<sup>7</sup>

The progression of the disease results in hematological and biochemical abnormalities. They could be used to reduce mortality and morbidity by early detection of the problems and the introduction of efficient management techniques. Patients with severe dengue infection may be effectively identified with plasma leakage by using a combination of hematological and biochemical indicators, such as HCT, albumin concentration, platelet count, and aspartate aminotransferase (AST).<sup>8</sup> Dengue infection is now increasingly linked to hepatic involvement of variable severity.<sup>9</sup> Abnormal values of liver function tests are frequently observed in dengue infection. In dengue-infected patients, increased ALT and reduced serum albumin were observed.<sup>10,11</sup> These parameters may be utilized to anticipate the start of the leaking phase in advance. Therefore, the present study aimed to identify the significance of hematological and biochemical parameters among patients with different severities of dengue infection.

## Materials & Methods

This cross-sectional study was conducted in Farooq Hospital Westwood Lahore during five months (1<sup>st</sup> June to 31<sup>st</sup> October) of the year 2023. Patients admitted to the dengue ward and diagnosed with DVS, DHF, and DSS according to WHO conventional classification of

dengue<sup>12</sup> were included. The diagnosis was made by disease specialists and patient record was maintained in the hospital data software.<sup>4</sup> Patients who were on long-term medication with underlying chronic disease and those with negative dengue NS-1 antigen tests were excluded. The relevant information of patients was collected using a structured data collection proforma with informed written consent (for children, a guardian consent was obtained). On admission, about three to five milliliters of blood was separately collected in ethylenediamine tetraacetic acid (EDTA) vacutainer for TLC, HCT, and platelets and in clotted vacutainer for biochemical investigations (ALT and serum albumin). Complete blood count to check hematological parameters (TLC, HCT, and platelets) was performed on Mindray BC-5000 while ALT and serum albumin were estimated through Selectra Pro-M using the photoelectric colorimetric principle. The collected data was analyzed through Statistical Package for the Social Sciences (SPSS) version 25.0. For quantitative variables, data was presented as mean + SD. Qualitative variables were presented as frequency and percentages. The multivariate analysis was used to find the estimated marginal means and association between study variables.

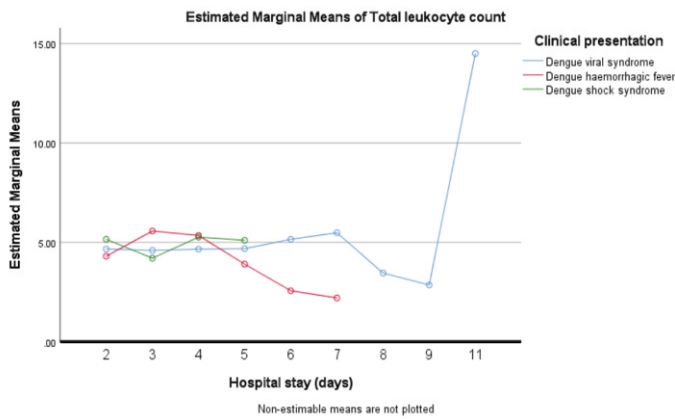
## Results

A total of 134 patients were included in this study, 70 (52.2%) were males and 64 (47.8%) were females. The range of age was 03 years to 86 years. The mean age of patients was 44.22+17.87 years. According to the clinical criteria, 95 patients (70.9%) had DVS, 27 patients (20.1%) had DHF, and 12 patients (9.0%) had DSS. The mean age of DSS (46.50+14.93) patients was higher than DHF (46.04+12.62), and DVS (43.42+19.48) patients (statistically non-significant). The mean duration of hospital stay of these patients was 4.38+1.85 days.

The normal range for hematological parameters was: TLC (4.00-11.00 ×10<sup>9</sup>/L), HCT (36.00-46.00 %), and platelets (150.00-450.00×10<sup>9</sup>/L). In total, 69 (51.49%) patients had leukopenia, 68 (50.74%) patients had increased HCT levels and 103 (76.86%) patients have thrombocytopenia.

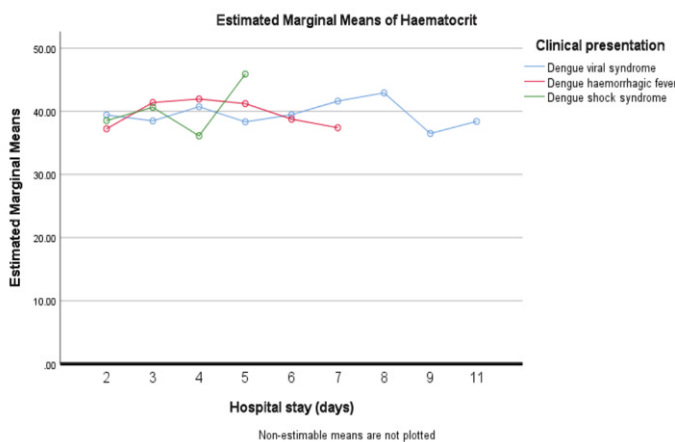
The highest mean value of TLC (14.50 + 2.23) was observed in DVS patients with 11 days of hospital stay, while the lowest mean value of TLC (2.85+1.57) was observed with 09 days of hospital stay. In DHF, the highest mean value of TLC (5.56+0.91) was observed in patients with 03 days of hospital stay, and the lowest mean value (2.20+2.23) with 07 days of hospital stay.

The highest and lowest mean values of TLC were (5.26 + 0.99), and (4.20 + 1.28) were observed in DSS patients with 04 days and 03 days of hospital stay respectively. Statistically significant distinct variations in TLC patterns are evident among different cases of DVS, DHF, and DSS (Figure 1).



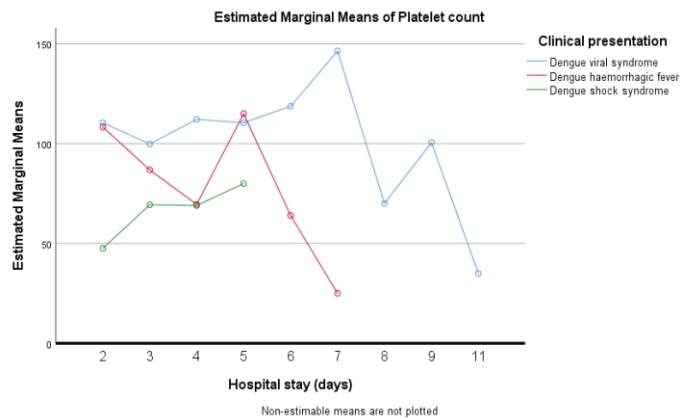
**Figure 1:** Pattern of Total Leukocyte Count Estimated Marginal Means in Dengue Infections

The highest mean value of HCT (42.92 + 2.04) was observed in DVS patients with 08 days of hospital stay, while the lowest mean value of HCT (36.50 + 4.09) was observed with 09 days of hospital stay. In DHF, the highest mean value of HCT (41.95 + 2.19) was observed in patients with 04 days of hospital stay, and the lowest mean value (37.23 + 3.34) with 02 days of hospital stay. The highest and lowest mean values of HCT were (45.90 + 5.79), and (36.12 + 2.59) were observed in DSS patients with 05 days and 04 days of hospital stay respectively but was statistically not significant. The pattern of HCT in DVS, DHF, and DSS patients is given (Figure 2).



**Figure 2:** Pattern of hematocrit estimated marginal mean values in dengue infections

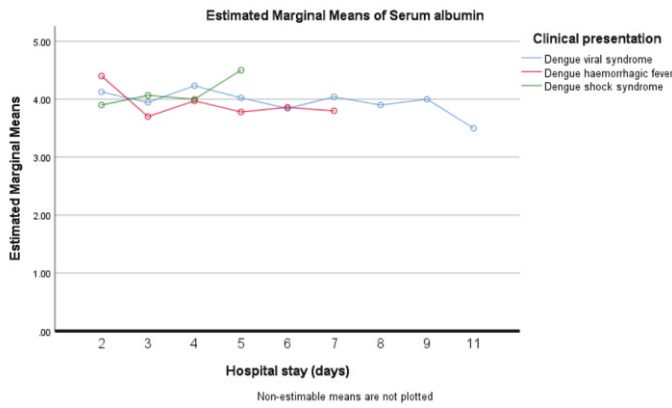
In DVS patients, statistically significant highest mean value of platelets (146.40 + 26.86) was observed with 07 days of hospital stay, while the lowest mean value of platelets (35.00 + 59.67) was observed with 11 days of hospital stay. In DHF, the highest mean value of platelets (115.0 + 26.68) was observed in patients with 05 days of hospital stay, and the lowest mean value (25.00 + 59.67) with 07 days of hospital stay. The highest mean values (80.00 + 59.67) and lowest mean values (47.50 + 42.19) of platelets were observed in DSS patients with 05 and 02 days of hospital stay respectively. The pattern of platelets in DVS, DHF, and DSS patients is given (Figure 3).



**Figure 3:** Pattern of Platelet estimated marginal mean values in dengue infections

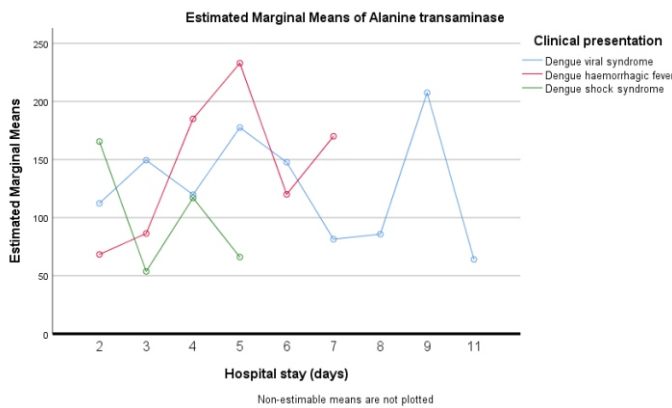
The normal ranges for biochemical parameters were: serum albumin (3.50-5.20 g/dL) and ALT (less than 41 U/L). In this study, out of 134 patients, 09 (6.71%) have decreased levels of serum albumin, and 122 (91.04%) have increased ALT levels. The mean values of serum albumin and ALT were also observed during the clinical course of DVS, DHF and DSS. The highest mean value of serum albumin (4.23 + 0.07) was observed in DVS patients with 04 days of hospital stay, while the lowest mean value of serum albumin (3.50 + 0.31) was observed with 11 days of hospital stay. In DHF, the highest mean value of serum albumin (4.40 + 0.18) was observed in patients with 02 days of hospital stay, and the lowest mean value (3.70 + 0.13) with 03 days of hospital stay. The highest and lowest mean values of serum albumin were (4.50 + 0.31), and (3.90 + 0.22) were observed in DSS patients with 05 days and 02 days of hospital stay respectively. All these findings were statistically non-significant. The pattern of serum albumin showed a marked difference between DVS, DHF, and DSS (Figure 4).





**Figure 4:** Pattern of serum albumin marginal mean values in dengue infections

The highest mean value of ALT (207.50+58.50) was observed in DVS patients with 09 days of hospital stay, while the lowest mean value of ALT (64.0+82.73) was observed with 11 days of hospital stay. In DHF, the highest mean value of ALT (233.0+36.99) was observed in patients with 05 days of hospital stay, and the lowest mean value (68.33+47.76) with 02 days of hospital stay. The highest and lowest mean values of ALT were (165.0 + 58.50), and (53.66+47.76) were observed in DSS patients with 03 days and 02 days of hospital stay respectively. All these findings were statistically non-significant. The pattern of ALT showed a marked difference between DVS, DHF, and DSS (Figure 5).



**Figure 5:** Comparison of alanine transaminase mean values in dengue infections

The association between study variables was determined by multivariate analysis. A statistically significant association was found among hospital stay (days) with TLC (0.002) and clinical presentation of dengue infection with platelets (0.012). The other variables were found statistically non-significant. The p-value of <0.05 was

**Table 1:** Observed association between study variables

Factors	Dependent variables	Mean square	p-value	Observed power
Hospital stay (days)	Total leukocyte count	16.21	0.002*	0.964
	Platelet count	3178.38	0.525	0.398
	Hematocrit	20.06	0.778	0.265
	Serum albumin	0.14	0.186	0.628
	Alanine transaminase	7653.15	0.356	0.498
Clinical presentation of dengue infection (DVS, DHF, and DSS)	Total leukocyte count	5.54	0.332	0.242
	Platelet count	16337.70	0.012*	0.767
	Hematocrit	0.71	0.979	0.053
	Serum albumin	0.11	0.333	0.241
	Alanine transaminase	6373.24	0.397	0.208

Statistical test: Multivariate analysis  
\*Significant p-value

considered statistically significant.

### Discussion

Differentiating dengue from other viral infections may be challenging due to the absence of specific early clinical features, besides Polymerase Chain Reaction (PCR) or NS1 antigen testing within the first 48 hours, which offers a greater likelihood of positive results. However, these tests cannot differentiate among those progressing to DVS, DHF, and DSS. The DHF and DSS are characterized by significant plasma leakage, resulting from various host factors emerging in the later stages of the illness. Changes in blood parameters during dengue infection could serve as predictive indicators for individuals at higher risk of plasma leakage and aid in the early detection of these complications. This approach enables clinicians to potentially identify prior development of DHF and DSS, facilitating effective patient management and reducing morbidity and mortality<sup>(9)</sup>. Previous studies have extensively presented the detailed clinical spectrum of dengue virus infection<sup>(13-15)</sup>. Our study, however, aimed to assess how TLC, HCT, platelets, serum albumin, and ALT vary among patients with different severities of dengue.

This study showed the raised incidence of dengue infection among males compared to females. In Pakistan, the male population typically spends extended periods outdoors due to employment, resulting in greater exposure to mosquitoes than females. Additionally, women in Pakistan tend to cover themselves more with clothing as compared to men. These study findings align with

previous research by Gandhi and Shetty<sup>16</sup> and Asghar et al.<sup>(17)</sup> The prevalence of dengue cases was notably higher among the age group of 11-50 years compared to the elderly (50-70 years of age). This elevated frequency within the younger age bracket can be attributed to the larger population size in this demographic and their increased exposure to mosquitoes, mainly due to their active engagement in outdoor activities. Consistent findings from other studies on dengue patients also endorsed this observation, highlighting an increased intensity of dengue within the younger age groups in contrast to the older population.<sup>18,19</sup> In this study, 70.9% of patients presented with mild dengue infection (DVS), and 29.1% of patients presented with severe dengue infections (DHF and DSS). The incidence of classic dengue fever of 70% was also found in other studies.<sup>20,21</sup> Our study showed that the mean duration of hospital stay was 4.38+1.85 days and this finding is consistent with another study which showed the mean duration of hospital stay ( $3.43 \pm 2.085$ ) days.<sup>22</sup>

In this study, thrombocytopenia, leukopenia, and high HCT were found in 76.86%, 51.49%, and 50.74% of the patients respectively. This finding is in agreement with a previous study showing 80% thrombocytopenia.<sup>4</sup> Another study from India has documented thrombocytopenia, leucopenia, and high HCT in dengue infection.<sup>25</sup>

The increase in HCT levels among dengue patients is often linked to plasma leakage caused by increased vascular permeability. While a 20% rise in HCT has been considered as a diagnostic threshold previously,<sup>23</sup> this study demonstrated less increase in HCT than expected. A similar observation of a lower-than-expected rise in HCT levels has been documented previously. This suggests the necessity for revised recommendations regarding HCT elevation for diagnosing dengue. The commonly observed leukopenia and thrombocytopenia in dengue patients result from bone marrow suppression and the binding of dengue antigens to platelets<sup>(24)</sup>. This study showed notable variations in TLC with severity of dengue infection but thrombocytopenia was not found significant in association with severity. This finding is in agreement with the previous study conducted in 2004.<sup>26</sup>

Our study revealed that 91.04% of dengue-infected patients have high ALT levels. These findings were consistent with a previous study conducted in Lahore, Pakistan.<sup>24</sup> In dengue patients, there was a consistent pattern of low serum albumin levels, with the severity

of the disease. The lowest levels were recorded in cases of DSS. This decline in albumin levels is linked to increased plasma leakage and increased vascular permeability seen in DSS. Consistent findings of decreased serum albumin levels were also noted in other studies conducted in India.<sup>20</sup>

## Conclusion

Based on the above findings, it is evident that hematological parameters like leukopenia (decreased total leukocyte count) vary with severity of disease (Hospital stay). Thrombocytopenia, increased HCT and biochemical parameters like increased ALT and decreased albumin may serve as a screening tool for early therapeutic response, however additional studies are required. Patients exhibiting compromised parameters should receive additional care to prevent the onset of complications.

**Conflict of Interest:** *None*

**Source of Funding:** *None*

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### Authors Contribution

**OF:** Conceptualization of Project

**EK:** Data Collection

**AF:** Literature Search

**ZY:** Statistical Analysis

**AA:** Drafting, Revision

**AM:** Writing of Manuscript