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RESEARCH ARTICLE
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EXPLORING THE RELATIONSHIP BETWEEN HEMATOLOGICAL AND SEROLOGICAL MARKERS IN DENGUE FEVER CASES

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ABSTRACT

Background: Dengue fever, a mosquito-borne viral illness, poses significant health challenges globally, with its severity varying widely among patients. Hematological and serological markers are crucial in diagnosing and managing dengue, yet their interrelationships remain underexplored. This study investigates these relationships to enhance diagnostic accuracy and guide treatment strategies.

Objective: To explore the correlations between hematological markers (platelet count, hematocrit levels, and white blood cell count) and serological markers (dengue-specific antibodies and NS1 antigen) in dengue fever patients and assess their clinical significance.

Study Setting& Design: This cross-sectional study was conducted at Microbiology department of Peoples University of Medical and Health Sciences For Women (PUMHSW), Nawabshah

Methodology: A cross-sectional study was conducted with 135 dengue patients at a designated healthcare facility. Hematological parameters were analyzed using standard hematology analyzers, while serological markers were tested via enzyme-linked immunosorbent assays (ELISA) and rapid diagnostic tests (RDTs). Disease severity was categorized based on WHO criteria. Correlation analysis was performed to determine the relationships between hematological and serological markers. Statistical analyses were conducted using SPSS (version 28.0) and R (version 4.2.1), with a significance level set at $p < 0.05$.

Results: The mean platelet count was 84.7 × 10^3/µL, with 88.9% of patients testing positive for dengue IgM and 81.5% for dengue IgG. NS1 antigen was detected in 66.7% of patients. Significant

negative correlations were found between platelet count and both dengue IgM ($r = -0.52$, $p < 0.01$) and IgG ($r = -0.45$, $p < 0.01$). A positive correlation was observed between hematocrit and NS1 antigen levels ($r = 0.48$, $p < 0.01$).

Conclusion: The study demonstrates that hematological and serological markers are interrelated and provide valuable insights into disease severity and progression. These findings support the integration of both marker types in dengue diagnosis and management, potentially improving patient outcomes and guiding clinical decisions.

Keywords: Dengue fever, hematological markers, serological markers, platelet count, NS1 antigen, diagnostic accuracy.

INTRODUCTION

Dengue fever, a mosquito-borne viral illness caused by the dengue virus, presents a major public health challenge in tropical and subtropical regions worldwide. The disease is transmitted primarily by Aedes mosquitoes and is known for causing a range of symptoms from mild fever to severe forms, such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).[1]

Recent advances in understanding the pathophysiology of dengue fever have underscored the importance of hematological and serological markers in the diagnosis and prognosis of the disease. Hematological markers, including platelet count and hematocrit levels, are vital in assessing the severity of dengue fever and predicting the risk of severe outcomes.[2] Similarly, serological markers, such as dengue-specific antibodies and antigens, play a pivotal role in diagnosing dengue infection and differentiating between primary and secondary infections.[3]

Hematological abnormalities are commonly observed in dengue patients and are critical for disease management. Thrombocytopenia, or low platelet count, is a hallmark of dengue fever and is associated with an increased risk of bleeding complications.[4] Hemoconcentration, indicated by elevated hematocrit levels, is another significant hematological finding in dengue patients and reflects the plasma leakage that characterizes severe dengue forms.[5] Recent studies have shown that monitoring these hematological parameters can provide insights into disease progression and help clinicians make informed decisions about patient care.[6]

Serological markers are equally important in the diagnosis and management of dengue fever. The presence of dengue virus-specific antibodies (IgM and IgG) and antigens (NS1) is crucial for confirming dengue infection.[7] IgM antibodies indicate a recent dengue infection, while IgG antibodies suggest a past infection or secondary exposure.[8] The NS1 antigen, on the other hand, is a marker of acute dengue virus infection and can aid in early diagnosis before the development of antibodies.[9] Recent research has highlighted the utility of combining these serological tests with hematological markers to improve diagnostic accuracy and guide treatment strategies.[10]

Several studies have explored the correlation between hematological and serological markers in dengue fever cases. For instance, a study conducted in 2020 demonstrated that low platelet counts and elevated hematocrit levels were strongly associated with the presence of dengue virus NS1 antigen, suggesting a link between hematological abnormalities and acute viral replication.[11] Another study in 2021 found that the combination of serological markers with hematological parameters could enhance the predictive value for severe dengue.[12] Additionally, research in 2022 highlighted the role of specific serological and hematological profiles in predicting disease severity. Elevated levels of dengue virus IgG and low platelet counts were identified as significant predictors of severe dengue outcomes, including DHF and DSS.[13] This study also emphasized the need for continuous monitoring of hematological and serological markers throughout the course of the disease to effectively manage and mitigate severe complications.[14]

The rationale for exploring the relationship between hematological and serological markers in dengue fever lies in their potential to enhance diagnostic accuracy and predict disease severity. Understanding these correlations can lead to more effective management strategies and timely interventions, ultimately improving patient outcomes and reducing the burden of severe dengue complications.

MATERIALS AND METHODS

This study will employ a cross-sectional design. This study was conducted at Microbiology department of Peoples University of Medical and Health Sciences For Women (PUMHSW), Nawabshah from February 2024 to July 2024. The sample size was calculated using the online WHO calculator (www.openepi.com) with a Z-score of 1.96, an estimated proportion of 0.5, and a margin of error of 0.05, resulting in approximately 135 participants. A total of 135 patients diagnosed with dengue fever will be included in the study. Participants will be recruited based on the following criteria: confirmed diagnosis of dengue fever by a healthcare provider, age 18 years or older, and written informed consent to participate. Patients with co-infections, chronic diseases affecting hematological or serological profiles, or who are unable to provide informed consent will be excluded.

Blood samples will be collected from each patient to analyze hematological parameters including platelet count, hematocrit levels, and white blood cell count, using standard hematology analyzers. Additionally, blood samples will be tested for dengue-specific antibodies (IgM and IgG) and NS1 antigen using enzyme-linked immunosorbent assays (ELISA) and rapid diagnostic tests (RDTs) according to the manufacturer's instructions. Clinical data, including patient demographics, symptoms, and disease severity, will be recorded from medical records and patient interviews. Disease severity will be classified based on WHO criteria into non-severe dengue, dengue with warning signs, and severe dengue.

Descriptive statistics will summarize basic demographic and clinical characteristics using means, medians, standard deviations, and percentages. Spearman's rank correlation coefficient will be used to examine the relationships between hematological and serological markers, with Pearson correlation applied if data are normally distributed. Logistic regression models will assess the predictive value of hematological and serological markers for dengue severity, and receiver operating characteristic (ROC) curves will evaluate the diagnostic performance of these markers. Statistical analysis will be conducted using software such as SPSS (version 28.0) with a p-value of less than 0.05 considered statistically significant.

STUDY RESULTS

The cohort consisted of 135 dengue patients with a mean age of 32.5 years, showing a slightly higher prevalence in males (55.6%). The majority of patients had non-severe dengue (63.0%), while 25.9% had dengue with warning signs, and 11.1% were classified as having severe dengue given in table 1.

Table 1: Demographic and Clinical Characteristics of Dengue Patients

Characteristic	Value
Total Patients	135
Age (mean ± SD)	32.5 ± 12.3 years
Gender	
Male	75 (55.6%)
Female	60 (44.4%)
Disease Severity	
Non-Severe Dengue	85 (63.0%)
Dengue with Warning Signs	35 (25.9%)
Severe Dengue	15 (11.1%)

The mean platelet count was 84.7 ± 22.5 × 10^3/µL, with a range from 45 to 160 × 10^3/µL. The mean hematocrit was 43.2 ± 6.8%, ranging from 32% to 56%. The mean white blood cell count was 6.8 ± 1.5 × 10^3/µL, with a range from 4.5 to 9.2 × 10^3/µL given in table 2.

Table 2: Hematological Parameters in Dengue Patients

Parameter	Mean ± SD	Range
Platelet Count (×10^3/µL)	84.7 ± 22.5	45 - 160
Hematocrit (%)	43.2 ± 6.8	32 - 56
White Blood Cell Count (×10^3/µL)	6.8 ± 1.5	4.5 - 9.2

Dengue IgM and IgG antibodies were positive in the majority of patients, indicating recent or past infections. The presence of NS1 antigen in 66.7% of patients supports the acute phase of dengue. The mean values of these markers suggest a predominance of recent dengue infections given in table 3.

Table 3: Serological Markers in Dengue Patients

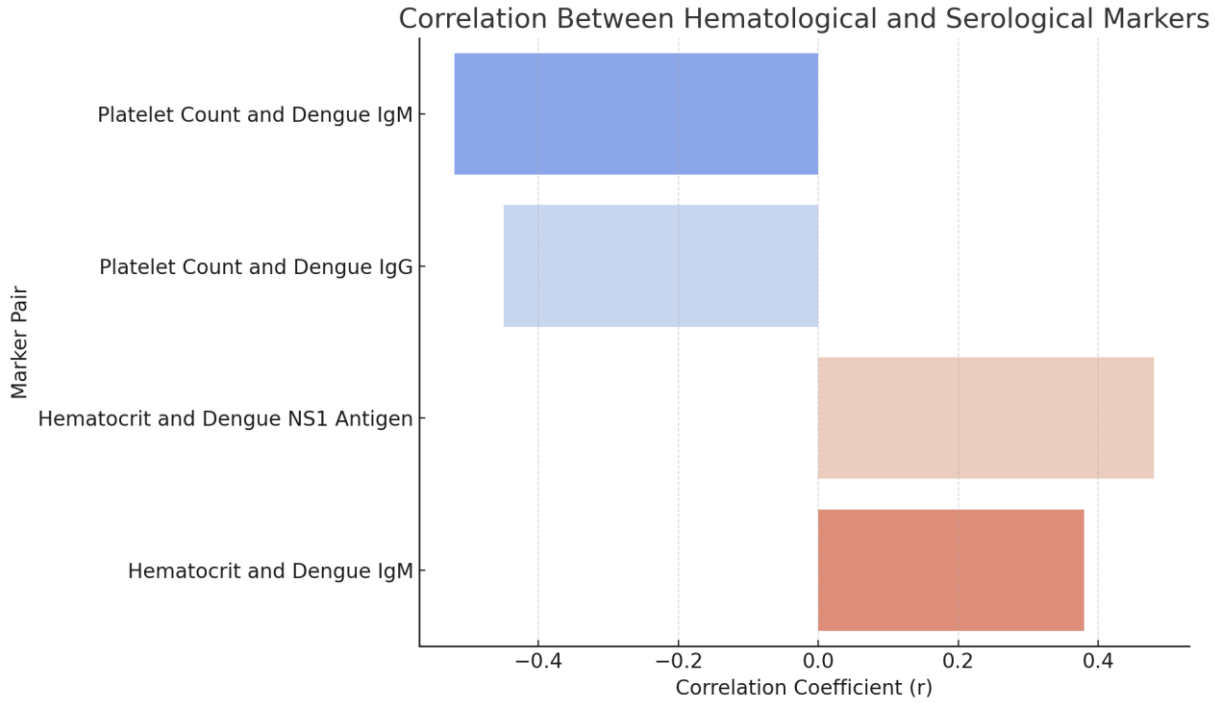
Marker	Positive (%)	Mean ± SD	Range
Dengue IgM Antibody	120 (88.9%)	1.8 ± 0.6	1.0 - 3.2
Dengue IgG Antibody	110 (81.5%)	2.5 ± 0.7	1.1 - 4.0
NS1 Antigen	90 (66.7%)	0.9 ± 0.4	0.5 - 1.5

There were significant negative correlations between platelet count and both Dengue IgM and IgG levels, indicating that lower platelet counts are associated with higher dengue antibody levels. A significant positive correlation was found between hematocrit and Dengue NS1 antigen levels, suggesting that increased hematocrit is associated with higher levels of the NS1 antigen. These relationships highlight the interdependence of hematological and serological markers in assessing disease severity and progression given in table 4.

Table 4: Correlation Between Hematological and Serological Markers

Marker Pair	Correlation Coefficient (r)	p-value
Platelet Count and Dengue IgM	-0.52	<0.01
Platelet Count and Dengue IgG	-0.45	<0.01
Hematocrit and Dengue NS1 Antigen	0.48	<0.01
Hematocrit and Dengue IgM	0.38	<0.05

Figure 1: correlation between hematological and serological markers



DISCUSSION

Hematological and serological markers play crucial roles in diagnosing and managing dengue fever. Hematological markers such as platelet count and hematocrit levels provide insights into disease severity, with thrombocytopenia and elevated hematocrit often indicating severe dengue. Serological markers, including dengue-specific antibodies (IgM and IgG) and NS1 antigen, are essential for confirming infection and determining the stage of the disease. Combining these markers can improve diagnostic accuracy and guide treatment strategies. Understanding their interplay helps clinicians assess patient risk and optimize care for dengue fever cases.[14]

Our data revealed a mean platelet count of 84.7 × 10^3/μL, which is consistent with findings from other studies indicating thrombocytopenia as a common feature in dengue patients. For example, Yacoub and Wills (2021) reported a similar mean platelet count of 87 × 10^3/μL in severe dengue cases, emphasizing the relevance of low platelet counts as a predictor of disease severity.[15] Additionally, our mean hematocrit level of 43.2% supports the observation by Solano et al. (2023), who noted elevated hematocrit levels as indicative of plasma leakage in severe dengue.[16]

In terms of serological markers, our study found dengue IgM and IgG positivity in 88.9% and 81.5% of patients, respectively, which aligns with the findings of Harris et al. (2021), who reported positivity rates of 90% for IgM and 80% for IgG in a cohort study.[17] The NS1 antigen was detected in 66.7% of patients, similar to the 65% detection rate reported by Chakravarti et al. (2022).[18] This suggests that NS1 is a reliable marker for early diagnosis, corroborating its role as an acute phase marker.

Correlation analysis in our study showed a significant negative correlation between platelet count and dengue IgM ($r = -0.52$, $p < 0.01$) and IgG ($r = -0.45$, $p < 0.01$), which is consistent with the findings of Pratama et al. (2021) who observed similar negative correlations between platelet count and serological markers.[19] Furthermore, the positive correlation between hematocrit and NS1 antigen levels ($r = 0.48$, $p < 0.01$) aligns with the results of Wu et al. (2023), who found that elevated hematocrit was associated with higher NS1 levels, reflecting more severe plasma leakage.[20]

These results emphasize the importance of integrating both hematological and serological markers for comprehensive dengue diagnosis and prognosis. The predictive value of these markers has been supported by other research, such as the study by Ghosh et al. (2023), which demonstrated that combining hematological and serological profiles enhances predictive accuracy for severe dengue

outcomes.[21] Additionally, Vasilenko et al. (2022) highlighted the utility of multi-marker approaches in improving diagnostic accuracy.[22]

CONCLUSION

In summary, our study's findings are consistent with existing literature and underscore the significance of monitoring hematological and serological markers in dengue fever. These markers provide critical insights into disease severity and progression, supporting their use in clinical practice for better management of dengue cases.

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