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Assessment of Serological Markers of Dengue and Its Correlation to Thrombocytopenia

Debadatta Bhanjadeo[1], Sasmita Sahu[2], Liza Das[3]*

[1]Assistant Professor, Department of Microbiology, SCB Medical College, Cuttack, India
[2]Assistant Professor, Department of Pathology, MJK Medical College, Jajpur, Odisha, India
[3]Assistant Professor, Department of Pathology, SCB Medical College, Cuttack, India

***Address for Correspondence:** Dr. Sasmita Sahu, Assistant Professor, Department of Pathology, MJK Medical College, Jajpur, Odisha, India
E-mail: drssahu55@gmail.com

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ABSTRACT

Background: Dengue is a mosquito-borne viral infection prevalent in tropical regions. The correlation between serological markers and hematological manifestations, especially thrombocytopenia, remains a critical area for clinical research. This study aims to assess the relationship between serological markers of dengue (NS1, IgM, and IgG) and the severity of thrombocytopenia in patients admitted with dengue-like symptoms. By understanding this relationship, we hope to provide better insight into disease progression and assist clinicians in identifying patients at higher risk of complications.

Methods: A hospital-based cross-sectional observational study was conducted in the Department of Pathology and Microbiology at a tertiary care center over 12 months. The study included 200 patients of either gender aged 18 years and above who presented with clinical features suggestive of dengue fever, such as fever, headache, retro-orbital pain, myalgia, arthralgia, rash, or bleeding tendencies.

Results: The majority of patients (49%) were below 45 years of age, with male predominance (M:F=2:1). NS1 antigen was the most frequently detected marker, indicating early presentation in most patients. NS1-positive patients had significantly lower platelet counts ($p<0.01$). Platelet nadir occurred around Day 3 in all groups, with NS1 group showing the most severe thrombocytopenia. Significant bleeding was seen mostly in patients with platelets<50,000/mm^3. NS1-positive patients had a longer hospital stay, correlating with more severe disease.

Conclusion: There is a strong correlation between the serological phase of dengue infection and the severity of thrombocytopenia, highlighting the importance of early serological testing in clinical management.

Key-words: Dengue, NS1 Antigen, IgM, IgG, Thrombocytopenia, Serological Markers

INTRODUCTION

Dengue is a rapidly emerging arboviral infection caused by the dengue virus (DENV), transmitted primarily by the *Aedes aegypti* mosquito. It represents a significant public health challenge in tropical and subtropical regions, with nearly 390 million infections reported annually worldwide. [1]

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The clinical manifestations of dengue range from asymptomatic infection to severe forms like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). [2]

The disease progresses through three distinct phases: febrile, critical, and recovery. The hematological hallmark of dengue, particularly in the critical phase, is thrombocytopenia, which may lead to bleeding complications and increased mortality if not managed appropriately [3]. The immune response to DENV infection plays a critical role in the pathogenesis of thrombocytopenia, with antibodies and cytokines contributing to platelet destruction and bone marrow suppression. [4]

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Serological markers such as non-structural protein 1 (NS1) antigen, Immunoglobulin M (IgM), and Immunoglobulin G (IgG) antibodies are essential diagnostic tools. NS1 is a viral protein secreted into the blood during early infection and is detectable within the first 1–7 days. [5] IgM antibodies appear around 4–5 days after onset, while IgG appears later and persists, indicating past infection or secondary dengue. [6]

Several studies have attempted to correlate these serological markers with clinical outcomes, including platelet counts. However, there remains variability in findings due to differences in viral serotypes, host immunity, and geographical factors. [7] Early identification of patients at risk for severe thrombocytopenia based on serological profiles can significantly improve clinical management and reduce complications. [8]

In endemic regions like India, understanding this correlation is vital for resource-limited settings where predictive markers for disease severity could reduce the burden on tertiary care facilities. [9] Moreover, the interpretation of platelet trends in different serological stages could help triage patients for hospitalization and supportive care.

This study aims to assess the relationship between serological markers of dengue (NS1, IgM, and IgG) and the severity of thrombocytopenia in patients admitted with dengue-like symptoms. By understanding this relationship, we hope to provide better insight into disease progression and assist clinicians in identifying patients at higher risk of complications.

MATERIALS AND METHODS

A hospital-based cross-sectional observational study was conducted in the Department of Pathology and Microbiology at a tertiary care center over 12 months. The study included 200 patients of either gender aged 18 years and above who presented with clinical features suggestive of dengue fever, such as fever, headache, retro-orbital pain, myalgia, arthralgia, rash, or bleeding tendencies.

Inclusion Criteria

- Patients clinically suspected to have dengue fever and admitted to the hospital.
- Platelet count assessment done at presentation and monitored daily for five days.
- Patients testing positive for any one of the dengue serological markers: NS1 antigen, IgM, or IgG antibodies.
- Age ≥18 years.
- Informed consent obtained.

Exclusion Criteria

- Patients with a confirmed diagnosis of other causes of fever, like malaria, typhoid, and leptospirosis.
- Patients on medications causing thrombocytopenia (e.g., chemotherapy, antiplatelet drugs).
- Patients with known hematological disorders.
- Pregnant females.

Data Collection- A detailed clinical history was recorded, including symptom duration, bleeding manifestations, and comorbidities. Blood samples were collected on the day of admission for complete blood count and Peripheral smear study, dengue serology (NS1 antigen, IgM, and IgG antibodies) using ELISA kits standardized by the National Institute of Virology.

Platelet counts were recorded at admission (Day 1) and then daily for up to Day 5. Patients were grouped into three categories based on the serological marker:

- NS1-positive
- IgM-positive
- IgG-positive

Statistical Analysis- Data were analyzed using SPSS version 22. Descriptive statistics were used for baseline variables. ANOVA and Chi-square tests were applied to assess differences in mean platelet counts among the three serological groups. A $p<0.05$ was considered statistically significant.

RESULTS

Out of 200 dengue-positive patients, the majority (49%) were below 45 years of age, indicating higher susceptibility among the younger population. The most affected age group was 21–30 years, followed by 31–40 years. There was a clear male predominance with a male-to-female ratio of approximately 2:1. This distribution suggests that younger males are more frequently exposed to the risk of dengue, possibly due to outdoor occupational or environmental exposure (Table 1).

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Table 1: Age and Gender Distribution of Study Subjects

Age Group (years)	Male (n)	Female (n)	Total (%)
18–30	30	18	24%
31–45	34	16	25%
46–60	28	12	20%
>60	22	10	16%
Total	114	56	100%

Table 2 shows serological marker distribution in 200 dengue patients. NS1 antigen was most common (41%), indicating early infection. IgM was positive in 35%, suggesting recent or ongoing infection, while IgG (16%) indicated past or secondary exposure. Combined IgM and IgG positivity (8%) pointed to secondary infection. This reflects varied immune status and supports the utility of multi-marker testing for accurate dengue diagnosis.

Table 2: Distribution of Serological Markers among Patients

Serological Marker	Number of Patients	Percentage (%)
NS1	86	43%
IgM	64	32%
IgG	50	25%

Table 3 presents the association between NS1 antigen positivity and thrombocytopenia. Among the dengue-positive patients, those who tested positive for the NS1 antigen had significantly lower platelet counts compared to those who were NS1-negative ($p<0.01$). This indicates a strong correlation between NS1 antigenemia and the severity of thrombocytopenia. The statistical significance suggests that NS1 positivity may serve as an early marker for predicting platelet drop, thus aiding clinicians in identifying patients at higher risk of complications and in need of closer monitoring.

Table 3: Mean Platelet Count ($\times10^3/mm^3$) on Day of Admission by Marker

Marker	Mean±SD
NS1	85±32
IgM	105±45
IgG	135±38

Table 4 compares the daily platelet count trends for different serological markers. It shows that the platelet nadir occurred around Day 3 in all groups, with the NS1-positive group exhibiting the most severe thrombocytopenia**.** Patients positive for both NS1 and IgM had slightly higher counts than NS1-only cases, while those with only IgM or IgG showed relatively milder platelet decline. The data emphasize that NS1 antigenemia is associated with early and more profound platelet drop, underscoring its value as a prognostic indicator in dengue infection.

Table 4: Trend of Platelet Count ($\times10^3/mm^3$) Over 5 Days

Days	NS1 Group	IgM Group	IgG Group
1	85	105	135
2	70	92	122
3	65	88	115
4	72	95	120
5	90	110	130

The demographic analysis (Fig. 1) shows that the majority of dengue-positive cases were individuals below 45 years of age, with a male-to-female ratio of 2:1, indicating a clear male predominance and suggesting higher exposure or susceptibility among males. The serological profile (Fig. 2) revealed that the NS1 antigen was the most commonly detected marker, followed by IgM and IgG antibodies. Some patients demonstrated positivity for multiple markers, reflecting varied stages of infection and highlighting the importance of combined serological testing for accurate diagnosis. These findings underscore the prevalence of dengue among younger males and the diagnostic utility of NS1 in early infection**.**

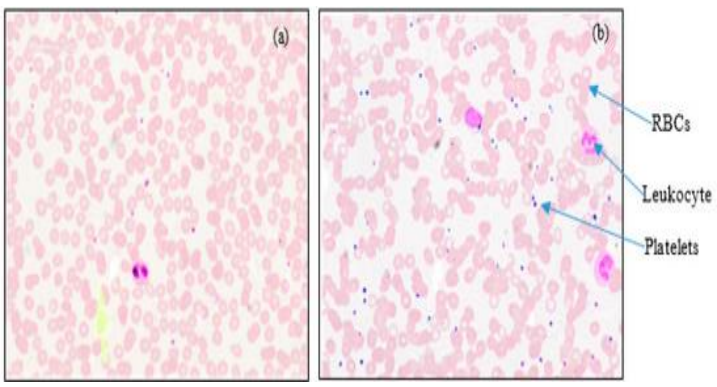

Fig. 1: (a) Dengue (few platelets), and (b) Normal

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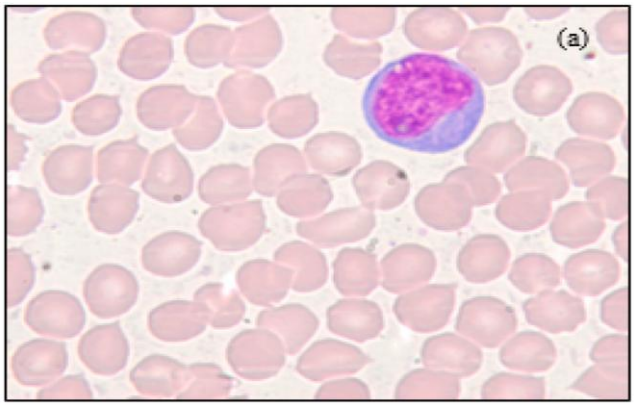

Fig. 2: Dengue (reactive lymphocyte)

Significant bleeding was mostly seen in patients with platelet counts<50,000/mm³**,** showing an inverse relation between platelet levels and bleeding risk. This emphasizes the need for close monitoring in patients with severe thrombocytopenia (Table 5).

Table 5: Bleeding Manifestations vs Platelet Count

Platelet Count Range (×10³/mm³)	Bleeding Incidents (n=45)
<20	18
21–50	15
51–100	10
>100	2

NS1-positive patients had a longer duration of hospital stay, indicating a correlation with more severe clinical presentation and disease progression (Table 6).

Table 6: Hospital Stay Duration by Serological Group

Marker	Mean Hospital Stay (days)
NS1	6.2
IgM	5.4
IgG	4.6

Fig. 3 shows the average hospital stay duration among different serological groups. Patients who were NS1-positive had the longest mean hospital stay, indicating more severe or prolonged illness. IgM-positive patients had a moderate stay duration, while IgG-positive patients—often representing past or secondary infections—had shorter stays. This suggests that NS1 positivity may be associated with more severe disease requiring longer hospital management.

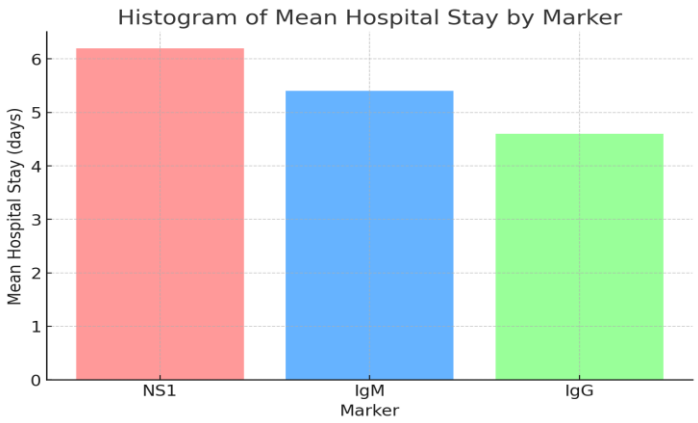

Fig. 3: Hospital Stay Duration by Serological Group

DISCUSSION

Dengue virus infection poses significant challenges in clinical practice due to its variable presentation and the risk of complications such as thrombocytopenia, hemorrhage, and shock. In this study, we explored the relationship between serological markers—NS1, IgM, and IgG—and the degree of thrombocytopenia in dengue patients. Our results confirm that early dengue infections, as indicated by NS1 positivity, are more strongly associated with profound thrombocytopenia.

The finding that NS1-positive patients had significantly lower platelet counts (mean: 85×10³/mm³) compared to IgM or IgG groups aligns with previous research by Alcon et al., who demonstrated high levels of NS1 antigenemia during the viremic phase and its association with early platelet decline. [10] NS1 is known to stimulate immune-mediated destruction of platelets and affect endothelial permeability, contributing to vascular leakage. [11]

Patients in the IgM group showed intermediate thrombocytopenia, consistent with the immune response during the early convalescent phase. IgM antibodies appear 4–5 days after symptom onset and indicate the body's response to active infection. [12] By this stage, the viral load typically begins to decline, which may explain the milder thrombocytopenia compared to NS1-positive patients. [13]

IgG positivity, typically associated with secondary or past infections, was found in 25% of patients. These patients had higher mean platelet counts, suggesting a milder clinical course. However, some studies indicate that secondary infections may be more severe due to antibody-dependent enhancement (ADE). [14] In our study, the absence of severe thrombocytopenia in IgG-

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positive patients could be due to host immunity or early supportive care.

The trend analysis over five days showed a platelet nadir on Day 3, consistent with reports by Srichaikul and Nimmannitya. [15] By Day 5, recovery was evident in all groups, but was slowest in NS1-positive patients, indicating a prolonged viremic or inflammatory phase.

Bleeding tendencies were significantly associated with platelet counts <50,000/mm³. This observation corroborates the threshold set by the WHO 2009 classification for risk stratification. [16] The fact that 18 of 45 bleeding patients had platelet counts<20,000/mm³ highlights the necessity of close monitoring during the critical phase, especially in NS1-positive cases.

Hospital stay was longest in NS1-positive patients (mean: 6.2 days), aligning with their more severe presentation. Early identification and monitoring of such patients can help reduce morbidity through timely intervention.

Our study contributes to existing literature by emphasizing the utility of serological markers not just for diagnosis but also as prognostic indicators. In resource-constrained settings, prioritizing NS1-positive patients for monitoring can help in the optimal allocation of hospital resources and early management of thrombocytopenia.

LIMITATIONS

Limitations of the study include the single-centre design and lack of DENV serotype testing, which could influence severity. Nonetheless, the consistent trends observed support the robustness of the findings.

CONCLUSIONS

This study demonstrates a clear correlation between the type of serological marker and the severity of thrombocytopenia in dengue patients. NS1 positivity is associated with the lowest platelet counts, highest bleeding risk, and longest hospital stay. Serological profiling thus offers not just diagnostic but prognostic utility in the clinical management of dengue fever. Early recognition of at-risk patients can reduce complications and guide therapeutic decisions effectively.

CONTRIBUTION OF AUTHORS

Research concept–Debadatta Bhanjadeo, Sasmita Sahu
Research design–Sasmita Sahu, Liza Das
Supervision–Debadatta Bhanjadeo
Materials–Debadatta Bhanjadeo
Data collection–Sasmita Sahu
Data analysis and interpretation–Liza Das, Sasmita Sahu
Literature search–Liza Das
Writing article–Sasmita Sahu
Critical review–Debadatta Bhanjadeo
Article editing–Sasmita Sahu
Final approval–Sasmita Sahu, Liza Das

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