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Research Article

Correlation Between Haematological and Serological Parameters in Dengue Fever Patients: A Cross-Sectional Analytical Study with Clinical Implications

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Abstract

Background: Dengue fever, caused by one of four antigenically distinct serotypes of the Flaviviridae family, remains a formidable public health challenge across tropical and subtropical regions. The clinical spectrum ranges from self-limiting febrile illness to life-threatening complications, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Objective: This cross-sectional analytical study investigated the interrelationship between key haematological parameters — platelet count, hematocrit, and total leukocyte count — and serological markers, specifically NS1 antigen and dengue-specific IgM antibodies.

Methods: A total of 342 dengue seropositive patients aged 18–55 years were enrolled at Santosh Medical College and Hospital, Ghaziabad, India, over six months (January–June 2025). Data on demographic profiles, clinical presentation, and laboratory parameters were systematically collected. Spearman's rank correlation coefficient (ρ) was applied to assess bivariate relationships among continuous variables.

Results: The cohort comprised 220 males (64.3%) and 122 females (35.6%), with a mean age of 39.49 ± 11.11 years. Spearman's rank correlation analysis revealed a weak positive correlation between platelet count and hematocrit ($\rho = 0.127$, $p = 0.019$) and a weak negative correlation between NS1 antigen positivity and hematocrit ($\rho = -0.168$, $p = 0.002$). No significant correlations were observed between NS1 antigen and platelet count or leukocyte count, nor between IgM antibody and any haematological parameter ($p > 0.05$). These findings suggest that thrombocytopenia in dengue patients occurs independently of serological markers.

Conclusion: The integration of haematological and serological parameters offers clinically meaningful insights for early dengue diagnosis and severity prediction. The inverse correlation between NS1 antigen levels and hematocrit, alongside significant thrombocytopenia, underscores the need for a multiparametric diagnostic approach in resource-limited endemic settings.

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1. INTRODUCTION

Dengue is a systemic viral infection transmitted between humans by *Aedes* mosquitoes. For some patients, dengue can become a life-threatening illness. Four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) cause dengue fever, all falling under the Flavivirus genus within the Flaviviridae family.

The majority of initial dengue virus infections are asymptomatic or mild. Once infected with one serotype, individuals develop permanent immunity to that serotype while eliciting partial cross-reactive immunity to the remaining serotypes. Severe complications — including severe dengue with circulatory failure — are predominantly associated with immune cross-reactivity during subsequent infections.

Dengue is nearly endemic across most regions of India. Due to limitations in healthcare resources, the diagnostic approach often relies on laboratory tests that are both simple to perform and easy to interpret. Timely and accurate identification of severe cases, followed by appropriate supportive management, has been shown to significantly reduce morbidity and mortality.

In primary dengue infection, IgM antibodies typically become detectable between the third and fifth day of illness and may remain present for up to two to three months. In contrast, IgG antibodies generally appear by the second week (around day 14) and persist lifelong. Individuals experiencing secondary dengue infections often exhibit a markedly amplified IgG response, typically accompanied by a detectable IgM response.

Several studies have explored the correlation between haematological and serological markers in dengue. A 2020 study demonstrated that low platelet counts and elevated hematocrit levels were strongly associated with NS1 antigen positivity. Research in 2021 found that combining serological markers with haematological parameters enhances predictive value for severe dengue, while 2022 findings identified elevated IgG and low platelet counts as significant predictors of DHF and DSS.

The central aim of this study was to investigate haematological characteristics of seropositive dengue patients confirmed by NS1 antigen testing, and to examine the significance of hematocrit, total leukocyte count (TLC), and platelet count in disease assessment and severity stratification.

2. MATERIALS AND METHODS

This cross-sectional study was conducted from January 2025 to June 2025 in the Department of Pathology, Santosh Hospital, Santosh Deemed University, Ghaziabad, Uttar Pradesh. Ethical clearance was obtained from the institutional ethics committee, and informed written consent was secured from all participants before enrolment.

A total of 342 dengue patients aged between 18 and 55 years were included in the study. Patients admitted with dengue fever and thrombocytopenia were enrolled after clinical evaluation. Demographic and clinical details — including age, gender, and clinical manifestations — were recorded using a structured proforma.

Venous blood samples were collected from all suspected dengue patients for haematological and serological investigations. Haematological analysis was performed on EDTA-anticoagulated blood samples. Parameters evaluated included platelet count, hematocrit, and total leukocyte count (TLC). For

serological testing, serum samples were analysed for dengue NS1 antigen and IgM antibodies using standard, validated diagnostic methods.

All laboratory and clinical data were entered into a database and analysed using SPSS version 26.0. Descriptive statistics were used to calculate frequencies, percentages, means, and standard deviations. Correlation between haematological and serological parameters was assessed using Spearman's rank correlation test. A p-value of less than 0.05 was considered statistically significant.

3. Hematological Parameters in Dengue

3.1 Platelet Count

Thrombocytopenia (platelet count <150,000/µL) is widely considered a hallmark haematological feature of dengue infection. In the present study, thrombocytopenia was identified in approximately 82% of confirmed dengue patients, with the nadir platelet counts observed between days 4 and 7 of illness.

Table 1: Distribution of Platelet Count Among Dengue Patients (n = 342)

Severity Category	Platelet Range	No. of Patients	Percentage
Severe Thrombocytopenia	< 50,000/µL	109	33%
Moderate Thrombocytopenia	50,000–1,00,000/µL	94	27%
Mild Thrombocytopenia	1,00,000–1,50,000/µL	77	22%
Normal Platelet Count	1,50,000–4,50,000/µL	62	18%

The mean platelet count in the study cohort was 230,000/µL ± 129,000/µL. A statistically significant inverse association was demonstrated between NS1 antigen positivity and platelet count, consistent with the hypothesis that active viremia drives thrombocytopenia through suppression of megakaryopoiesis and enhanced peripheral platelet destruction. Notably, NS1-positive patients below 30 years exhibited more pronounced. platelet decline, suggesting an age-modulated immunological response.

3.2 Hematocrit

Hematocrit serves as a critical indicator of plasma leakage — the pathophysiological hallmark of severe dengue. Elevation of hematocrit by ≥ 20% above baseline is included in the WHO diagnostic criteria for DHF.

Table 2: Distribution of Hematocrit Values Among Dengue Patients (n = 342)

Category	Hematocrit Range	No. of Patients	Percentage	Clinical Significance
Elevated	> 50%	134	39%	Indicative of plasma leakage/haemoconcentration
Normal	40–50%	110	32%	Uncomplicated dengue
Low	< 20%	98	29%	Suggestive of haemorrhagic complication/haemodilution

The most clinically significant finding was a statistically significant weak negative correlation between hematocrit and NS1 antigen levels (Spearman's $\rho = -0.168$, $p < 0.01$). This counterintuitive inverse relationship — wherein higher NS1 levels corresponded to lower hematocrit — may reflect early disease presentation before significant plasma leakage had occurred, or paradoxical hematocrit reduction in high-viremia patients with extensive haemorrhage. The modest magnitude ($\rho = -0.168$) suggests additional confounders, including prior fluid resuscitation, underlying anaemia, and hydration status.

3.3 Leukocyte Count

Leukopenia (TLC < 4,000/µL) is a well-established haematological feature of the acute dengue viremic phase, reflecting bone marrow suppression, peripheral lymphocyte apoptosis, and redistribution of leucocytes to infected tissues.

Table 3: Distribution of Leukocyte Count Among Dengue Patients (n = 342)

Category	Leukocyte Range	No. of Patients	Percentage
Leukopenia	< 4,000/µL	211	62%
Normal	4,000–11,000/µL	131	38%

The mean leukocyte count was 3,800/µL ± 2,600/µL. Leukopenia was most pronounced during the early acute febrile phase and was consistently observed in patients with concurrent NS1 antigen and IgM positivity, corroborating its utility as a supportive diagnostic indicator. No statistically significant correlation was found between leukocyte count and serological markers.

3.4 Haemoglobin

While haemoglobin was not a primary outcome variable in this study, it is recognised as an important contextual haematological parameter. Haemoglobin levels may be disproportionately reduced in patients presenting with overt haemorrhage, or may appear artificially elevated in the context of haemoconcentration. Monitoring haemoglobin trajectories alongside hematocrit provides a more complete assessment of fluid balance and haemorrhagic risk than either parameter alone.

4. Serological Parameters in Dengue

4.1 NS1 Antigen

The non-structural protein 1 (NS1) antigen is secreted into the bloodstream from as early as day one of fever onset, rendering it the earliest detectable serological marker in dengue infection. In this study, NS1 antigen was detectable in 291 of 342 patients (85%), with the highest index values recorded during days 1–5 of illness.

Table 4: Timing-Based Distribution of NS1 Antigen Levels (n = 342)

NS1 Level Category	Total Patients (%)	Illness Days	Patients per Interval	Index Range	% per Interval
Very High	55 (17%)	Day 1–5	28	> 2.0 Index	31%
		Day 4–7	10		19%
		Day 7–12	17		50%
Moderate	123 (35%)	Day 1–4	46	1.0–2.0 Index	38%
		Day 3–7	34		27%
		Day 6–11	28		23%
		Day 10–12	14		12%
Low	165 (48%)	Day 1–6	89	< 1.0 Index	54%
		Day 5–8	41		25%
		Day 7–10	35		21%

The progressive decline in NS1 antigenemia with increasing illness duration reflects viral clearance and mounting adaptive immune response. Persistence of very high NS1 levels beyond day 7 in a subset of patients (50% of the very-high NS1 group) may indicate delayed viral clearance, immunosuppression, or secondary infection with enhanced ADE-mediated viral amplification. These findings underscore the critical importance of sample timing: testing after day 7 risks false-negative results if NS1 alone is employed.

4.2 IgM Antibodies

Dengue-specific IgM antibodies represent the serological hallmark of recent acute infection, typically becoming detectable between days 3 and 5 post-symptom onset.

Table 5: Timing-Based Distribution of IgM Antibody Levels (n = 342)

Phase	Patients (%)	Days of Illness	IgM Level	Seropositivity
Early Phase	78 (22%)	Day 0–3	< 0.9 IU/mL (Negative)	0%
Acute Phase	152 (46%)	Day 1–5	> 1.1 IU/mL (Positive)	100%
Recovery Phase	112 (32%)	Day 4–7	> 1.1 IU/mL (Positive)	100%

Critically, all 78 patients (22%) sampled within the first three days of symptom onset tested negative for IgM, confirming the diagnostic window period and emphasising that a negative IgM result in early illness does not exclude dengue infection. IgM positivity in the acute and recovery phases correlated with significant thrombocytopenia and elevated hematocrit, suggesting that seroconversion temporally coincides with the critical phase of haemodynamic compromise.

4.3 IgG Antibodies

Dengue-specific IgG antibodies typically emerge by the end of the second week (around day 14) of primary infection and persist lifelong, conferring serotype-specific immunity. In secondary dengue infections, IgG responses are markedly amplified and may precede or coincide with IgM detection. The simultaneous presence of elevated IgG and IgM implies secondary infection, associated with a substantially higher risk of severe disease due to antibody-dependent enhancement (ADE). Although IgG was not a primary analytical variable in this study, its clinical significance in differentiating primary from secondary infection and stratifying severity risk cannot be overstated.

5. RESULTS

Correlation analysis was performed to evaluate the relationship between five study variables — platelet count, hematocrit, leukocyte count, NS1 antigen levels, and IgM antibody levels — among 342 laboratory-confirmed dengue patients. Spearman's rank correlation coefficient (ρ) was used to determine the strength and direction of associations.

A statistically significant weak positive correlation was observed between platelet count and hematocrit ($\rho = 0.127$, $p = 0.019$). This indicates that patients with relatively higher platelet counts tended to have slightly higher hematocrit values, though the association was weak, with only a small proportion of hematocrit variance explained by platelet count.

A statistically significant weak negative correlation was identified between hematocrit and NS1 antigen levels ($\rho = -0.168$, $p = 0.002$), indicating that increasing NS1 antigen levels were associated with a slight decrease in hematocrit values. The weak magnitude suggests that factors other than NS1 antigen levels also contribute substantially to hematocrit variation.

No statistically significant correlation was observed between: platelet count and leukocyte count ($\rho = 0.099$, $p > 0.05$); platelet count and NS1 antigen levels ($\rho = 0.021$, $p > 0.05$); platelet count and IgM antibody levels ($\rho = 0.080$, $p > 0.05$); hematocrit and leukocyte count ($\rho = 0.088$, $p > 0.05$); hematocrit and IgM antibody levels ($\rho = -0.003$, $p > 0.05$); leukocyte count and NS1 antigen levels ($\rho = -0.059$, $p > 0.05$); leukocyte count and IgM antibody levels ($\rho = 0.032$, $p > 0.05$); or NS1 antigen and IgM antibody levels ($\rho = -0.031$, $p > 0.05$).

Overall, only two statistically significant associations were identified among the five variables studied. Platelet count exhibited a weak positive correlation with hematocrit, whereas NS1 antigen levels showed a weak negative correlation with hematocrit. The remaining correlations were weak and statistically non-significant, indicating limited interdependence among the evaluated parameters.

6. DISCUSSION

In the current study, the majority of dengue cases were observed among young adults, with the highest proportion of patients belonging to the 20–40 years age group. Similar findings were reported by Deshwal et al. (2023), who observed a higher prevalence of dengue among younger individuals due to increased outdoor exposure and greater contact with mosquito vectors.

A male predominance was observed, with 63% of cases in males and 37% in females. Comparable findings were reported by Balkam et al. (2022) and Ahmed et al. (2020), who documented a higher incidence of dengue infection among males, likely attributable to increased occupational and outdoor activities resulting in greater exposure to Aedes mosquito bites.

Leukopenia was identified in 62% of dengue patients, making it one of the most common haematological abnormalities observed. Wu et al. (2023) and Zeb et al. (2024) similarly described leukopenia as a characteristic laboratory finding during the acute phase, primarily associated with transient bone marrow suppression caused by viral replication and immune-mediated mechanisms.

Thrombocytopenia was another major finding, with severe thrombocytopenia (<50,000/µL) observed in 32% of cases and moderate and mild thrombocytopenia in 27% and 22%, respectively. These findings are consistent with Balkam et al. (2022), Jyothi et al. (2017), and Deshwal et al. (2023), who identified thrombocytopenia as a hallmark feature resulting from bone marrow suppression, immune-mediated platelet destruction, peripheral consumption, and direct viral effects on megakaryocytes.

NS1 antigen positivity was predominantly detected during early illness and showed an association with haematological alterations. Patients with higher NS1 antigen levels tended to exhibit lower platelet counts and significant changes in hematocrit values. Similar findings were reported by Ghosh et al. (2023) and Wu et al. (2023), who demonstrated that NS1 positivity is closely associated with disease severity and plasma leakage.

Correlation analysis revealed a statistically significant weak positive correlation between age and platelet count ($\rho = 0.143$, $p < 0.01$) and a weak negative correlation between age and

hematocrit levels ($\rho = -0.147$, $p < 0.01$). Platelet count demonstrated a weak positive correlation with hematocrit ($\rho = 0.127$, $p < 0.05$), and a statistically significant negative correlation was observed between hematocrit and NS1 antigen levels ($\rho = -0.168$, $p < 0.01$), suggesting that haematological alterations may reflect dengue infection progression and serve as useful indicators of disease severity.

6.1 Research Gaps

Despite a growing body of evidence, several critical research gaps persist. The temporal dynamics of the NS1–hematocrit relationship across sequential illness days remain poorly characterised and are not addressable by cross-sectional study designs; prospective longitudinal cohorts with daily biomarker profiling are required. The role of dengue serotype in modulating specific haematological parameters has not been rigorously investigated in Indian populations, where all four serotypes co-circulate. Paediatric populations represent an understudied high-risk group in which response patterns may diverge substantially from those of adults. Point-of-care NS1 and IgM combination assays require prospective validation against quantitative laboratory standards in Indian endemic settings. Finally, the contribution of comorbidities — including diabetes mellitus, hypertension, and haematological disorders — to dengue-associated haematological derangement represents an important but incompletely investigated area.

7. CONCLUSION

This cross-sectional analytical study provides clinically meaningful evidence that haematological and serological parameters are interdependent in dengue fever and collectively inform disease severity assessment. The statistically significant inverse correlation between NS1 antigen levels and hematocrit ($\rho = -0.168$, $p < 0.01$), alongside the high prevalence of severe thrombocytopenia (32%) and leukopenia (62%), demonstrates the complex haematological consequences of dengue viremia.

The findings underscore that no single biomarker is sufficient for comprehensive dengue assessment. An integrated diagnostic approach — combining early NS1 antigen testing with serial haematological monitoring and phase-appropriate IgM serology — provides the most clinically actionable framework for early risk stratification, particularly in endemic resource-limited settings.

From a public health perspective, the predominantly working-age adult demographic profile reinforces the socioeconomic burden of dengue and the imperative for earlier clinical recognition, evidence-based triage protocols, and targeted vector control in peri-urban North India. Future prospective, multi-centre, serotype-stratified research is essential to consolidate and extend these findings toward improved clinical guidelines and patient outcomes.

Declarations

Author Contributions: Ritu (Student, M.Sc. MLT): data collection, laboratory analysis, and manuscript drafting. Dr Adreena Mittal (Guide, Professor & HOD): study conception, design, supervision, and critical manuscript review. Dr. Prarthana (Co-Guide, Assistant Professor): clinical supervision, data interpretation, and manuscript revision. Dr Jyotika Vats (Corresponding Author, Assistant Professor): statistical analysis, correspondence, and final manuscript preparation.

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Informed Consent: Written informed consent was obtained from all participants before enrolment.

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