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The pattern of hematological abnormalities in NS1-positive dengue fever

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Abstract

Introduction: Dengue fever is a mosquito-borne viral illness that poses a significant public health threat in tropical and subtropical regions, including Bangladesh. The detection of non-structural protein 1 (NS1) antigen has emerged as a valuable tool for identifying dengue infection in its early phase, often before the appearance of immunoglobulin M or immunoglobulin G antibodies. This study aims to investigate the pattern of hematological abnormalities in NS1-positive dengue fever patients.

Methods: This cross-sectional observational study was conducted in Bangladesh Medical College, from January 2024 to January 2025, and included 120 patients who tested positive for dengue NS1 antigen. Descriptive statistics were used to summarize data. All analyses were carried out using Statistical Package for the Social Sciences software version 25.

Result: Among 120 NS1-positive dengue patients, the majority were aged 19–40 years (48.3%) and male (57.5%), with 85% presenting within 5 days of illness. Thrombocytopenia was present in all cases, with 36.7% showing severe levels. Leukopenia affected 68.3%, and hemoconcentration was seen in 41.7% of patients. Hematological abnormalities, particularly severe thrombocytopenia and hemoconcentration, were more pronounced with longer illness duration.

Conclusion: This study concludes that thrombocytopenia, leukopenia, and hemoconcentration are the most consistent hematological abnormalities, with severity increasing alongside illness duration. Thrombocytopenia was universal, while leukopenia and hemoconcentration were more prevalent in patients presenting after 5 days and among males.

Keywords: Dengue fever, dengue shock syndrome, hematological abnormalities, non-structural protein 1 positive

Introduction

Dengue fever, a mosquito-borne viral illness caused by the dengue virus (DENV), is a growing public health challenge in tropical and subtropical regions. With an estimated 390 million infections and 96 million symptomatic cases annually, dengue poses a significant burden, especially in densely populated developing countries.[1] The virus is primarily transmitted by *Aedes aegypti* mosquitoes and exists in four distinct serotypes (DENV-1 to DENV-4), each capable of causing disease ranging from mild febrile illness to life-threatening complications, such as dengue hemorrhagic fever and dengue shock syndrome.[2] Early and accurate

diagnosis of dengue is crucial for reducing complications and mortality. Among the diagnostic markers, the non-structural protein 1 (NS1) antigen has gained attention due to its high sensitivity in the early phase of infection, often detectable from day 1 of fever to day 5 to seven.[3] NS1 antigen detection is particularly useful before seroconversion occurs, providing an opportunity for prompt diagnosis and intervention.[4] In addition to confirming infection, NS1 positivity may also be associated with certain clinical and laboratory trends, particularly hematological abnormalities that offer prognostic value.[5] Hematological abnormalities are central to the pathogenesis, diagnosis, and monitoring of dengue fever. Thrombocytopenia, leukopenia, and elevated hematocrit are considered hallmark laboratory findings in dengue patients and are closely monitored during hospitalization.[6] Thrombocytopenia, defined as a platelet count below 150,000/mm^3, occurs due to bone marrow suppression, increased platelet destruction, and immune-mediated clearance. In severe cases, platelet counts may drop below 50,000/mm^3, increasing the risk of bleeding and contributing to disease severity.[7] Leukopenia is another common abnormality, especially during the febrile and critical phases. The suppression of bone marrow progenitor cells by the DENV leads to a drop in total white blood cell (WBC) counts, most notably neutrophils.[8] As the disease progresses to the recovery phase, relative lymphocytosis and the appearance of atypical lymphocytes often emerge, reflecting immune activation and viral clearance.[9] A rise in hematocrit is also frequently observed in dengue and is considered a surrogate marker for plasma leakage, a key event in the transition to severe dengue. An increase in hematocrit by more than 20% from baseline is indicative of capillary leakage and is often accompanied by clinical signs of hypovolemia or shock.[10] Monitoring hematocrit levels in NS1-positive patients is therefore essential for early detection of disease progression and timely fluid management. The pattern and severity of hematological abnormalities can vary based on several factors, including age, sex, host immune status, and viral virulence. Some studies suggest that NS1-positive patients may present with more pronounced thrombocytopenia and hemoconcentration compared to NS1-negative counterparts, although findings remain inconsistent across populations.[11] Regional and seasonal differences in dengue epidemiology also play a role in these variations, making localized studies important for clinical decision-making. In dengue-endemic countries, such as Bangladesh, where outbreaks are recurrent and healthcare resources are limited, hematological monitoring offers a cost-effective method for early risk stratification. Identifying abnormal trends in platelet count, white cell count, and hematocrit in NS1-positive patients can help clinicians predict severe disease, prioritize admissions, and guide supportive care.[12] Therefore, this study aims to investigate the pattern of hematological abnormalities in NS1-positive dengue fever patients.

Methods

This cross-sectional observational study was conducted in Bangladesh Medical College, from January 2024 to January 2025, and included 120 patients who tested positive for dengue NS1 antigen. Patients of all age groups and both sexes who presented within the first 7 days of illness and had confirmed NS1 antigen positivity by enzyme-linked immunosorbent assay were enrolled after obtaining informed consent. Patients with pre-existing hematological disorders, concurrent infections, or chronic liver disease were excluded to avoid confounding hematological parameters. Detailed clinical history and examination findings were recorded in a structured data collection form. Venous blood samples were collected at admission for complete blood count, which included hemoglobin, total leukocyte count, platelet count, and hematocrit. Hematological parameters were analyzed using an automated hematology analyzer. Thrombocytopenia was defined as a platelet count <150,000/mm^3, leukopenia as a total leukocyte count <4,000/mm^3, and hemoconcentration as a hematocrit >45% in males or >40% in females. Patients were also grouped according to the duration of illness at presentation (≤3 days, 4–5 days, >5 days) to assess the temporal pattern of hematological changes.

Descriptive statistics were used to summarize data. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were reported for continuous variables. Comparisons of hematological parameters across sex and illness duration were performed using appropriate statistical tests (Chi-square and *t*-test), with a $P < 0.05$ considered statistically significant. All analyses were carried out using Statistical Package for the Social Sciences software version 25.

Results

Most patients (48.3%) were aged between 19–40 years, and 57.5% were male. About 85% presented within the first 5 days of illness, reflecting early detection through NS1 testing [Table 1].

Mean platelet count remained low, indicating thrombocytopenia. Leukopenia and elevated hematocrit values were frequently observed, suggesting early plasma leakage [Table 2].

All patients had thrombocytopenia, with severe forms in 36.7%. Leukopenia was seen in over two-thirds, and 41.7% had hemoconcentration – suggestive of disease severity [Table 3].

A clear trend of worsening hematological abnormalities was seen with increasing illness duration. Severe thrombocytopenia and hemoconcentration were markedly more common after 5 days of illness [Table 4].

Platelet and WBC counts were comparable across sexes. However, males had significantly higher hematocrit levels and more frequent hemoconcentration, suggesting greater plasma leakage risk [Table 5].

Table 1: Demographic profile of NS1-positive dengue patients (*n*=120)

Variable	Category	Frequency (%)
Age group (years)	≤18	26 (21.7)
	19–40	58 (48.3)
	41–60	25 (20.8)
	>60	11 (9.2)
Sex	Male	69 (57.5)
	Female	51 (42.5)
Duration of illness at presentation (days)	≤3 days	43 (35.8)
	4–5 days	59 (49.2)
	>5 days	18 (15.0)

NS1: Non-structural protein 1

Discussion

This study highlights the demographic and hematological characteristics of NS1-positive dengue patients during the early phase of

Table 2: Hematological parameters at presentation (*n*=120)

Parameter	Mean±SD	Range
Hemoglobin (g/dL)	13.1±1.6	9.4–16.8
Total leukocyte count (/mm^3)	3,800±1,250	1,800–7,200
Platelet count (/mm^3)	78,500±29,200	18,000–145,000
Hematocrit (%)	41.2±5.3	30.1–55.0

SD: Standard deviation

Table 3: Frequency of hematological abnormalities (*n*=120)

Hematological abnormality	Frequency (%)
Thrombocytopenia (<150,000/mm^3)	120 (100.0)
Moderate (50,000–150,000)	76 (63.3)
Severe (<50,000)	44 (36.7)
Leukopenia (<4,000/mm^3)	82 (68.3)
Hemoconcentration (elevated HCT)	50 (41.7)
Anemia	23 (19.2)
Atypical lymphocytosis	31 (25.8)

Table 4: Hematological abnormalities by duration of illness (*n*=120)

Parameter	≤3 days (*n*=43) (%)	4–5 days (*n*=59) (%)	>5 days (*n*=18) (%)
Severe thrombocytopenia	7 (16.3)	26 (44.1)	11 (61.1)
Leukopenia	27 (62.8)	43 (72.9)	12 (66.7)
Hemoconcentration	11 (25.6)	24 (40.7)	15 (83.3)

Table 5: Hematological parameters by sex (*n*=120)

Parameter	Male (*n*=69)	Female (*n*=51)	*P*-value
Platelet count (mean±SD)	76,000±28,900	80,800±29,600	0.34
WBC count (mean±SD)	3,750±1,270	3,950±1,230	0.27
Hematocrit (%)	43.2±4.7	38.5±3.8	<0.001
Hemoconcentration (%)	38 (55.1)	12 (23.5)	0.001

WBC: White blood cell, SD: Standard deviation

infection. The most commonly affected age group was 19–40 years (48.3%), followed by ≤18 years (21.7%), indicating that young and middle-aged adults were predominantly affected, which is consistent with findings by Sahana and Sujatha, who reported that 47% of dengue cases occurred in the 20–40 years group.[13] Similarly, Khan *et al*. observed a high prevalence in the 21–30 years group (45.7%) in a tertiary hospital-based study in India.[14] The male predominance (57.5%) noted in this study also aligns with previous reports that show a male-to-female ratio ranging from 1.3:1 to 2:1, possibly due to higher outdoor exposure among males.[15,16] Early detection was evident as nearly 85% of patients presented within the first 5 days of fever, in line with the NS1 antigen's diagnostic utility during the early febrile phase.[17] Comparable early presentation rates were reported by Kulkarni *et al*., where 82% of NS1-positive cases were detected within 5 days of illness.[18] Hematologically, thrombocytopenia was universal (100%) in our cohort, with 36.7% having severe thrombocytopenia (<50,000/mm^3). These findings correspond with those of Anand *et al*., who reported thrombocytopenia in 96% of NS1-positive cases and severe thrombocytopenia in 34%.[19] Leukopenia was observed in 68.3%, closely matching the 64–74% range reported by a study from Southeast Asia.[20] The mean WBC count in our study was 3,800/mm^3, consistent with the values seen in earlier studies.[21] A significant proportion (41.7%) exhibited hemoconcentration, reflecting early plasma leakage, a hallmark of severe dengue. Hemoconcentration and severe thrombocytopenia were more prevalent in patients presenting after 5 days of illness, reinforcing the notion that hematological derangements worsen as the disease progresses.[22] Sex-based comparisons showed that males had significantly higher hematocrit levels (43.2% vs. 38.5%) and higher hemoconcentration rates (55.1% vs. 23.5%), which is in agreement with Chacko *et al*., who found higher hematocrit and plasma leakage rates among male patients.[23] Atypical lymphocytosis was present in 25.8% of patients, a finding somewhat lower than that of studies reporting rates up to 40%, possibly due to variability in the timing of sample collection.[24] Overall, the hematological trends observed in this study – particularly thrombocytopenia, leukopenia, and hemoconcentration – reinforce their role as early indicators of dengue severity and highlight the value of NS1-based detection in initiating timely clinical management.

Limitations of the study

The study was conducted in a single hospital with a small sample size. Hence, the results may not represent the whole community.

Conclusion

This study concludes that thrombocytopenia, leukopenia, and hemoconcentration are the most consistent hematological abnormalities, with severity increasing alongside illness duration. Thrombocytopenia was universal, while leukopenia and hemoconcentration were more prevalent in patients presenting after 5 days and among males.

Recommendation

Routine and early hematological monitoring – including platelet count, white blood cell count, and hematocrit – should be integrated into the management protocol for all NS1-positive dengue patients to enable timely risk stratification, guide fluid therapy, and reduce the risk of severe complications.

Funding

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Conflict of Interest

None declared.

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