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Clinical and Hematological correlates of dengue infection: Findings from a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Dengue, a mosquito-borne viral infection, is endemic in tropical regions like Bangladesh, where it has led to a significant public health burden. Hematocrit and neutrophil counts are critical indicators in diagnosing and managing dengue, especially when assessing plasma leakage and immune response.

Objective: To assess hematocrit and neutrophil status in clinically suspected dengue patients and correlate these findings with IgM, IgG, and NS1 antigen levels.

Materials and Methods: A cross-sectional descriptive study was conducted at a general hospital in Dhaka city, Bangladesh on 168 patients clinically suspected of having dengue. Blood samples were analyzed for hematocrit, neutrophil counts, NS1 antigen, and IgM/IgG antibody levels. Hematological tests were performed using a Sysmex 1800i Hematology Analyzer. Descriptive statistics, Chi-square tests, and p-value analysis were conducted using SPSS version 25.

Results: Among the 168 patients, 29.8% tested positive for dengue. Hematocrit analysis showed that 57.1% had below-normal levels, 40.5% were normal, and 2.4% had elevated levels. Neutrophil analysis revealed that 52.9% of patients with raised neutrophil counts were dengue positive ($p = 0.019$). Additionally, a significant association was found between low platelet counts and dengue positivity ($p < 0.001$).

Conclusion: Hematocrit and neutrophil counts, along with serological markers, are valuable in diagnosing and managing dengue. This study highlights the importance of neutrophil count as a key indicator of dengue positivity, alongside hematocrit and serological markers. Early identification of these hematological abnormalities can help guide timely therapeutic interventions.

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Keywords: Dengue; Hematocrit; Neutrophil Count; NS1 Antigen; IGM/IGG

1. Introduction

Dengue is a mosquito-borne viral infection caused by the dengue virus (DENV), which is transmitted primarily through the bite of infected *Aedes aegypti* mosquitoes[1]. It is a major public health concern in tropical and subtropical regions, with over 100 countries reporting cases of dengue every year. The clinical manifestations of dengue range from mild febrile illness to severe life-threatening conditions such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)[2].

In recent years, dengue outbreaks have surged globally, including in Bangladesh, which has seen one of the worst dengue epidemics in its history. In 2019, approximately 90,000 individuals in Bangladesh were affected by dengue, marking an alarming increase in incidence[3]. The clinical symptoms of dengue, which appear after an incubation period of 4–10 days, typically include high fever, severe headache, retro-orbital pain, myalgia, arthralgia, rash, nausea, vomiting, and swollen glands. Although these symptoms last for 2–7 days in uncomplicated cases, some patients progress to severe dengue, which is characterized by plasma leakage, fluid accumulation, respiratory distress, and organ impairment[4].

The dengue virus has four distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4[5]. While infection with one serotype provides lifelong immunity to that specific virus, there is no cross-protection against other serotypes, leading to the possibility of multiple infections throughout a person's life. Secondary infections have been associated with an increased risk of developing severe dengue, particularly DHF and DSS[6].

One of the key clinical indicators monitored in dengue patients is the hematocrit (HCT), which is the proportion of blood volume occupied by red blood cells. Hematocrit measurement is used to assess hemoconcentration, a marker of plasma leakage in severe dengue[7]. Hemoconcentration, defined as a 20% or more increase in hematocrit compared to baseline values, is a critical sign of hypovolemia and vascular permeability[8]. Hematocrit levels fluctuate during the different phases of dengue infection and can provide valuable information regarding the severity of the disease. A persistently high hematocrit level, along with unstable vital signs, suggests ongoing plasma leakage and necessitates fluid replacement therapy. On the other hand, a sudden drop in hematocrit levels may indicate hemorrhage, requiring urgent blood transfusions[9].

Given the critical role that hematocrit plays in the diagnosis and management of dengue, monitoring hematocrit levels can help in the timely identification of complications and guide clinical management strategies[10]. This study aims to explore the hematocrit status of clinically suspected dengue patients in Bangladesh, and to correlate it with serological findings, including NS1 antigen, IgM, and IgG antibody levels. By doing so, this research seeks to contribute to a better understanding of the hematological profile of dengue patients, particularly with respect to plasma leakage and hemoconcentration, which are pivotal in the management of severe cases. To assess hematocrit and neutrophil counts in clinically suspected dengue patients and correlate these findings with IgM, IgG levels, and NS1 antigen status.

2. Methods and materials

2.1. Study Settings and Population

This study was cross-sectional descriptive research focusing on observational data collection to explore and describe the clinical and hematological characteristics of patients suspected of having dengue. Conducted a general hospital in Dhaka city, Bangladesh and the study included 168 patients aged 18 to 75 years. These patients were identified as clinically suspected dengue cases and were drawn from both outpatient and inpatient services of the hospital. Data collection spanned two months, from July 1st to August 31st , 2023.

2.2. Selection Criteria

Inclusion criteria for the study encompassed patients who were clinically suspected of having dengue and had either a positive NS1 antigen test by the immunochromatographic test (ICT) method or detectable levels of IgG and IgM antibodies via ELISA. Additionally, hematological parameters, including hematocrit, platelet count, and neutrophil count, were considered. Exclusion criteria included patients younger than 18 years, as well as pregnant women, surgical patients, those in the ICU, and immunocompromised individuals.

2.3. Hematological Procedures

The NS1 antigen test was conducted to detect the presence of the non-structural protein NS1, which is secreted into the bloodstream during dengue infection. Detection was performed using the immunochromatographic (ICT) method with commercially available diagnostic kits. The procedure involved using a 100 µl serum sample, of which 40 µl was applied to the cassette test device. After a 20-minute incubation period, the presence of a test band alongside the control band on the cassette indicated a positive result for the NS1 antigen.

For the complete blood count (CBC), several key blood components were measured, including red blood cells, white blood cells, hemoglobin, hematocrit (packed cell volume), and platelets. A 2 ml blood sample was collected and processed in a centrifuge to separate the red blood cells, plasma, and anticoagulant. Automated analysis of the sample was performed using the Sysmex 1800i Hematology Analyzer, which provided precise and reliable results.

2.4. Sample Collection Technique

Blood samples were collected by certified lab technicians using standard phlebotomy procedures. The blood was typically drawn from the patient's elbow or hand. The collection process involved cleaning the site with antiseptic, applying a tourniquet to engorge the vein, and then drawing the blood into vials. After the sample was collected, the site was bandaged to ensure that bleeding was controlled and to promote healing.

2.5. Laboratory Investigation

2.5.1. Dengue Duo Rapid Test

The Dengue Duo Rapid Test, produced by Standard Diagnostics, was employed to categorize patients as having primary or secondary dengue infections. This one-step immunochromatographic assay detects both NS1 antigen and IgM/IgG antibodies against the dengue virus from whole blood, serum, or plasma[11].

2.5.2. NS1 Antigen Detection and Antibody Testing (IgM and IgG)

NS1 glycoprotein, indicative of acute dengue infection, was detected in serum samples using the immunochromatographic (ICT) method, which is effective within the first 6 days after fever onset. To differentiate between acute and past dengue infections, enzyme-linked immunosorbent assays (ELISA) were employed. The IgM test identified early-phase antibodies by incubating serum samples with anti-human IgM antibodies and dengue virus antigen, with results detected colorimetrically using horseradish peroxidase-conjugated anti-dengue virus antibodies. The IgG test, used to detect antibodies from past infections, involved incubating serum samples with dengue virus antigens and anti-human IgG antibodies conjugated with peroxidase, with results measured through optical density readings where an index value above 1.00 was considered positive[12].

2.6. Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS (Statistical Package for the Social Sciences), version 25. Descriptive statistics were employed to summarize patient demographics, clinical characteristics, and laboratory findings. Chi-square tests were conducted to examine the associations between clinical variables and dengue test results. A p-value < 0.05 was considered statistically significant.

2.7. Ethical Considerations

The study adhered to the ethical guidelines established by the hospital's Ethical Committee. Informed consent was obtained from all participants, and patient confidentiality was maintained by recording only unique hospital identification numbers, along with age and sex. No personally identifiable information was collected.

3. Results

A total of 168 patients were included in this study. The gender distribution revealed that 80 (48%) of the patients were male, and 88 (52%) were female (Fig. 1). The age range of the patients was from 18 to 75 years, and they were categorized into two age groups: 18-35 years and above 35 years. The majority of the patients (52.4%) were aged 18-35 years, while 47.6% were above 35 years (Table 1).

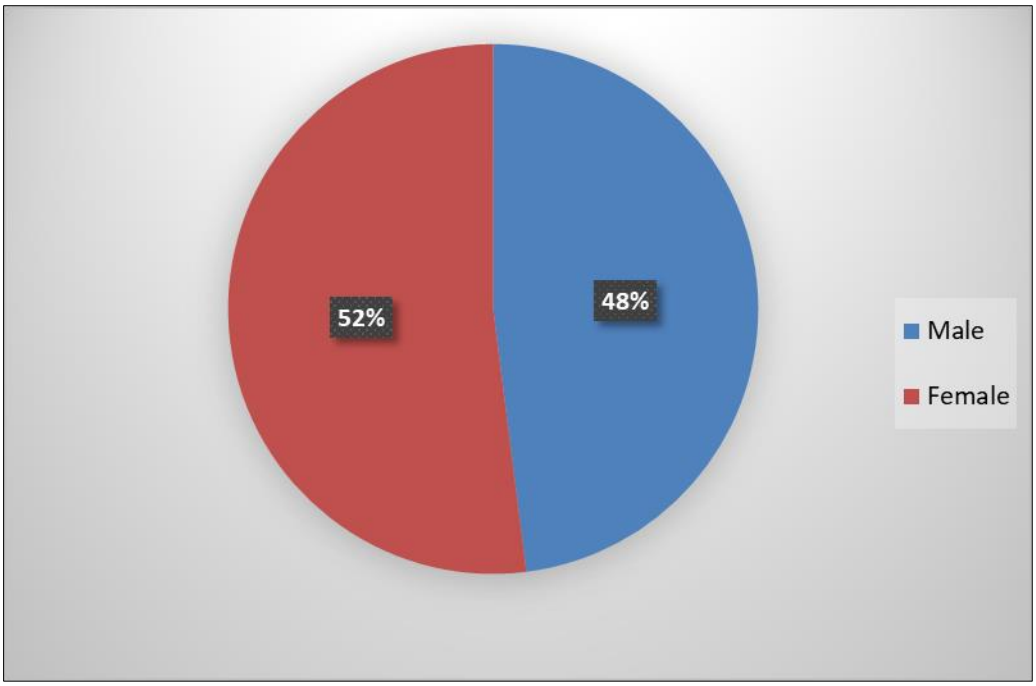

Figure 1 Gender distribution

Table 1 Age-wise distribution of patients

Age Group	Frequency	Percentage
18-35 years	88	52.4%
Above 35 years	80	47.6%
Total	168	100%

Among the patients, 29.8% (50/168) tested positive for dengue, while 70.2% (118/168) were negative for the disease (Table 2).

Table 2 Dengue fever status according to laboratory results

Dengue Status	Frequency	Percentage
Dengue Positive	50	29.8%
Dengue Negative	118	70.2%
Total	168	100%

In the dengue-positive group, 15.5% of patients were positive for NS1 antigen, 1.2% were positive for IgM antibody, and 11.9% were positive for IgG antibody. Among the dengue-negative group, 84.5% were negative for NS1, 98.8% were negative for IgM, and 88.1% were negative for IgG (Table 3).

Table 3 Serological profile of dengue patients

Serological Marker	Positive (n = 168)	% Positive	Negative (n = 168)	% Negative
NS1	26	15.5%	142	84.5%
IgM	2	1.2%	166	98.8%
IgG	20	11.9%	148	88.1%

Analysis of hematocrit levels revealed that 57.1% of patients had below-normal hematocrit, 40.5% had normal levels, and 2.4% had raised hematocrit (Table 4).

Table 4 Hematocrit status of patients

Hematocrit Level	Frequency	Percentage
Below Normal	96	57.1%
Normal	68	40.5%
Raised	4	2.4%
Total	168	100%

When analyzing the relationship between hematocrit status and dengue positivity, it was found that 31.3% of patients with below-normal hematocrit were dengue positive, while 68.8% were dengue negative. Among patients with normal hematocrit, 29.4% were dengue positive, and 70.6% were dengue negative. Interestingly, all patients with raised hematocrit were dengue negative (Table 5). The hematocrit levels did not show a significant association with dengue positivity ($p = 1.000$).

Table 5 Association between hematocrit status and dengue positivity

Hematocrit Level	Dengue Positive	% Positive	Dengue Negative	% Negative	Total	X^2	P-value
Below Normal	30	31.3%	66	68.8%	96	0.544	1.000
Normal	20	29.4%	48	70.6%	68		
Raised	0	0%	4	100%	4		
Total	50	29.8%	118	70.2%	168		

A significant correlation was observed between neutrophil status and dengue positivity. Of the patients with raised neutrophil counts, 52.9% were dengue positive, while 47.1% were dengue negative. For patients with normal neutrophil counts, 23.9% were dengue positive, and 76.1% were dengue negative. This relationship was statistically significant ($p = 0.019$) (Table 6). There was a significant association between neutrophil status and dengue positivity, with elevated neutrophil counts more frequently observed in dengue-positive patients ($p = 0.019$).

Table 6 Association between neutrophil status and dengue positivity

Neutrophil Status	Dengue Positive	% Positive	Dengue Negative	% Negative	Total	X^2	P-value
Normal	32	23.9%	102	76.1%	134	5.478	0.019
Raised	18	52.9%	16	47.1%	34		
Total	50	29.8%	118	70.2%	168		

Analysis of platelet counts in dengue-positive patients showed that 64.0% had a low platelet count, while 36.0% had normal platelet levels. Among dengue-negative patients, 84.7% had normal platelet counts, and only 15.3% had low levels (Table 7). There is a highly significant association between low platelet count and dengue positivity, with low platelets more commonly observed in dengue-positive patients ($p < 0.001$).

Table 7 Association between platelet count and dengue positivity

Platelet Count	Dengue Positive	% Positive	Dengue Negative	% Negative	Total	X^2	P-value
Low	32	64.0%	18	15.3%	50	25.78	<0.001
Normal	18	36.0%	100	84.7%	118		
Total	50	29.8%	118	70.2%	168		

This table 8 summarizes the findings of hematocrit, neutrophil count, platelet count, and serological markers (NS1, IgM, and IgG) among dengue-positive and dengue-negative patients. It also includes the p-values showing statistical significance where relevant.

Table 8 Hematological and Serological Findings in Dengue Suspected Patients with Statistical Significance

Parameter	Dengue Positive (%)	Dengue Negative (%)	Total (%)	p-value
Hematocrit Status				
Below Normal	30 (31.3%)	66 (68.8%)	96 (57.1%)	1.000
Normal	20 (29.4%)	48 (70.6%)	68 (40.5%)	
Raised	0 (0%)	4 (100%)	4 (2.4%)	
Neutrophil Count				0.019
Normal	32 (23.9%)	102 (76.1%)	134 (79.8%)	
Raised	18 (52.9%)	16 (47.1%)	34 (20.2%)	
Platelet Count				<0.001
Low	32 (64.0%)	18 (15.3%)	50 (29.8%)	
Normal	18 (36.0%)	100 (84.7%)	118 (70.2%)	
Serological Markers				
NS1 Positive	26 (15.5%)	142 (84.5%)	168 (100%)	
IgM Positive	2 (1.2%)	166 (98.8%)	168 (100%)	
IgG Positive	20 (11.9%)	148 (88.1%)	168 (100%)	

4. Discussion

This study aimed to assess the clinical and hematological characteristics of dengue patients in Bangladesh, focusing on the association between neutrophil status, platelet count, hematocrit levels, and dengue positivity. The findings from 168 patients provide valuable insights into the epidemiology of dengue in this population and contribute to the growing body of research on dengue's hematological manifestations.

The gender distribution in this study showed that 40.48% of the patients were male and 44.52% were female, which differs from studies conducted in other regions where males are often overrepresented among dengue cases. However, the gender distribution in this study suggests that dengue affects both genders relatively equally, consistent with research conducted in Bangladesh13. The age distribution in this study revealed that the majority of patients (52.4%) were aged between 18 and 35 years, with the remaining 47.6% over 35 years old. This age pattern is in line with previous studies that have noted that dengue predominantly affects younger adults. The age group between 18 and 35 years is more mobile and may be more exposed to dengue vectors, which could explain this trend. In this study, 29.8% of patients tested positive for dengue, a finding consistent with earlier research conducted in similar settings14. Dengue positivity rates can vary significantly based on the region and the season of data collection. The presence of NS1 antigen in 15.5% of the dengue-positive patients and IgG antibodies in 11.9% of the patients suggests a mixture of both acute and past dengue infections, which is consistent with findings from previous studies15.

The analysis of hematocrit levels revealed that 57.1% of patients had below-normal hematocrit levels, while 40.5% had normal levels. However, the study did not find a significant association between hematocrit levels and dengue positivity ($p = 1.000$), contradicting earlier findings where elevated hematocrit was considered a marker for dengue severity. This discrepancy may be due to the timing of blood collection, as hematocrit levels fluctuate during the course of dengue illness16.

A significant association between neutrophil status and dengue positivity was observed in this study ($p = 0.019$). Among patients with raised neutrophil counts, 52.9% were dengue positive, while only 23.9% of patients with normal neutrophil counts were dengue positive. This is in agreement with findings from other studies that have reported

neutrophilia in the early stages of dengue infection, often before a drop in white blood cells occurs17. Neutrophil count is often elevated in response to viral infections, but in dengue, this finding is more commonly associated with secondary infections18. This underscores the importance of neutrophil count as a potential marker for early dengue infection, especially in secondary cases.

This study found a highly significant association between low platelet count and dengue positivity ($p < 0.001$). Among dengue-positive patients, 64.0% had low platelet counts, which is a well-documented hematological feature of dengue. Thrombocytopenia (low platelet count) is a common indicator of dengue infection and often correlates with disease severity19. Previous studies have noted that platelet counts drop significantly in dengue patients, especially during the critical phase of the illness. These results reinforce the importance of monitoring platelet levels for early detection and management of dengue, particularly in patients showing clinical signs of bleeding or plasma leakage20.

The serological and hematological findings of this study align with other research conducted in tropical regions where dengue is endemic21. Studies in Vietnam22 have reported a similar prevalence of thrombocytopenia and raised neutrophil counts among dengue patients. Additionally, the association between low platelet count and dengue positivity has been consistently reported across various studies conducted in Southeast Asia23.

However, the lack of a significant correlation between hematocrit levels and dengue positivity in this study contrasts with findings from studies in Sri Lanka24 and Thailand25, where hematocrit is often used as a marker for disease severity and plasma leakage. This difference could be due to variations in patient population, timing of blood sample collection, and the specific stage of dengue progression when patients presented to the hospital.

5. Conclusion

This study confirms the significant association between neutrophil status, platelet count, and dengue positivity, highlighting their potential as early diagnostic markers in dengue management. While hematocrit did not show a significant correlation with dengue status in this study, further research with serial measurements may provide more definitive answers. Given the rising incidence of dengue in Bangladesh and other tropical regions, early diagnosis and management based on clinical and hematological parameters remain crucial in reducing morbidity and mortality.

Study Limitations

While the findings of this study contribute valuable data on dengue in Bangladesh, certain limitations should be acknowledged. First, the study was limited to a single hospital, which may affect the generalizability of the results. Second, hematocrit levels were measured at a single time point, which may not reflect the dynamic changes that occur throughout the course of the illness. Lastly, due to resource constraints, the study did not assess other biomarkers like C-reactive protein (CRP) or cytokine levels, which could provide more insights into the inflammatory response in dengue.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Contribution to authors

All authors contributed equally to the work. All authors read and approved the final manuscript for publication.

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