

Original Article

Evaluation of Hematological Changes in Dengue Fever: Experience of 2023 outbreak from Jashore, Bangladesh

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Abstract

Background: Dengue fever is a painful febrile illness caused by a mosquito-borne Arbovirus. Epidemic episodes often occur during the rainy season. Complete blood count (CBC) is essential in patients with dengue fever and serological tests are necessary to confirm it. This study aimed to evaluate the hematological changes in dengue fever patients in Jashore Medical College Hospital, Bangladesh.

Methods: This prospective cross-sectional study was conducted in the Department of Medicine, Jashore Medical college Hospital, Bangladesh from July 2023 to Decembar 2023. The study involved 177 dengue fever patients identified through NSI and/or IgM antibody tests. Purposive sampling was used for patient selection, and data analysis utilized SPSS version 23.0.

Results: Analysis of hematological parameters on the day 1 and day 3 indicated significant shifts in platelet, leucocyte, neutrophil, and lymphocyte counts. Platelet count decreased from $99.67 \pm 96.17 \times 10^9/L$ to $82.72 \pm 60.84 \times 10^9/L$ ($p=0.048$). Leucocyte count rose from $6.43 \pm 3.01 \times 10^9/L$ to $7.85 \pm 5.58 \times 10^9/L$ ($p=0.003$), while neutrophil count decreased from $6.31 \pm 1.38 \times 10^9/L$ to $5.44 \pm 1.36 \times 10^9/L$ ($p<0.001$). Lymphocyte count also increased from $3.06 \pm 1.80 \times 10^9/L$ to $3.78 \pm 1.19 \times 10^9/L$ ($p<0.001$). No significant shifts were observed in hemoglobin ($p=0.579$) or hematocrit ($p=0.639$) levels.

Conclusion: Among dengue fever patients, platelet and neutrophil counts decrease while leukocyte and lymphocyte counts increase significantly between the day 1 and day 3. However, there are no significant shifts observed in hemoglobin or hematocrit levels in the same tenure.

Keywords: Hematological changes, Dengue, Fever, Platelet.

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Introduction

Dengue fever is a vector-borne viral infection prevalent in tropical and subtropical regions worldwide.¹ The World Health Organization estimates approximately 50 million

cases of dengue infection annually worldwide.² The incidence of dengue has risen significantly over the years, contributing to substantial morbidity and mortality, particularly in tropical regions¹. The viruses responsible for dengue are transmitted by mosquitoes, particularly the *Aedes aegypti* species, which are active during the day and tend to feed on humans. Dengue is caused by various serotypes, including DEN-1, DEN-2, DEN-3, and DEN-4, which can lead to dengue fever or more severe forms like dengue hemorrhagic fever (DHF).³ Plasma leakage is a critical pathological characteristic of dengue hemorrhagic fever, and the timely and precise diagnosis and management of this phase are crucial for improving patient outcomes.⁴ Throughout the course of the illness, various biochemical and hematological changes occur. Hematological and biochemical parameters, including hematocrit levels, albumin concentration, platelet count, and the aspartate

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aminotransferase ratio, have been demonstrated to be effective in identifying patients experiencing plasma leakage in severe cases of dengue infection.^{5,6} Hepatic involvement of varying severity is increasingly recognized in relation to dengue infection.⁷ Alterations in liver function tests, characterized by mildly elevated serum total bilirubin, increased levels of alanine transaminase (ALT) and aspartate transaminase (AST), and decreased serum albumin, are commonly observed in dengue infection and can serve as prognostic markers.^{8,9} Additionally, during the plasma leakage phase of the illness, there is a reduction in serum levels of calcium, albumin, and cholesterol.¹⁰ NS1 antigen production triggers the generation of antiplatelet antibodies, which cross-react with integrins and adhesins, resulting in platelet aggregation.^{11,12} While both antibodies may indicate a prior infection, determining the ratio of IgM to IgG or observing rising titers in paired sera can aid in determining the recency of the infection. Since fatalities in these patients often result from hematological complications, conducting a study could significantly reduce the mortality and morbidity associated with dengue.¹³ In primary infection, IgM antibodies typically emerge around 5 days after symptom onset, peak within approximately 21 days, and gradually decline within 1–2 months from the onset. They may persist for up to 6 months. IgG antibodies, on the other hand, become detectable around 14 days after symptom onset and persist at a lower level for the individual's lifetime.¹⁴ Diagnosis of acute dengue infection is typically conducted using an in vitro immunochromatographic assay to identify Nonstructural 1 (NS1) protein as well as IgM and IgG anti-dengue virus antibodies.¹⁵ Hematological parameters are often altered in dengue infection, with common findings including thrombocytopenia, leukopenia, elevated hematocrit (Hct), and the presence of atypical lymphocytes.¹⁶ Nucleic acid amplification tests are considered the gold standard for detecting dengue infection, but they are often not readily available in resource-limited settings. Therefore, lateral flow assays (LFA) or immunochromatography (ICT)-based methods are commonly used for dengue diagnosis in many developing countries.¹⁷ While ICT offers user-friendly and rapid results, it suffers from lower sensitivity and specificity, as well as increased cross-reactivity, leading to more false positives. In this context, hematological parameters can serve as a supportive tool for dengue diagnosis in conjunction with rapid ICT methods.¹⁸ ICT detects dengue-specific antibodies or antigens in the patient's blood, while hematological parameters help identify dengue-related changes such as thrombocytopenia and hemoconcentration.¹⁹ The objective of this study was to evaluate the hematological changes in dengue fever in Jashore Medical College Hospital, Bangladesh.

Methodology

This was cross-sectional study that took place at the Department of Medicine, Jashore Medical College Hospital, Bangladesh, from July 2023 to December 2023. A total of 177 patients diagnosed with dengue fever, based on NS1 and/or IgM antibody tests, were included in the study. Purposive sampling was employed to select participants. All patients presenting to the hospital with symptoms and signs indicative of dengue fever underwent testing for NS1 antigen and IgM/IgG dengue antibody serology, depending on the day of fever, using the enzyme-linked immunosorbent assay (ELISA) technique. Written consent was obtained from all participants before data collection. Patients under the age of 12 and those with previously diagnosed blood disorders were excluded from the study according to the exclusion criteria. Data analysis was performed using the SPSS version 23.0 program. In statistical analysis, significance was determined by a p-value of less than 0.05.

Result

Regarding the age distribution of our participants, it was noted that the highest proportion (27.7%) belonged to the 26–35 years age group, followed by 19.8%, 19.2%, 14.1%, 11.3%, and 7.9% from the 36–45, 19–25, 46–60, 12–18, and over 60 years age groups, respectively. Nearly three-fourths of cases (76%) were male and the rest of the cases (24%) were female (Figure 1). In our study, the most common presenting complaints among patients were as follows: headache (83.1%), generalized pain (65.0%), vomiting (51.4%), arthralgia (45.2%), pain on eye movement (31.6%), depression (28.2%), and diarrhea (26.6%). The mean \pm SD duration of fever was 6.7 ± 3.41 days. Analysis of hematological parameters over the day 1 and day 3 revealed significant changes in platelet count, leucocyte count, neutrophil count, and lymphocyte count. Platelet count decreased from a mean of $99.67 \pm 96.17 \times 10^9/L$ on the 1st day to $82.72 \pm 60.84 \times 10^9/L$ on the 3rd day ($p=0.048$). Leucocyte count increased from $6.43 \pm 3.01 \times 10^9/L$ to $7.85 \pm 5.58 \times 10^9/L$ ($p=0.003$), while neutrophil count decreased from $6.31 \pm 1.38 \times 10^9/L$ to $5.44 \pm 1.36 \times 10^9/L$ ($p<0.001$). Lymphocyte count also increased from $3.06 \pm 1.80 \times 10^9/L$ to $3.78 \pm 1.19 \times 10^9/L$ ($p<0.001$). However, there were no significant changes in hemoglobin level ($p=0.579$) or hematocrit level ($p=0.639$) between the 1st and 3rd days. Raised ALT, AST and serum creatinine were found in 22.0% and 24.3% and 2.3% of the cases respectively. In the current study, the majority of cases (75.7%) tested positive for NS1, while 27.1% were positive for IgM antibodies (Table 2).

Table 1. Age and sex distribution

Age (Years)	n	%
12-18	20	11.3%
19-25	34	19.2%
26-35	49	27.7%
36-45	35	19.8%
46-60	25	14.1%
>60	14	7.9%
Total	177	100%
Sex Distribution	Male	76%
	Female	24%

Table 2. Hematological, biochemical parameters and diagnostic findings

Variables	Hematological parameter		
	1 st day	3 rd day	p-value
	Mean \pm SD		
Hemoglobin (g/dl)	12.96 \pm 1.98	13.07 \pm 1.74	0.579
Hematocrit (%)	39.50 \pm 6.60	39.8 \pm 5.34	0.639
Platelet (n x 10 ⁹ /L)	99.67 \pm 96.17	82.72 \pm 60.84	0.048
Leucocyte (n x 10 ⁹ /L)	6.43 \pm 3.01	7.85 \pm 5.58	0.003
Neutrophil (n x 10 ⁹ /L)	6.31 \pm 1.38	5.44 \pm 1.36	<0.001
Lymphocyte (n x 10 ⁹ /L)	3.06 \pm 1.80	3.78 \pm 1.19	<0.001
Biochemical parameters			
Variables	N	%	
Raised ALT	39	22.0%	
Raised AST	43	24.3%	
Raised serum creatinine	4	2.3%	
Diagnostic findings			
Variables	N	%	
NS1 Positive	134	75.7%	
IgG antibody positive	54	30.5%	
IgM antibody positive	48	27.1%	

Discussion

In terms of the age distribution among our participants, the majority (27.7%) were in the 26-35 years age bracket, followed by 19.8%, 19.2%, 14.1%, 11.3%, and 7.9% from the 36-45, 19-25, 46-60, 12-18, and over 60 years age groups, respectively. In contrast, another study²⁰ reported a wider age range from 1 year to 65 years, with the highest proportion (51.6%) in the 0-10 years age group. Upon analyzing the gender distribution among the cases, approximately three-

quarters (76%) were male, while the remaining quarter (24%) were female. In a similar study²¹, out of 438 confirmed dengue patients admitted, 254 were male (58%) and 184 were female (42%). The most frequently reported complaints among our patients included headache (83.1%), generalized pain (65.0%), vomiting (51.4%), arthralgia (45.2%), pain on eye movement (31.6%), depression (28.2%), and diarrhea (26.6%). In contrast, a different study²² found that fever (96.5%), headache (40.6%), gastrointestinal symptoms (30%), nausea or vomiting (23.1%), myalgia (19.0%), rash (4.6%), and bleeding (3.2%) were the most common symptoms among admitted cases, demonstrating variations from our study's findings. In this study, analysis of hematological parameters over the 1st and 3rd days revealed significant changes. Platelet count decreased from a mean of 99.67 \pm 96.17 x 10⁹/L on the 1st day to 82.72 \pm 60.84 x 10⁹/L on the 3rd day (p=0.048). Leukocyte count increased from 6.43 \pm 3.01 x 10⁹/L to 7.85 \pm 5.58 x 10⁹/L (p=0.003), while neutrophil count decreased from 6.31 \pm 1.38 x 10⁹/L to 5.44 \pm 1.36 x 10⁹/L (p<0.001). Lymphocyte count also increased from 3.06 \pm 1.80 x 10⁹/L to 3.78 \pm 1.19 x 10⁹/L (p<0.001). However, there were no significant changes in hemoglobin level (p=0.579) or hematocrit level (p=0.639) between the 1st and 3rd days. Nearly similar findings were observed in some previous studies.^{20,21} In our study, elevated levels of alanine transaminase (ALT), aspartate transaminase (AST), and serum creatinine were observed in 22.0%, 24.3%, and 2.3% of the cases, respectively. A study by Ferede et al.²³ reported elevated AST (45.1%) and ALT (17.6%) levels. Additionally, Kularatam et al. found that AST and ALT levels begin to rise in the early febrile phase, with median concentrations of AST at 746 u/L and ALT at 118 u/L.²⁴ In the present study, the majority of cases (75.7%) tested positive for NS1, while 27.1% were positive for IgM antibodies. In a previous study²¹, it was demonstrated that most patients were positive for NS1 (70.3%). However, in the same study, IgM was positive in 62.1% of cases, and IgG was positive in 14.8%. Dengue, a self-limiting infection, manifests a spectrum of illnesses from asymptomatic cases to severe conditions like DHF/dengue shock syndrome. Symptoms overlap with other infections, often leading to underreporting and misdiagnosis.²⁵ This disease is a significant cause of morbidity and mortality in over 100 tropical and subtropical countries, putting approximately 2.5 billion people at risk worldwide. Dengue's prevalence has surged in recent decades, notably in the Americas, Western Pacific, and Southeast Asia.²⁶ Timely diagnosis, coupled with aggressive fluid replacement and attentive nursing, can slash

fatality rates to 1% or lower. Currently, serological testing stands as the gold standard for confirming dengue infection. As the global burden of dengue rises, early detection and effective management become imperative in combating its spread and mitigating its impact on public health.^{27,28}

Limitation of the study:

The study's limitations include its single-centered design, small sample size, and short duration, which may restrict the generalizability of findings to the entire country. Therefore, caution is warranted when extrapolating the results, as they may not fully represent the diverse scenarios across the nation.

Conclusion

Among dengue fever patients, notable hematological changes occur between the 1st and 3rd days of illness. Specifically, platelet and neutrophil counts decrease, reflecting the characteristic thrombocytopenia and leukopenia associated with the disease. Conversely, leukocyte and lymphocyte counts increase significantly during this period.

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