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Research article

Comparison of Thrombocyte Nadir between Dengue Fever and Dengue Hemorrhagic Fever Patients

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Abstract

Dengue infection remains a major public health problem and is frequently accompanied by thrombocytopenia. Declining platelet levels during illness may reflect disease severity and assist clinical monitoring in hospitalized patients. This study aimed to compare thrombocyte nadir between patients with dengue fever (DF) and dengue hemorrhagic fever (DHF). A retrospective cross-sectional study was conducted using medical record data from 150 hospitalized dengue patients at Sanjiwani Hospital during 2022-2024. Dengue infection was confirmed by anti-dengue IgM testing based on available medical records. DF and DHF were classified according to clinical-laboratory criteria, with DHF supported by evidence of plasma leakage, including a hematocrit increase of at least 20% from the reference value documented in the medical record. Because thrombocyte nadir data were not normally distributed, differences between groups were analyzed using the Mann-Whitney U test and reported as median (min-max). Of 150 patients, 119 (79.3%) were classified as DF and 31 (20.7%) as DHF. The thrombocyte nadir was significantly lower in DHF than in DF, with median values of 38.5 (10-129) compared with 56 (13-147) x 10^3 cells/μL; p = 0.001. These findings suggest that thrombocyte nadir differs according to dengue severity and support serial platelet monitoring as part of clinical surveillance in hospitalized dengue patients.

Keywords : dengue fever, dengue hemorrhagic fever, thrombocyte nadir, platelet count, thrombocytopenia

Abstrak

Infeksi virus dengue tetap menjadi masalah kesehatan masyarakat utama dan sering disertai trombositopenia. Penurunan kadar trombosit selama perjalanan penyakit dapat mencerminkan derajat keparahan dan membantu pemantauan klinis pada pasien rawat inap. Penelitian ini bertujuan membandingkan nadir trombosit antara pasien dengue fever (DF) dan dengue hemorrhagic fever/demam berdarah dengue (DHF/DBD). Penelitian ini menggunakan desain potong lintang retrospektif berdasarkan data rekam medis 150 pasien dengue yang dirawat di RS Sanjiwani selama tahun 2022-2024. Infeksi dengue dikonfirmasi melalui pemeriksaan IgM anti-dengue berdasarkan data rekam medis yang tersedia. DF dan DHF diklasifikasikan berdasarkan kriteria klinis-laboratoris, dengan DHF didukung oleh bukti kebocoran plasma, termasuk peningkatan hematokrit sekurang-kurangnya 20% dari nilai rujukan yang digunakan dalam rekam medis. Karena data nadir trombosit tidak berdistribusi normal, perbedaan antarkelompok dianalisis menggunakan uji Mann-Whitney U dan dilaporkan sebagai median (min-maks). Dari 150 pasien, 119 pasien (79,3%) diklasifikasikan sebagai DF dan 31 pasien (20,7%) sebagai DHF/DBD. Nadir trombosit secara signifikan lebih rendah pada kelompok DHF dibandingkan dengan DF, dengan nilai median 38,5 (10-129) dibandingkan dengan 56 (13-147) x 10^3 sel/μL; p = 0,001. Temuan ini menunjukkan bahwa nadir trombosit berbeda menurut derajat keparahan dengue dan mendukung pemantauan trombosit serial sebagai bagian dari surveilans klinis pasien dengue yang dirawat di rumah sakit.

Kata kunci : demam dengue, demam berdarah dengue, nadir trombosit, jumlah trombosit, trombositopenia

INTRODUCTION

Dengue fever remains an important public health challenge, particularly in endemic regions and areas with high population mobility. Aedes mosquitoes are increasingly affected by urbanization, climate variation, and travel-related movement, which may contribute to changes in dengue transmission and outbreak patterns (Messina et al., 2019; Pisaneschi et al., 2025; World Health Organization, 2024). Recent global reports indicate that dengue continues to cause a substantial disease burden, including clinically confirmed cases, severe cases, and dengue-related deaths, emphasizing the need for early recognition and clinical monitoring (Natu et al., 2024; World Health Organization, 2024).

The occurrence of dengue infection among travelers and in non-endemic areas also highlights the importance of surveillance and risk stratification in clinical settings

(Masyeni et al., 2018; Masyeni, Yohan & Sasmono, 2019; Hitchings et al., 2025; Sasmono et al., 2025).

Dengue infection has a wide clinical spectrum, ranging from mild febrile illness to severe disease with bleeding, plasma leakage, shock, or organ involvement (Paraná et al., 2024). Thrombocytopenia is a common hematologic abnormality in dengue and may reflect disease progression, platelet consumption, immune-mediated destruction, or impaired platelet production (Castilho et al., 2020; Khazali et al., 2024). Therefore, the lowest platelet count during illness, or thrombocyte nadir, may provide useful information for comparing clinical severity between dengue groups.

Although thrombocyte nadir is frequently monitored in dengue patients (Lam et al., 2017), data comparing thrombocyte nadir between DF and DHF in hospitalized patients remain clinically relevant. This study aimed to compare thrombocyte nadir between patients with DF and DHF admitted to Sanjiwani Hospital.

RESEARCH METHOD

Ethical approval for the study was obtained from the Ethics Review Committee of Sanjiwani Hospital with document number 67/PEPK/X/2025. This retrospective cross-sectional study used medical record data from 150 patients admitted to Sanjiwani Hospital with dengue infection during 2022-2024. Dengue infection was confirmed by detection of anti-dengue IgM antibodies in available medical records from patients with fever for 2-5 days and thrombocytopenia <150 x 10^3 cells/µL. DF and DHF were classified using clinical-laboratory criteria based on previous institutional classification and dengue guideline principles; DHF was operationally defined by evidence of plasma leakage, including a hematocrit increase of at least 20% from the reference value used in the medical record, supported by thrombocytopenia and clinical evaluation (World Health Organization, 2009; Masyeni et al., 2025). Patients with a history of idiopathic thrombocytopenic purpura were excluded. Demographic and clinical data were presented descriptively. Normality of continuous variables was assessed before group comparison. Because complete blood count variables and thrombocyte nadir were not normally distributed, data were presented as median (min-max), and differences

between DF and DHF groups were analyzed using the Mann-Whitney U test. A p-value of < 0.05 was considered statistically significant.

RESULT

In this study, 150 patients diagnosed with dengue were divided into two groups: dengue fever (DF) and dengue hemorrhagic fever (DHF). Of the total, 119 patients (79.3%) were classified as DF, while 31 patients (20.7%) were classified as DHF based on clinical and laboratory criteria, including evidence of plasma leakage with a hematocrit increase of at least 20%. The complete demographic data are presented in Table 1. The mean fever duration before hospital admission was 4.3 ± 1.2 days.

Table 1. Demographic characteristics of the subjects

Variable	Frequency	Percentage (%)
Age, years		
< 15	13	8.7%
15-24	34	22.7%
25-44	61	40.7%
45-64	38	25.3%
≥ 65	4	2.7%
Gender		
Male	98	65.3%
Female	52	34.7%

Figure 1 shows the percentage of subjects reporting clinical symptoms. All participants experienced fever; retroorbital pain was reported by 50.7% and vomiting by 50.6%. Bleeding was noted in only 4% of participants. The sources of bleeding were gum bleeding and petechiae.

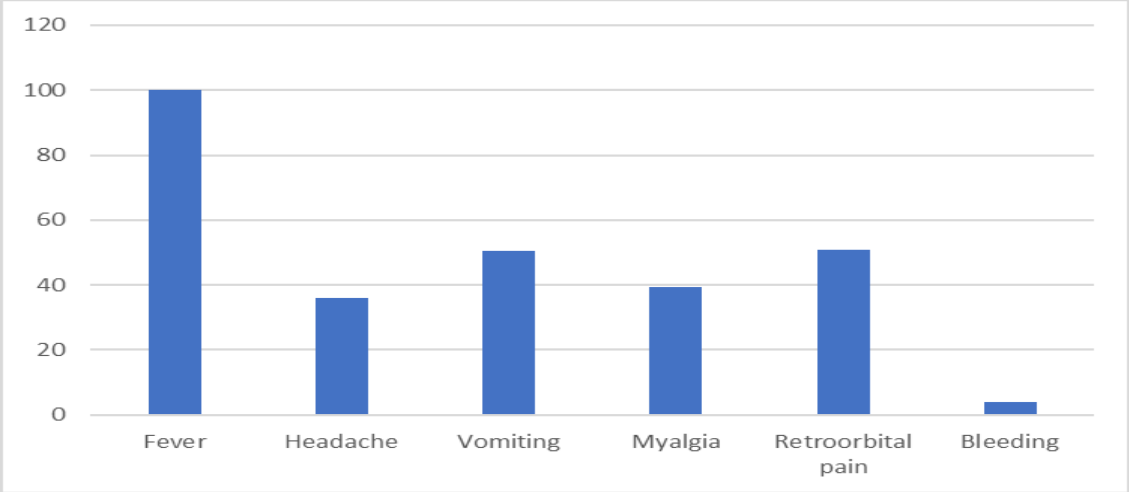

Figure 1. Characteristics of symptoms in subjects

The study did not identify any unusual manifestations of dengue, such as fulminant transaminitis, altered consciousness, or acute respiratory distress syndrome.

The study found no subjects with severe leukopenia, defined as a leukocyte count below 1 x 10^3 cells/µL. The complete laboratory results on admission are presented in Table 2.

Table 2. Complete blood count results on admission by dengue severity

Variable	Median (min-max)		p-value
	DF	DHF	
White blood cells, x 10^3 cells/µL	3.9 (1.9-9.8)	3.5 (1.3-4.1)	0.335
Hemoglobin, g/dL	13.9 (8.5-16.3)	16.3 (14.8-19.4)	< 0.001
Hematocrit, %	40.2 (25.3-43.8)	47.2 (46.8-55.7)	< 0.001
Thrombocyte, x 10^3 cells/µL	97 (17-301)	73 (11-176)	0.014

Note: * Mann-Whitney U test

Because the distribution of complete blood count variables was not normal, laboratory values were reported as median (min-max). The thrombocyte nadir by dengue severity is presented in Table 3. The median thrombocyte nadir was significantly lower in DHF than in DF, with median values of 38.5 (10-129) compared with 56 (13-147) x 10^3 cells/µL; p = 0.001.

Table 3. Comparison of thrombocyte nadir between DF and DHF patients

Dengue severity	Median (min-max)	*p-value**
DF	56 (13-147)	**0.001**
DHF	38.5 (10-129)	

Note: * Mann-Whitney U test; DF: dengue fever; DHF: dengue hemorrhagic fever

DISCUSSION

In this study of 150 dengue patients (119 with DF and 31 with DHF), the thrombocyte nadir was significantly lower in the DHF group than in the DF group. This finding supports the concept that DHF is associated with more pronounced hematologic abnormalities than DF, particularly thrombocytopenia. The more profound thrombocytopenia observed in DHF may be related to suppressed megakaryopoiesis, increased peripheral platelet destruction or consumption, immune-mediated mechanisms, and plasma leakage during the critical phase of dengue infection (Castilho et al., 2020; Khazali et al., 2024).

Recent studies support that thrombocytopenia in dengue is a dynamic process involving both reduced platelet production and increased platelet loss. Khazali et al. (2024) explained that dengue-associated thrombocytopenia may result from impaired megakaryopoiesis and thrombopoiesis, along with increased platelet activation, apoptosis, and immune-mediated clearance. This mechanism is clinically relevant because platelet depletion may contribute to more severe dengue manifestations, especially when it occurs together with immune activation and plasma leakage. Therefore, the lower thrombocyte nadir observed in the DHF group in this study may reflect a more intense hematological disturbance during the critical phase of dengue infection.

The present finding is also consistent with recent clinical evidence. Faridah et al. (2022), in a retrospective Indonesian study, reported that platelet-related parameters were associated with DHF and may help identify patients at higher risk of more severe dengue. Similarly, Jean Pierre et al. (2024) identified platelet count, along with other

laboratory parameters, as a marker of dengue severity. Pulock et al. (2025) also reported that severe dengue was associated with warning signs and laboratory abnormalities, including low platelet counts and plasma leakage. In addition, Guo et al. (2025) emphasized that platelet counts in dengue should be interpreted dynamically, as platelet counts decline over the course of acute infection. These findings support serial platelet monitoring rather than relying only on a single platelet measurement at admission.

The lower thrombocyte nadir in DHF should be interpreted primarily as a marker associated with dengue severity in this study population. Although age and comorbidities may influence dengue outcomes in other studies, this study did not perform stratified analysis by age; therefore, age was not used as the main explanation for the difference in thrombocyte nadir. The present findings are more directly consistent with the pathophysiology of DHF, in which thrombocytopenia, immune activation, and plasma leakage may occur together during disease progression.

In clinical practice, thrombocyte nadir should not be interpreted as a stand-alone determinant of severity. It should be assessed together with hematocrit changes, warning signs, bleeding manifestations, hemodynamic status, and evidence of plasma leakage. This is important because thrombocytopenia may indicate disease progression, but the clinical risk of DHF is strongly influenced by the combination of platelet decline and vascular leakage. Recent studies on dengue severity also emphasize the importance of combining clinical and laboratory parameters to improve risk stratification in hospitalized patients (Paraná et al., 2024; Masyeni et al., 2025).

The higher hematocrit and hemoglobin values recorded in the DHF group should also be interpreted cautiously because the increase in hematocrit was part of the operational classification of DHF in this study. Rather than being treated as an independent finding, elevated hematocrit in this context supports evidence of hemoconcentration and plasma leakage, which are important components in the assessment of dengue severity (World Health Organization, 2009). Therefore, serial monitoring of platelet count and hematocrit remains clinically relevant in hospitalized dengue patients.

When interpreting these findings, several limitations should be considered. The use of retrospective cross-sectional data from a single center may limit generalizability and cannot establish causal or prognostic relationships between thrombocyte nadir and dengue severity. The reliance on available serological confirmation, variation in timing of diagnostic testing, absence of dengue serotype data, and limited information on each patient's baseline hematocrit may also introduce misclassification or measurement bias. Future prospective multicenter studies with standardized diagnostic criteria and broader virological data are needed to validate thrombocyte nadir thresholds and clarify their prognostic significance.

CONCLUSION

This study suggests that thrombocyte nadir differs significantly between dengue severity groups in hospitalized patients, with DHF patients showing a lower nadir than DF patients. These findings support the use of serial platelet monitoring as part of clinical observation in hospitalized dengue patients, particularly during the critical phase. However, because this was a retrospective single-center study and did not evaluate a predictive cut-off, the clinical implications should be interpreted cautiously. Further prospective studies are needed to determine whether thrombocyte nadir can be used as a reliable prognostic marker for dengue severity.

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