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A Relationship of Bleeding Manifestation with Platelet Counts in Dengue Patients in a Tertiary Care Hospital

Muhammad Jamil[1], Javeria Iqbal[1], Hafiz Ahmad Iqrash Qureshi[1], Ayesha Waheed[2], Mariyam Rashid[3], Adeel Ahmed[1], Muhammad Irfan Jamil[4]

[1]Nishtar Hospital, Multan, Pakistan
[2]Bakhtwar Amin Hospital, Multan, Pakistan
[3]Services Hospital, Lahore, Pakistan
[4]Lahore General Hospital, Lahore, Pakistan

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Corresponding Author: Adeel Ahmed, Nishtar Hospital, Multan, Pakistan
Email: mohammodadeel786@gmail.com

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ABSTRACT

Background and Objective: Dengue fever is a prevalent cause of febrile illness, often associated with thrombocytopenia and bleeding manifestations. The study aims to investigate the relationship between platelet counts and bleeding manifestations among dengue patients admitted to a tertiary care hospital. **Material & Methods:** A Cross-sectional study was conducted at the Department of Medicine, Nishtar Hospital, Multan, involving 140 confirmed dengue cases with platelet counts below 150,000/µL. This study was conducted over a period of 15 months from July 2023 to September 2024. Patients were categorized by platelet levels and bleeding manifestations and data were analyzed using SPSS version 26. **Results:** A total of 140 patients with a mean age of 44.23 ± 11.95 years were included in the study. Bleeding manifestations were observed in 57.1% of patients, categorized as single-site bleeding in 36.4% and multiple-site bleeding in 20.7%. Petechiae were the most common manifestation (52.1%), followed by purpura (39.3%) and gum bleeding (37.1%). Severe thrombocytopenia was significantly associated with petechiae (65.6%, p=0.042) and purpura (75.0%, p=0.000), while melena was more frequent in mild thrombocytopenia (35.6%, p=0.000). Hematuria and bleeding gums were significantly correlated with moderate thrombocytopenia (42.9%, p=0.018; 38.1%, p=0.036, respectively). Bleeding status showed no significant trend across platelet count categories (p=0.198). **Conclusions:** Thrombocytopenia severity is significantly associated with specific bleeding manifestations in dengue patients, highlighting the need for vigilant platelet monitoring to mitigate complications.

INTRODUCTION

Dengue fever (DF) is an acute systemic viral infection caused by the dengue virus, a member of the Flaviviridae family [1]. It is transmitted worldwide by the vector species *Aedes aegypti* and *Aedes albopictus*, manifesting in four serotypes (DENV 1-4) [2]. Immunity to one serotype increases the risk of severe dengue upon reinfection [3]. The World Health Organization has identified dengue fever as a critical global health challenge, ranking it among the top ten threats to public health [4]. Annually, the dengue virus is estimated to infect approximately 390 million individuals, of whom 96 million present with clinically significant symptoms [5]. Dengue fever have been reported in 129 countries. Dengue remains a significant endemic disease in Pakistan, with the most recent major outbreak occurring from September to December 2019, resulting in 53,498 reported cases and 95 deaths [6].

Dengue patients present with a broad clinical spectrum, from mild fever to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [7]. The World Health Organization classified the clinical manifestations of DHF into four classes: Class I includes fever with a positive tourniquet test; Class II includes the above plus mild bleeding; Class III is characterized by weak and rapid pulse accompanied by narrowing of pulse pressure or hypotension; and Class IV involves profound shock with undetectable pulse, unmeasurable blood pressure, and cold, clammy extremities. Grades III and IV are collectively regarded as DSS [8]. Individuals diagnosed with dengue fever often exhibit a spectrum of symptoms such as fever, headache, retro-orbital discomfort, joint pain, vomiting, lethargy, fatigue, sore throat and diverse bleeding manifestations [9]. The hemorrhagic features observed in dengue include petechiae, rashes, bleeding gums,

conjunctival suffusion, hematuria, per-rectal bleeding and melena [10].

Among the clinical signs of dengue infection, thrombocytopenia—a reduction in platelet count—is a hallmark finding that plays an important role in the pathophysiology and progression of the disease [11]. According to WHO guidelines, thrombocytopenia serves as a diagnostic criterion for dengue hemorrhagic fever (DHF) [12]. The etiology of thrombocytopenia in dengue is likely multifactorial, involving both impaired platelet production and accelerated peripheral platelet destruction [13]. Elements such as platelet dysfunction, coagulopathy, and the host immune response are believed to influence bleeding risk, indicating that thrombocyte count alone may not adequately predict the clinical severity of hemorrhagic symptoms [14]. The enzyme-linked immunosorbent assay (ELISA) for detecting non-structural protein 1 (NS1) antigen and immunoglobulin M (IgM) antibodies is the diagnostic method of choice in regions where dengue is endemic. Dengue fever management is primarily supportive, emphasizing hydration, paracetamol for fever (avoiding NSAIDs to prevent bleeding), and vigilant monitoring for severe dengue signs, including persistent vomiting, abdominal pain, and bleeding [15]. The study aims to investigate the relationship between platelet counts and bleeding manifestations in dengue patients admitted to a tertiary care hospital.

MATERIALS AND METHODS

A Cross-sectional study was conducted at the Department of Medicine, *Nishtar Hospital*, *Multan*, after obtaining ethical approval from the Ethical Review Committee (IRB: 8041) and informed consent from all participants. This study was conducted over a period of 15 months from July 2023 to September 2024. A total of 140 participants were enrolled through a non-probability consecutive sampling technique that were diagnosed with dengue and were admitted to the hospital.

Inclusion & Exclusion Criteria

Patients of both gender (male and female), aged 14 years or older, presenting with an acute febrile illness lasting 2 to 7 days, and having a laboratory-confirmed diagnosis of dengue fever—evidenced by positive dengue serology (NS1 antigen, IgM, or IgG antibodies) or polymerase chain reaction (PCR) test results—with a platelet count <150,000/µL, were included in this study. Patients with a documented history of bleeding disorders or underlying conditions predisposing to bleeding—such as peptic ulcer disease, chronic liver disease (CLD), immune thrombocytopenic purpura, hemophilia, von Willebrand disease (vWD), or hematological malignancies—were excluded from the study. Additionally, participants with concurrent infections (e.g., malaria, typhoid, or other viral illnesses), those undergoing treatments affecting coagulation or platelet function and patients who declined participation were not included.

Data Collection Procedure

Patients presenting with acute febrile illness lasting 2–7 days were identified from the outpatient and emergency department. Following an initial screening based on clinical suspicion of dengue, cases were confirmed through laboratory testing, including positive results for NS1 antigen, IgM or IgG antibodies or polymerase chain reaction (PCR). Written informed consent was taken from all patients after providing information about the study's objectives, methodology and potential risks. Demographic and clinical details such as age, gender, duration of fever and clinical symptoms (e.g., myalgia, retro-orbital pain, headache, nausea/vomiting, joint pain and abdominal pain) were documented using a predesigned data collection Performa. Patients were categorized into three diagnostic groups—DF, DHF or DSS—according to WHO-defined clinical and laboratory criteria.

Platelet counts were measured using automated hematology analyzers and stratified into three categories: mild (>100,000/µL), moderate (50,000–100,000/µL) and severe (<50,000/µL) thrombocytopenia. Bleeding manifestations, including petechiae, purpura, gum bleeding, epistaxis, hematemesis, hemoptysis, hematuria, melena, and per vaginal bleeding, were assessed by clinical examinations and patient histories and categorized them as no, single-site or multiple-site bleeding.

Data were analyzed using SPSS version 26.0. Descriptive statistics were used to sumup the baseline clinical and demographic characteristics of the study population. Continuous variables (age, duration of fever) were presented as means and standard deviations, while categorical variables (gender, clinical symptoms, bleeding manifestations, platelets count or degree of thrombocytopenia) were presented as frequencies and percentages. The Chi-square test was employed to evaluate associations between platelet count, bleeding manifestations and bleeding status. A p-value <0.05 was considered statistically significant.

RESULTS

There were 140 patients included in our study, with a mean age of 44.23 ± 11.95 years and an average duration of fever of 4.96 ± 1.05 days. The majority of participants belonged to the 36–45 years age group (30.7%), with males constituting 68.6% and females 31.4%. Fever was reported in all cases (100%), while the most frequent additional symptoms included headache (81.4%) and myalgia (75.7%). Dengue fever (DF) was the predominant clinical diagnosis (75%), followed by DHF (15%) and DSS (10%). Platelet counts revealed moderate thrombocytopenia (50,000–100,000/µL) in 45% of cases, with 22.9% showing severe

thrombocytopenia (<50,000/µL). Bleeding manifestations were primarily petechiae or rash (52.1%) and purpura (39.3%), with bleeding status categorized as no bleeding in 42.9%, single-site bleeding in 36.4%, and multiple-site bleeding in 20.7%. Further clinical demographic characteristics are detailed in Table 1.

Table 1
Clinical and Demographic Characteristics of Study Participants

Clinical and Demographic Characteristics		Frequency	(%)age
Age group	Below 25 years	5	3.6
	25 to 35 years	33	23.6
	36 to 45 years	43	30.7
	46 to 55 years	31	22.1
	Above 55 years	28	20.0
Gender	Male	96	68.6
	Female	44	31.4
Clinical manifestations	Fever	140	100.0
	Joint pain	61	43.6
	Headache	114	81.4
	Myalgia	106	75.7
	Abdominal pain	64	45.7
	Retro-orbital pain	50	35.7
	Nausea or vomiting	40	28.6
Clinical Diagnosis	DF	105	75.0
	DHF	21	15.0
	DSS	14	10.0
Platelet count	>100,000/µL	45	32.1
	50,000–100,000/µL	63	45.0
	<50,000/µL	32	22.9
Bleeding Manifestations	Petechiae or rash	73	52.1
	Purpura	55	39.3
	Epistaxis	32	22.9
	Bleeding gums	52	37.1
	Hematemesis	19	13.6
	Hemoptysis	14	10.0
	Hematuria	44	31.4
	Melena	27	19.3
	Per vaginal bleed	10	7.1
Bleeding Status	No bleeding	60	42.9
	Single-site bleeding	51	36.4
	Multiple site bleeding	29	20.7

Table 2 reveals that petechiae were observed in 65.6% of patients with severe thrombocytopenia, compared to 55.6% and 37.8% in moderate and mild thrombocytopenia, respectively (P = 0.042). Purpura was most prevalent in severe thrombocytopenia at 75.0%, followed by 33.3% in moderate and 22.2% in mild thrombocytopenia (P = 0.000). Bleeding gums occurred in 53.1%, 38.1%, and 24.4% of patients with severe, moderate, and mild thrombocytopenia, respectively (P = 0.036). Hematuria was observed in 42.9% of patients with moderate thrombocytopenia, 26.7% with mild, and 15.6% with severe thrombocytopenia (P = 0.018). Melena was most common in mild thrombocytopenia (35.6%), followed by moderate thrombocytopenia (17.5%), and was absent in severe thrombocytopenia (P = 0.000).

Table 2
Relationship between Platelet Counts and Bleeding Manifestations

Bleeding Manifestation	Platelet Count/ µL			p-value
	Mild Thrombocytopenia (>100,000)	Moderate Thrombocytopenia (50,000–100,000)	Severe Thrombocytopenia (<50,000)	
Petechiae	17 (37.8%)	35 (55.6%)	21 (65.6%)	0.042
Purpura	10 (22.2%)	21 (33.3%)	24 (75.0%)	0.000
Epistaxis	7 (15.6%)	17 (27.0%)	8 (25.0%)	0.358
Bleeding Gums	11 (24.4%)	24 (38.1%)	17 (53.1%)	0.036
Hematemesis	4 (8.9%)	11 (17.5%)	4 (12.5%)	0.431
Hemoptysis	2 (4.4%)	11 (17.5%)	1 (3.1%)	0.028
Hematuria	12 (26.7%)	27 (42.9%)	5 (15.6%)	0.018
Melena	16 (35.6%)	11 (17.5%)	0 (0%)	0.000
Per-Vaginal Bleed	2 (4.4%)	7 (11.1%)	1 (3.1%)	0.251

The distribution of bleeding status across platelet count categories showed no statistically significant difference (P = 0.198). No bleeding was observed in 46.7% of patients with mild thrombocytopenia, 39.7% with moderate thrombocytopenia, and 43.8% with severe thrombocytopenia. Single-site bleeding occurred in 44.4%, 33.3%, and 31.3% of patients with mild, moderate, and severe thrombocytopenia, respectively. Multiple-site bleeding was noted in 8.9% of mild, 27.0% of moderate, and 25.0% of severe thrombocytopenia cases (Table 3).

Table 3
Relationship between Bleeding Status and Platelet Count Distribution

Bleeding Status	Platelet Count/ µL			P-value
	Mild Thrombocytopenia (>100,000)	Moderate Thrombocytopenia (50,000–100,000)	Severe Thrombocytopenia (<50,000)	
No bleeding	21 (46.7%)	25 (39.7%)	14 (43.8%)	0.198
Single site bleeding	20 (44.4%)	21 (33.3%)	10 (31.3%)	
Multiple site bleeding	04 (8.9%)	17 (27.0%)	08 (25.0%)	

DISCUSSION

Dengue fever is a prevalent cause of febrile illness, often associated with thrombocytopenia and bleeding manifestations. The mean age in our study was 44.23 ± 11.95 years, with the majority of participants aged 36–45 years (30.7%). This aligns partially with Gupta et al. (2021), who reported a mean age of 43.25 ± 3.68 years and found the largest proportion of participants in the 25–35 years group (33.3%) [16]. Shabir et al. (2022) found a lower mean age of 35.5 ± 10.6 years, while Pal et al. (2023) reported an age distribution of 13.7% under 20 years, 20.6% aged 20–30 years, and 26.8% aged 30–40 years, consistent with our findings of a substantial proportion of middle-aged participants [17,18]. Similarly, K.R. et al. (2013) observed that 60% of participants were aged 21–40 years[19].

In our study, males constituted 68.6% of participants, while females accounted for 31.4%. This male predominance is consistent with Shabir et al. (2022) (73% males), Pal et al. (2023) (65% males), Bashir et al. (2015) (65% males), and Gupta et al. (2021) (62.5% males). K.R. et al. (2013) observed a similar gender distribution (57% males, 43% females). This male predominance may reflect differential exposure risks or healthcare-seeking behaviors among males in endemic regions [17–20].

The average duration of fever in our study was 4.96 ± 1.05 days. Fever was present in all cases (100%), consistent with findings from Singh et al.**,** Sreenivasa et al., and Bashir et al., where fever was universally observed in all cases [7,20,21]. Headache was observed in 81.4% of our participants, similar to Bashir et al. (84.4%) and higher than Pal et al. (55%). Myalgia was present in 75.7% of cases in our study, significantly higher than Shabir et al. (2022) (25%) but consistent with Gupta et al. (2021), where joint pain and myalgia were reported in 78.4% and 46.7%, respectively [16–18,20]. Abdominal pain was noted in 45.7% of our participants, higher than K.R. et al. (20%) and Pal et al. (8.7%). Retro-orbital pain was observed in 35.7%, aligning with Bashir et al. (46.4%). Nausea or vomiting (28.6%) in our study was comparable to Pal et al. (20%) and Shabir et al. (43%) [18,19].

Dengue fever (DF) was the predominant clinical diagnosis in our study (75%), with DHF and DSS comprising 15% and 10%, respectively. This is consistent with Bashir et al. (2015), where DF accounted for 86.5% of cases, and DHF and DSS were less frequent. K.R. et al. (2013) similarly reported DF in 76% of cases, DHF in 18%, and DSS in 6%, while Gupta et al. (2021) observed DF in 66.67% of cases and DHF/DSS in 33.33% [16,19,20]. Moderate thrombocytopenia (50,000–100,000/µL) was observed in 45% of participants in our study, while severe thrombocytopenia (<50,000/µL) was present in 22.9%, and mild thrombocytopenia (>100,000/µL) in 32.1%. These results align with Gupta et al. (2021), where 45.83% had moderate thrombocytopenia and 29.17% had severe thrombocytopenia. Similarly, Pal et al. (2023) reported 35% with moderate thrombocytopenia and 6.9% with severe thrombocytopenia. Shabir et al. (2022) reported a higher proportion of severe thrombocytopenia (<20,000/µL, 14%) [16–18].

Bleeding manifestations were present in 57.1% of our participants, with petechiae or rash (52.1%) and purpura (39.3%) being the most frequent. These findings are consistent with Shabir et al. (2022), where petechiae were observed in 43% of cases. Bleeding gums were noted in 37.1% of participants, higher than Shabir et al. (28%) and Gupta et al. (27.5%). Hematuria was observed in 31.4%, similar to Gupta et al. (33.33%) but higher than Bashir et al. (1.8%). A significant correlation was observed between platelet count and specific bleeding manifestations [16,17,20]. Petechiae were most frequent in severe thrombocytopenia (65.6%, P=0.042), consistent with Shabir et al., where petechiae occurred in 92.8% of cases with <20,000/µL platelets. Purpura (75%, P<0.001) and bleeding gums (53.1%, P=0.036) were also significantly associated with severe thrombocytopenia, corroborating findings from Gupta et al.. Melena was most common in mild thrombocytopenia (35.6%, P<0.001), similar to Singh et al., where melena occurred in 26% of cases [8,16].

No bleeding was observed in 42.9% of our participants, single-site bleeding in 36.4%, and multiple-site bleeding in 20.7%. These findings are consistent with Shabir et al., where 41% had no bleeding, 14% had single-site bleeding, and 43% had multiple-site bleeding. Pal et al. reported no bleeding in patients with platelet counts >50,000/µL, while 36.3% with platelet counts 20,000–50,000/µL had bleeding, consistent with our results [17,18].

This study's strengths include an analysis of clinical and hematological parameters in dengue patients, demonstrating significant correlations between platelet counts and bleeding manifestations. The findings provide insights into the relationship between thrombocytopenia and clinical outcomes. However, the single-center design limits external validity, and the study did not assess coagulation profiles, endothelial dysfunction markers, or longitudinal outcomes such as thrombocytopenia progression. Future research should focus on multi-center studies encompassing diverse populations and include additional factors to better understand bleeding pathophysiology. Developing standardized guidelines for bleeding risk stratification is essential to enhance clinical management and improve outcomes for dengue patients across varying healthcare settings.

CONCLUSION

This study reveals a strong association between platelet

counts and bleeding manifestations in dengue patients. Severe thrombocytopenia was linked to higher occurrences of petechiae and purpura, while melena was more common in mild thrombocytopenia. Significant correlations were also observed with bleeding gums and hematuria. However, bleeding status showed no consistent trend across platelet categories. Therefore, other biomarkers should also be considered to identify the patients at higher risk of bleeding. These findings underscore the critical role of platelet monitoring in predicting bleeding risks and optimizing management strategies for dengue patients in tertiary care settings.

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