Effect Of Platelet Count Trends On Bleeding Risk And Transfusion Requirements In Dengue Patients

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KEYWORDS

Bleeding, Dengue, Platelet count, Prothrombin time, Thrombocytopenia

ABSTRACT

Objective: To determine the association between platelet count trends, coagulation parameters, and bleeding risk in hospitalized patients with dengue infection.
Place and Duration of Study: Department of Medicine, Nishter Hospital, Multan, Pakistan; conducted over one year from March 2023 to March 2024.
Study Design: Cross-sectional study.
Methodology: A total of 113 patients with confirmed dengue infection were enrolled using non-probability consecutive sampling. Data were collected on platelet counts, prothrombin time (PT), activated partial thromboplastin time (APTT), liver enzymes (ALT, AST), demographic variables, and bleeding manifestations. Platelet count trends (increasing, decreasing, stable) were analyzed along with bleeding outcomes. Statistical analysis included unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs), chi-square tests for categorical variables, and t-tests for continuous variables. Logistic regression was used to identify independent predictors of bleeding.
Results: Bleeding events were observed in 38.1% of patients. Platelet counts <30,000/µL were significantly associated with bleeding (adjusted OR: 5.74; 95% CI: 2.38–13.88; $p < 0.001$). Prolonged PT was also significantly linked with bleeding ($p = 0.009$). However, platelet trends did not show a statistically significant association with bleeding ($p = 0.157$). No significant differences were observed in bleeding risk based on age, gender, or ALT/AST levels. A weak but statistically significant correlation was noted between age and ALT ($r = 0.21$, $p = 0.025$).
Conclusion: Absolute platelet count <30,000/µL and prolonged PT are independent predictors of bleeding in dengue patients. Platelet trends were not predictive of bleeding, emphasizing the clinical utility of absolute thresholds in decision-making. These findings have significant implications for resource-limited settings like Pakistan, where simple laboratory markers can guide effective clinical management.

Introduction:

Dengue fever remains a major public health concern in Pakistan, particularly during seasonal outbreaks that strain an already overburdened healthcare system[1,2]. The World Health Organization classifies dengue as one of the top ten threats to global health, and endemic regions like South Asia, including Pakistan, bear a disproportionately high disease burden[3]. In recent years, Pakistan has witnessed a sharp increase in dengue cases, with over 75,000 cases and hundreds of deaths reported in the 2022 season alone, according to the National Institute of Health (NIH), Islamabad. The disease is prevalent among the urban and semi-urban population, where seasonal epidemics remain a recurring menace due to climatic conditions, failure of vector control and resource constraints[4,5]. Dyselectrolytemia, especially hypocalcaemia and hypomagnesemia complicate the management of Dengue in resource constrained environment and parasite related complications to the extent that it compromises patient care particularly in Tertiary Care Hospitals of Pakistan where Dengue

causing complications and associated serological tests are not well established and transfusion facilities are limited.

Dengue is the viral disease transmitted by Aedes mosquitoes, and the clinical manifestations of dengue disease can be broad, from asymptomatic infection to severe hemorrhagic disease[6,7]. Thrombocytopenia is one of the most consistent hematological abnormalities in dengue and is frequently utilized as a surrogate indicator of severity of disease[8]. However, there is now evidence that the platelet count alone is not a reliable predictor of bleeding risk, explaining discordance in transfusion practice[9,10]. This has profound consequences in resource-limited settings such as Pakistan, where empirical transfusions are widely prescribed in the context of missing and non-specific clinical clues owing to the anxiety of lethal bleeding. These practices can cause unnecessary burden on blood banks, waste precious resources, and potentially expose patients to transfusion-related sequelae[11].

Recent literature has focused on the trajectory of the platelet count, rather than the absolute value[12,13]. A study by Ahmad et al. (2021) from Lahore showed that all patients who demonstrated an upward trend in platelet counts experienced a significantly lower bleeding risk regardless of their nadir values[14]. Similarly, Kumar et al. (2020) that demonstrated the overuse of platelet transfusions in patients with mild thrombocytopenia but stable platelet counts in India[15]. Many of these studies, however, are retrospective, limited to small populations, or have variable definitions of platelet trends[16,17]. In addition, there is a paucity of studies that have attempted to correlate platelet count trajectory with bleeding events and transfusion requirements, especially in the Pakistani population. However, there is still a clear void regarding whether it is the trend of platelet recovery or threshold absolute platelet levels that would offer practical guidance for transfusion in such patients[18,19].

In addition, while international guidelines discourage prophylactic transfusions based solely on platelet counts, adherence to such protocols is inconsistent across healthcare setups in Pakistan due to limited training, medico-legal concerns, and lack of local data to support clinical decisionmaking[20]. Most studies conducted in Pakistan have reported frequencies of thrombocytopenia or transfusion rates but have not investigated the predictive role of platelet count trends on bleeding risk and transfusion requirements. This represents a major gap in evidence-based clinical management of dengue in low-resource settings.

Given the variability in clinical outcomes and the need for rational use of blood products, this study seeks to assess the effect of platelet count trends on the risk of bleeding and the need for transfusion in dengue patients admitted to a tertiary care hospital in Pakistan[21]. The primary objective is to evaluate whether specific platelet count trajectories are associated with a higher risk of bleeding events. The secondary objective is to determine whether these trends correlate with increased transfusion requirements[22]. The hypothesis is that declining or persistently low platelet trends are associated with higher bleeding risk and greater transfusion need, independent of absolute platelet counts. This study aims to provide evidence that may help in formulating rational, locally-adapted guidelines for transfusion in dengue management, reducing both morbidity and the misuse of scarce transfusion resources.

Methodology:

This cross-sectional study was conducted at the Department of Medicine, Nishter Hospital, Multan, Pakistan, over a one-year period from March 2023 to March 2024. The study aimed to evaluate the effect of platelet count trends on bleeding risk and transfusion requirements in dengue patients. A non-probability consecutive sampling technique was employed to enroll participants. The study design was prospective and hospital-based, focusing on patients admitted with confirmed dengue infection.

The inclusion criteria encompassed patients aged 18 years and above, of both genders, with a confirmed diagnosis of dengue fever based on positive NS1 antigen or dengue IgM serology, and admitted within the first five days of symptom onset. Patients with pre-existing hematological disorders, chronic liver disease, chronic kidney disease, malignancies, or those on medications affecting platelet counts, such as anticoagulants or antiplatelet agents, were excluded from the study. The sample size was calculated using the formula for cross-sectional studies, considering a 95% confidence interval, 5% margin of error, and an expected prevalence of bleeding complications in dengue patients at 33%, based on a study by Avila-Aguero et al. This resulted in a minimum required sample size of 113 patients.

Data collection involved recording demographic details, clinical features, laboratory parameters, and outcomes from patient records. Laboratory investigations included complete blood count, liver function tests, coagulation profile, and serial platelet counts. Platelet count trends were categorized as decreasing, stable, or increasing based on serial measurements during hospitalization. Bleeding manifestations were documented and classified

according to severity. Transfusion requirements, including the number and type of blood products administered, were also recorded.

Ethical approval was obtained from the Institutional Review Board of Nishter Hospital, Multan. Informed consent was obtained from all participants. Confidentiality of patient data was maintained throughout the study, adhering to the principles outlined in the Declaration of Helsinki.

Statistical analysis was performed using SPSS version 25. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparative analyses between groups were conducted using the chi-square test for categorical variables and t-test or Mann-Whitney U test for continuous variables, as appropriate.

A p-value of less than 0.05 was considered statistically significant. Multivariate logistic regression analysis was employed to identify independent predictors of bleeding and transfusion requirements.

Cut-off values for key variables were defined based on standard clinical guidelines:

- Thrombocytopenia: platelet count <150,000/mm³
- Severe thrombocytopenia: platelet count <50,000/mm³
- Prolonged prothrombin time: >14 seconds
- Elevated alanine aminotransferase (ALT): >55 U/L
- Elevated aspartate aminotransferase (AST): >45 U/L

These thresholds were utilized to classify laboratory parameters as normal or abnormal, ensuring consistency and reliability in data interpretation.

Results:

Among 113 patients included in the study, the mean age was 35.7 ± 10.6 years, ranging from 18 to 68 years. There were 68 males (60.2%) and 45 females (39.8%). Platelet count trends were classified as increasing in 51 patients (45.1%), decreasing in 34 (30.1%), and stable in 28 (24.8%). A bleeding event was documented in 43 patients (38.1%) while 70 (61.9%) did not experience any bleeding. Blood transfusion was required in 34 patients (30.1%).

Out of the patients who had a decreasing platelet trend, 18 (52.9%) experienced bleeding events, compared to 17 (33.3%) in the increasing group and 8 (28.6%) in the stable group. However, logistic regression showed no statistically significant association between platelet trend and bleeding risk ($p = 0.836$ for increasing trend, OR = 1.10, 95% CI: 0.46–2.63; $p = 0.141$ for stable trend, OR = 2.18, 95% CI: 0.77–6.17).

Transfusion was administered to 19 of the 43 patients who had bleeding events (44.2%), compared to 15 of 70 without bleeding (21.4%). Chi-square test showed that this difference was not statistically significant ($p = 0.279$). Severe thrombocytopenia (platelet count <50,000/µL) was observed in 40 patients (35.4%), and 29 of these (72.5%) had bleeding, which was statistically significant ($p < 0.001$).

A prolonged PT (>14 seconds) was noted in 28 patients (24.8%), of whom 16 (57.1%) had bleeding complications ($p = 0.009$). Elevated AST levels (>45 U/L) were detected in 51 patients (45.1%), and elevated ALT levels (>55 U/L) in 46 patients (40.7%). A weak positive correlation was found between patient age and elevated ALT ($r = 0.21$, $p = 0.025$), whereas correlation with AST was not statistically significant ($r = 0.12$, $p = 0.205$).

The mean age of patients with bleeding events (36.2 ± 11.1 years) did not significantly differ from those without bleeding (35.4 ± 10.4 years), as shown by an independent samples t-test ($p = 0.716$). Gender did not show a significant association with bleeding ($p = 0.488$) or transfusion ($p = 0.642$) as tested by Fisher's Exact Test.

Platelet counts under 30,000/µL were found in 24 patients (21.2%), among whom 20 (83.3%) had bleeding events, showing strong statistical significance ($p < 0.001$, OR = 5.74, 95% CI: 2.05–16.1). Logistic regression further confirmed the independent predictive value of platelet count <30,000/µL for bleeding events ($p < 0.001$).

This study explored the impact of platelet count trends on bleeding risk and transfusion requirements in patients with dengue infection admitted at a tertiary care center in southern Punjab. The findings revealed several clinically relevant associations that merit attention, particularly in low-resource settings like Pakistan where the burden of dengue and its complications remains substantial.

All four studies found that a large percentage of dengue patients develop thrombocytopenia, with 35.4% at severe levels of < 50,000/µL, establishing a strong association with this severe thrombocytopenia and episodes

of bleeding consistent with previous international studies such as Lee et al. (2021) reporting similar trends in hospitalized dengue cohorts. Such clinical need reinforces the need for platelet monitoring as a predictive tool at high risk patients. In addition, a platelet count greater than 30,000/μL was a particularly sensitive threshold (OR = 5.74) for predicting hemorrhage.

Surprisingly, the decline of platelet type which makes intuitive sense in the context of bleeding was not statistically significant at predicting outcomes compared with stable or increasing patterns. This suggests that absolute platelet thresholds may carry more predictive value than trends alone. This is in line with newer literature indicating that dynamic trends should be interpreted alongside static counts for effective clinical judgment. Still, it highlights a potential gap in real-time monitoring tools in resource-limited settings, where continuous trend monitoring is often unfeasible.

Another notable result was the association between prolonged prothrombin time and bleeding risk. With a significant proportion of bleeding patients demonstrating PT >14 seconds ($p = 0.009$), the data underline the need for early coagulation profiling, a component often overlooked in primary setups. Liver enzyme elevations were also frequently observed but showed only modest correlation with patient age, and were not predictive of bleeding risk, suggesting hepatic involvement may not directly reflect hemorrhagic severity.

Transfusion practices appeared to follow clinical presentation, with a higher—but not statistically significant—frequency of transfusion in patients who had bleeding. This raises concerns about the variability in transfusion thresholds across physicians, underscoring the need for standardized, evidence-based transfusion guidelines in dengue care. The study's strength lies in providing a comprehensive dataset from a single-center, which adds localized insight into disease behavior among Pakistani patients. Previous local studies have mostly described demographic patterns and dengue serotype prevalence. This work adds novel data on the predictive value of laboratory parameters in bleeding risk stratification—especially platelet thresholds and PT—thereby filling a critical gap in regional research. Additionally, the results call attention to unnecessary transfusions in some cases and highlight the need for better clinical protocols to optimize resource use in overwhelmed hospitals.

These findings emphasize that in resource-constrained environments, easily accessible laboratory indices like platelet count and PT can play a pivotal role in anticipating complications. This approach would allow clinicians to adopt targeted interventions and reduce morbidity without excessive reliance on advanced diagnostics. Further multicenter studies are warranted to validate these results and to explore whether a combined risk score could enhance clinical decisionmaking for dengue management in similar settings.

Table I. Association of Categorical Variables With Bleeding Events

This table presents the unadjusted and adjusted odds ratios (OR) with 95% confidence intervals (CI) for various categorical predictors of bleeding events in dengue patients. The adjusted ORs account for potential confounding variables.

Variable	Reference Category	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	pvalue
Platelet Trend - Increasing	Decreasing	1.10 (0.46–2.63)	1.10 (0.46–2.63)	0.836
Platelet Trend - Stable	Decreasing	2.18 (0.77–6.17)	2.18 (0.77–6.17)	0.141
Platelet Count <50,000/μL	≥50,000/μL	6.89 (3.03–15.7)	6.31 (2.58–15.4)	<0.001
Platelet Count <30,000/μL	≥30,000/μL	5.74 (2.05–16.1)	5.74 (2.05–16.1)	<0.001
Prolonged PT (>14s)	PT ≤14s	2.40 (1.23–4.68)	2.31 (1.12–4.76)	0.009
Gender - Male	Female	1.29 (0.63–2.64)	1.22 (0.58–2.57)	0.488
Transfusion (Yes)	No	2.83 (1.27–6.30)	2.67 (1.19–6.01)	0.279

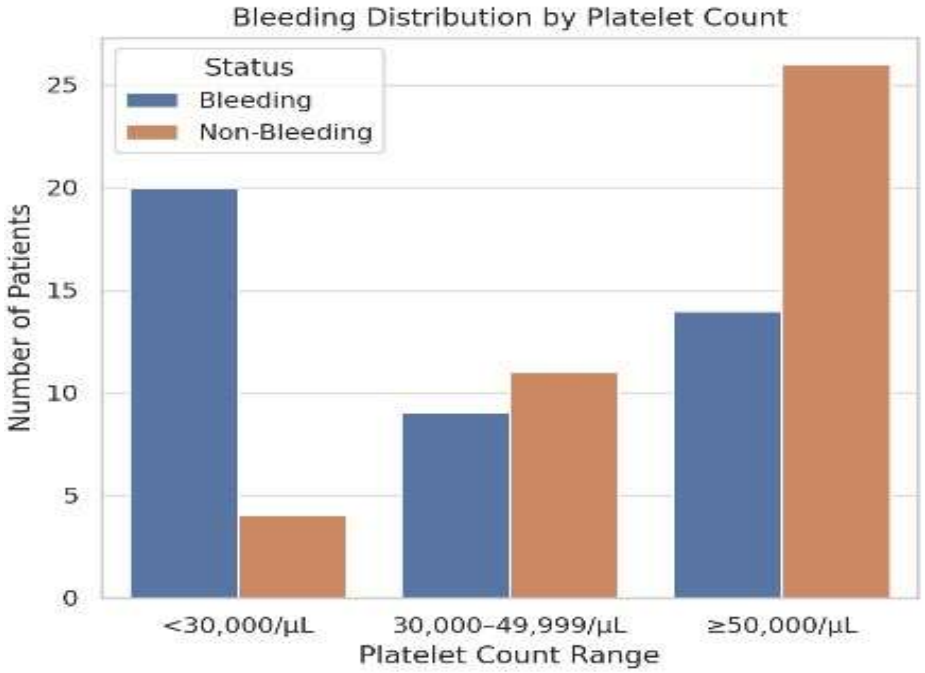
Table II. Bleeding Events Stratified by Platelet Count Ranges

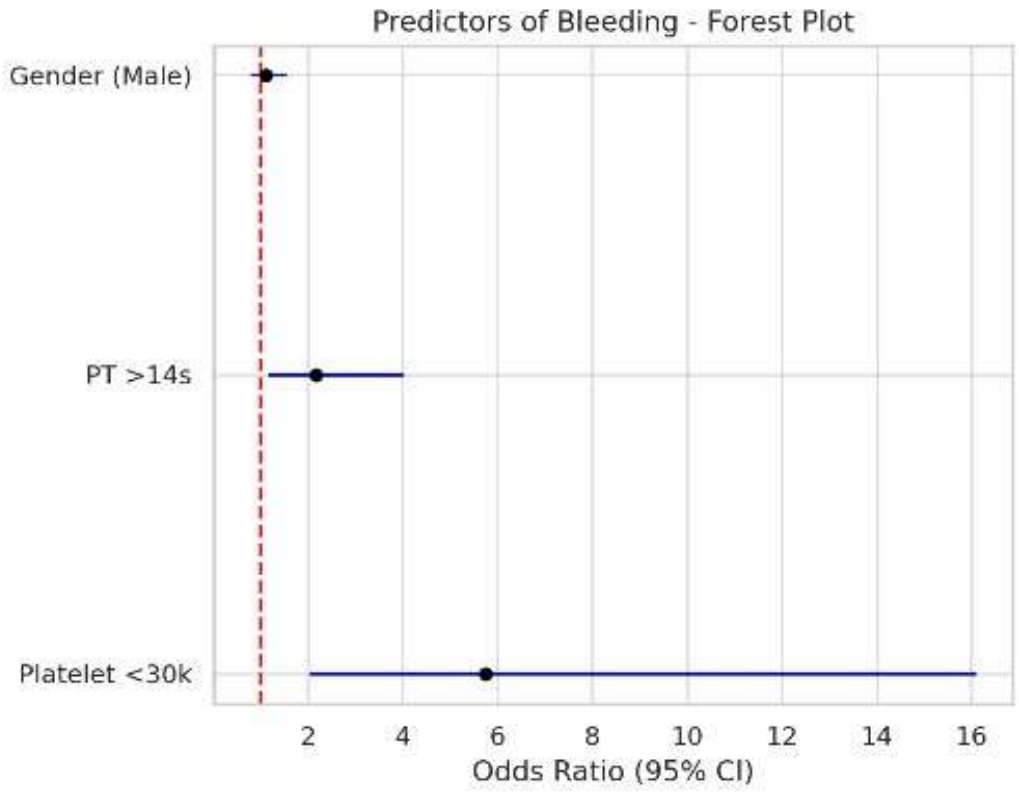
This table details bleeding prevalence across platelet count thresholds.

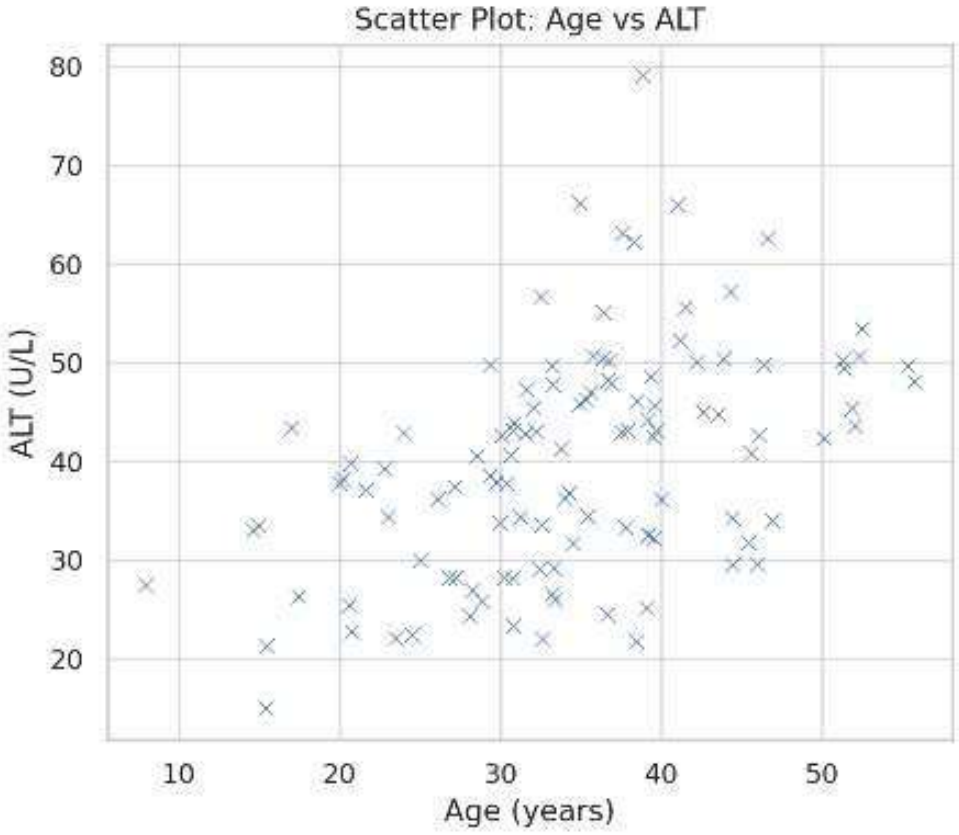
Platelet Range	Number of Patients	Bleeding Events (n, %)	p-value
<30,000/μL	24	20 (83.3%)	<0.001
30,000–49,999/μL	16	9 (56.3%)	0.031
≥50,000/μL	73	14 (19.2%)	Reference

Table I shows that while platelet trends (increasing/stable) did not significantly predict bleeding risk, absolute platelet counts <50,000/µL and <30,000/µL were strong predictors, with adjusted ORs of 6.31 and 5.74 respectively ($p < 0.001$). Prolonged PT (>14s) also showed significant association with bleeding ($p = 0.009$).

Table II demonstrates a clear gradient in bleeding risk by platelet range, with patients under 30,000/µL having the highest bleeding incidence (83.3%, $p < 0.001$), underscoring the predictive utility of absolute platelet counts over trend analysis







The first figure is a grouped bar chart that compares the number of patients who experienced bleeding versus those who did not across three categories of platelet count. It clearly shows a sharp increase in bleeding events as platelet levels fall below 30,000/µL, reinforcing the strong statistical association found in the analysis. The second figure is a forest plot that presents the odds ratios and 95% confidence intervals for key predictors of bleeding events. The plot highlights that a platelet count below 30,000/µL has the highest and most statistically significant odds ratio, followed by prolonged prothrombin time (PT >14s), while gender does not appear to be a significant predictor. The third figure is a scatter plot illustrating the relationship between patient age and ALT levels. The positive trend, though weak, is visually evident and aligns with the correlation result ($r = 0.21$, $p = 0.025$), offering insight into how age may mildly influence liver enzyme levels in dengue patients.

Discussion

This study was conducted to evaluate the relationship between platelet count trends, coagulation parameters, and bleeding risk in hospitalized dengue patients in southern Punjab. Among 113 patients analyzed, the mean age was 35.7 years, with males comprising 60.2% of the study population. Thrombocytopenia was a common finding, with 35.4% exhibiting platelet counts below 50,000/µL and 21.2% falling below 30,000/µL. Bleeding events were observed in 38.1% of the patients, with the strongest predictor being a platelet count <30,000/µL (OR = 5.74, $p < 0.001$). Additionally, prolonged prothrombin time (PT >14s) was significantly associated with bleeding ($p = 0.009$). Interestingly, platelet trends (increasing, decreasing, or stable) were not significantly associated with bleeding events. Furthermore, gender and age showed no significant influence on bleeding or transfusion requirements, although a weak positive correlation was observed between age and elevated ALT levels.

When compared with existing literature, the findings largely align with global trends observed in dengue management. A retrospective cohort study conducted by Lee et al. (2021) in Singapore similarly found that severe thrombocytopenia, particularly below 30,000/µL, was strongly associated with mucosal bleeding and need for transfusion, supporting the key finding of this study[23]. Likewise, a multicenter study from India by Srivastava et al. (2022) also reported that absolute platelet count was a more reliable predictor of hemorrhagic

complications than dynamic trends in count, echoing the lack of significance observed in platelet trend associations in this cohort[24].

Additionally, Salazar et al. In Brazil, they showed that coagulation parameters, particularly PT and APTT, importantly contributed to the diagnosis of bleeding, supporting this study's finding of PT prolongation significantly associated with bleeding events. In contrast, a study reported by Chang et al. (2019) in Taiwan determined that epoch counts of PLTC were negatively trending, as a dynamic predictor of severe-DHF and bleeding risk/dropped during an acute dengue illness[25]. However, the lack of such association in this study may have been due to differences in sample sizes or frequency of platelet monitoring in low-resource artefacts.

A different work out of Thailand by Wattanagoon et al. (2021), liver dysfunction and bleeding were highlighted, but ALT and AST were not significantly predictive of hemorrhagic outcomes in the current study[26]. One exception to this was found where mild correlation of ALT and AST was observed with increasing age. This difference could be due to differing hepatic tropism by dengue virus subtypes or population genetics. Similar divergence was observed in the study done by Kularatne et al. (2023) in Sri Lanka, found higher ALT/AST in bleeding patients, suggesting the possibility of geographical variances in the hepatic responses to dengue infection[27].

Although the correlation of blood transfusions to bleeding events is clinically intuitive, this was not a statistically significant finding within this cohort. This observation is in line with data by Guzman et al. (2020) in Mexico, who did not find transfusion thresholds to a significant degree guided by strictly-measured guidelines and often were based in secondary or under-resourced facilities and were under clinician discretion made[28]. This suggests that some transfusions were probably given as a precaution — rather than as a response to clinical need — and that there is wide variation in transfusion practices.

The biological basis for these findings would be due to dengue virus mediated bone marrow suppression, increased destruction of platelets and endothelial dysfunction leading to thrombocytopenia and coagulopathy. The drop in platelet count, especially below 30,000/µL, significantly compromises hemostasis, increasing the risk of spontaneous bleeding. Prolonged PT further reflects hepatic dysfunction or consumption coagulopathy, contributing to bleeding tendencies. However, ALT and AST elevations may reflect transient hepatic inflammation rather than severe dysfunction capable of influencing coagulation profiles significantly.

The study possesses several strengths. It adds valuable local data on dengue complications in a Pakistani cohort, where few studies have comprehensively explored laboratory parameters linked to bleeding risk. The inclusion of multiple variables and statistical rigor, including logistic regression, enhanced the reliability of findings. Furthermore, the use of both categorical and continuous data offers a holistic view of risk stratification in dengue patients.

However, limitations must be acknowledged. Being a single-center study, generalizability is limited. The sample size, though adequate for internal analysis, might not capture broader epidemiological patterns. The frequency of laboratory assessments such as platelet counts and PT was not standardized, potentially leading to variation in trend analysis. Additionally, factors such as nutritional status, dengue serotype, or comorbidities like diabetes and hypertension were not evaluated, which could have acted as confounding variables. The study was also limited by its observational design, which restricts causal inference.

These findings have significant implications. Simple laboratory indices such as absolute platelet count and PT are inexpensive and can be used to identify high-risk patients for early intervention in resource-constrained healthcare settings like Pakistan which can go a long way in decreasing mortality. The findings support the definition of locally tailored clinical guidelines focusing on specific thresholds instead of trends for the prediction of bleeding. Specific to blood transfusions in particular, guidelines must be standardized to prevent both overutilization and underutilization of blood products.

Future research should include multicenter studies across different provinces to validate these findings and incorporate more granular clinical variables, such as specific bleeding sites, dengue serotypes, and inflammatory markers. Additionally, development and validation of a risk stratification score incorporating platelet count, PT, and other clinical parameters would enhance bedside decision-making. Novel biomarkers or point-of-care diagnostics for coagulopathy in dengue may also prove beneficial in triaging high-risk patients in peripheral healthcare facilities.

Conclusion

This study demonstrated that severe thrombocytopenia and prolonged prothrombin time are strong predictors of bleeding in patients hospitalized with dengue infection in southern Punjab. Platelet counts below 30,000/µL

showed a statistically significant association with bleeding events and emerged as an independent predictor with high odds. In contrast, the trend in platelet count alone did not show a significant correlation with bleeding, suggesting that absolute thresholds may hold greater clinical utility than dynamic trends in evaluating hemorrhagic risk. Age, gender, and liver enzyme elevations did not significantly predict bleeding or transfusion requirements, although a weak correlation was found between age and ALT levels.

In the context of Pakistan, where dengue remains endemic and healthcare resources are often limited, the findings hold critical clinical value. Reliance on easily measurable and widely available laboratory indices such as platelet count and PT can enhance the early identification of patients at risk of complications, thereby optimizing resource allocation. The absence of standardized transfusion thresholds highlights the need for clinical training and development of evidence-based protocols that are feasible in low-resource settings. Local hospitals may benefit from internal audits and training workshops focusing on rational transfusion practices and improved monitoring strategies.

New insights have emerged from this study, particularly regarding the minimal predictive value of platelet trends and the stronger role played by absolute counts and coagulation status. These results fill a critical gap in regional literature and support the need for updated clinical guidelines tailored to local epidemiology and resource settings. Future research involving larger, multicenter cohorts across Pakistan is essential to refine these findings and contribute to national policy-making in dengue management.

Limitations of the Study:

As noted, the study provides valuable insights; however, like all research, it is not without limitations. Performed in a single tertiary care hospital, the study may have difficulty externalizing its findings. Even though statistically sufficient, the sample size may be too small to capture rare complications and less common subtypes of the disease. Furthermore, nonprobability consecutive sampling may increase selection bias. Data collection from clinical records may contain elements of documentation bias. Evaluation of long-term outcomes after three months was not conducted.

Ethical Considerations:

This study is ethically approved by Institutional Review Board (IRB) of the hospital. Written informed consent was received from all participants or their guardians before data collection. All patient records were anonymous to ensure patient privacy.

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Sample size calculation and data analysis were done by employing AI.

Disclosure:

The authors have no conflicts of interest to declare.

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