RESEARCH PAPER

Activated Partial Thromboplastin Time (aPTT) as a Predictor of Bleeding Manifestations and Severity in Adult Patients with Dengue – A Cross Sectional Study

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ABSTRACT

Background: Dengue fever is a leading cause of acute febrile illness in tropical regions. Thrombocytopenia alone correlates poorly with bleeding in dengue. Activated partial thromboplastin time (aPTT) reflects intrinsic coagulation dysfunction and may serve as a superior predictor.

Objectives: To assess deranged aPTT as a predictor of bleeding manifestations and to evaluate its association with severity of dengue in adult patients.

Methods: Cross-sectional observational study at SVMCH & RC, Puducherry (January–March 2026). Forty adult patients with serologically confirmed dengue were enrolled. aPTT at admission was the primary exposure variable; patients were observed for bleeding and severe dengue (CDC 2015 criteria).

Results: Twenty of the forty patients exhibited prolonged aPTT (mean 54.8 ± 9.3 s) and twenty had normal aPTT (mean 34.6 ± 2.9 s). Any bleeding (RR=3.25; p=0.026), substantial bleeding (RR=3.00; p=0.048), and severe dengue (RR=3.75; p=0.001) were all strongly correlated with prolonged aPTT. For significant bleeding, the negative predictive value (NPV) was 95.0%. There was no discernible relationship between platelet count and bleeding symptoms.

Conclusion: aPTT is a reliable rule-out screening tool for major bleeding and severity in dengue, with an NPV of 95%. Platelet count alone is insufficient to predict bleeding risk.

Keywords: Dengue, activated partial thromboplastin time (aPTT), coagulopathy, bleeding, severe dengue

How to cite this article: Ram TB, Rammohan G, Umarani R, Subrahmanyam DKS, Suresh K. Activated partial thromboplastin time (aPTT) as a predictor of bleeding manifestations and severity in adult patients with dengue – a cross sectional study. Int J Drug Deliv Technol. 2026;16(73s): 339-343. DOI: 10.25258/ijddt.16.73s.37

INTRODUCTION

Dengue fever is one of the most serious vector-borne illnesses in the world, with an estimated 390 million cases every year. Dengue morbidity and hospitalization are disproportionately high in India, a tropical nation. Although thrombocytopenia has historically been the primary hematological indicator in dengue surveillance, numerous studies have consistently shown a weak relationship between platelet count and actual bleeding symptoms [1,2].

Dengue-induced inflammatory cytokines, especially interleukin-6, which downregulate intrinsic coagulation factors, most notably Factor XII, are responsible for coagulopathy, which is becoming more widely acknowledged as a unique pathophysiological condition [3,4]. Prothrombin time (PT) is mostly unaltered, but the activated partial thromboplastin time (aPTT), which indicates intrinsic pathway failure, is selectively prolonged.

aPTT is inexpensive, widely available, and measurable as part of routine workup. If aPTT derangement demonstrates a reliable association with bleeding and severity, it can serve as a practical screening tool at admission, enabling timely triage and targeted intervention. Limited data exist from Puducherry and broader South India. Hence, this study was undertaken to evaluate aPTT derangement as a predictor of bleeding manifestations and severity in adult dengue patients.

MATERIALS AND METHODS

Study Design and Setting: Cross-sectional observational study conducted in the Department of General Medicine in a tertiary care centre at Puducherry, over three months (January–March 2026). IEC approval was obtained (IEC Ref: SVMCH&RC/IEC/2025). Written informed consent was obtained from all participants. Adults (≥18 years) with serologically confirmed dengue (NS1 antigen or IgM antibody positive) were included. Patients who received FFP before aPTT testing, those with known coagulation disorders, patients on anticoagulants, and those with chronic liver disease were excluded.

Sample Size: Based on Thomas RS et al. (2024): normal aPTT mean 34.7 ± 3.5 s vs prolonged 49.2 ± 12.8 s. Minimum 7 per group (80% power, 5% alpha, OpenEpi v3.0); augmented to 20 per group; total n = 40 [5].

Procedure: Structured proforma captured demographics, clinical features, serology (NS1/IgM/IgG), and laboratory parameters. Blood was drawn at admission for CBC, platelet count, and aPTT (upper limit of normal 40 s). Patients were observed throughout admission for bleeding events and severe dengue.

Minor bleeding: petechiae, purpura, epistaxis, gum bleed, subconjunctival hemorrhage.

Major bleeding: hematemesis, melena, hematuria, hemoptysis, hematochezia.

Severe dengue: as per CDC 2015 criteria — severe plasma leakage with shock, severe bleeding, or severe organ impairment.

STATISTICAL ANALYSIS

Categorical data as frequencies and proportions; continuous data as mean ± SD. Chi-square test for associations; relative risk (RR)

with 95% CI. Diagnostic performance (sensitivity, specificity, PPV, NPV) calculated. $p<0.05$ considered significant. SPSS v23.0 used.

RESULTS

Baseline Characteristics

Forty patients were enrolled and analyzed. Mean age: 41.2 ± 15.9 years; male 19 (47.5%), female 21 (52.5%). Distribution: urban 17 (42.5%), rural 14 (35.0%), semi-urban 9 (22.5%). Mean day of illness at admission: 4.9 days. NS1 positive: 28 (70%); IgM positive: 32 (80%); secondary dengue (IgG+): 17 (42.5%). Twenty patients each had normal and prolonged aPTT.

Primary Outcome: aPTT vs Bleeding and Severity

Seventeen of 40 patients (42.5%) had at least one bleeding manifestation; 4 had major bleeding. In the normal aPTT group, only 4/20 (20%) had any bleeding versus 13/20 (65%) in the prolonged group (RR=3.25; p=0.026). Major bleeding occurred in 1/20 (5%) vs 3/20 (15%) respectively (RR=3.00; p=0.048). Severe dengue was present in 4/20 (20%) normal vs 15/20 (75%) prolonged aPTT patients (RR=3.75; p=0.001). (Table 1, Figure 1, 2a, 2b).

Table 1. Association of aPTT with Outcomes (Primary Outcome)

Outcome Variable	Normal aPTT (n=20), n (%)	Prolonged aPTT (n=20), n (%)	p-value	RR (95% CI)
Any bleeding	4 (20.0)	13 (65.0)	0.026	3.25 (1.28–8.27)
Minor bleeding	4 (20.0)	12 (60.0)	0.019	3.00 (1.18–7.63)
Major bleeding	1 (5.0)	3 (15.0)	0.048	3.00 (0.34–26.3)
Severe dengue	4 (20.0)	15 (75.0)	0.001	3.75 (1.56–9.02)

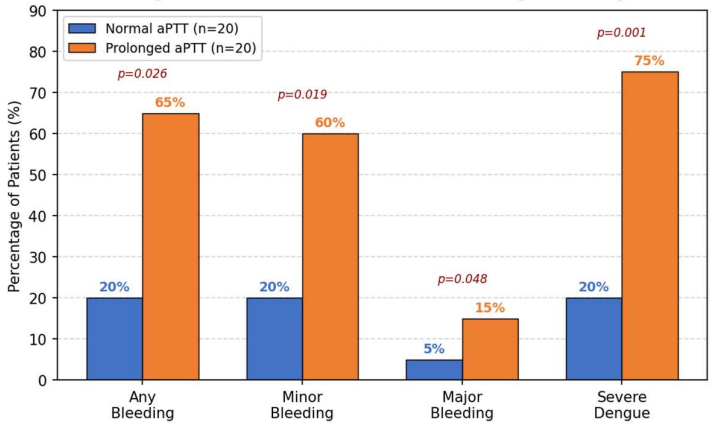

Figure 1: Proportion of patients with bleeding and severe dengue by aPTT group. p-values shown above bars

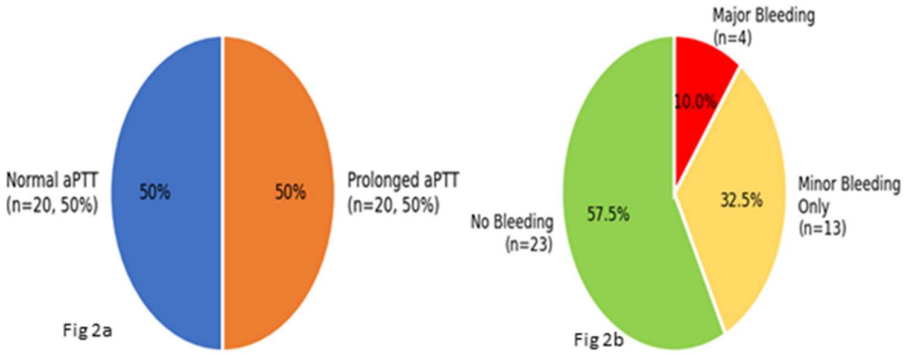

Figure (2a) aPTT group distribution; (2b) Bleeding category distribution among all 40 patients

Diagnostic Test Performance of aPTT

aPTT demonstrated an NPV of 95.0% for major bleeding – the study's key clinical finding. Sensitivity and specificity for major bleeding were 75.0% and 52.8% respectively. For severe dengue, sensitivity was 78.9%, specificity 76.2%, NPV 80.0%, and PPV 75.0% (Table 2 and Figure 3-4).

Table 2. Diagnostic Test Characteristics of aPTT

Measure	Major Bleeding	Minor Bleeding	Any Bleeding	Severe Dengue
Sensitivity (%)	75.0	75.0	76.5	78.9
Specificity (%)	52.8	50.0	65.2	76.2
PPV (%)	15.0	60.0	65.0	75.0
NPV (%)	95.0	62.5	77.3	80.0

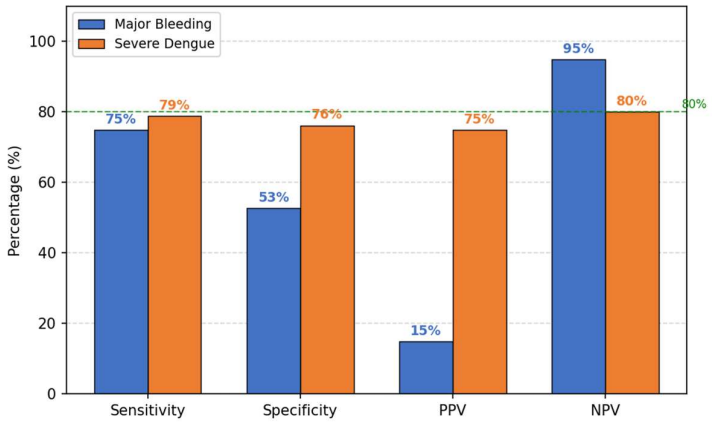

Figure 3: Diagnostic test characteristics (Sensitivity, Specificity, PPV, NPV) of aPTT for major bleeding and severe dengue. Green dashed line = 80% threshold

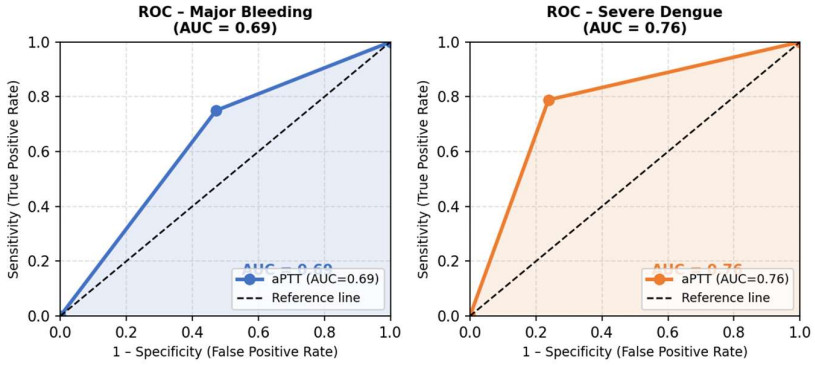

Figure 4: ROC curves for aPTT predicting major bleeding (AUC 0.69) and severe dengue (AUC 0.76)

Platelet Count and Outcomes

Platelet count was stratified into three categories. No statistically significant association was found between platelet category and bleeding manifestations (p=0.114 for any bleeding; p=0.822 for major bleeding). A statistically significant association with severe dengue was observed (p=0.045), though this was driven primarily by the 50,000–99,999/µL group. Results are shown in Table 3 and Figure 5.

Table 3. Platelet Count vs Bleeding and Severe Dengue

Outcome	<50,000 (n=15)	50,000–99,999 (n=15)	≥1,00,000 (n=10)	p-value
Any bleeding, n (%)	9 (60.0)	7 (46.7)	1 (10.0)	0.114
Major bleeding, n (%)	2 (13.3)	1 (6.7)	1 (10.0)	0.822
Severe dengue, n (%)	8 (53.3)	10 (66.7)	1 (10.0)	0.045

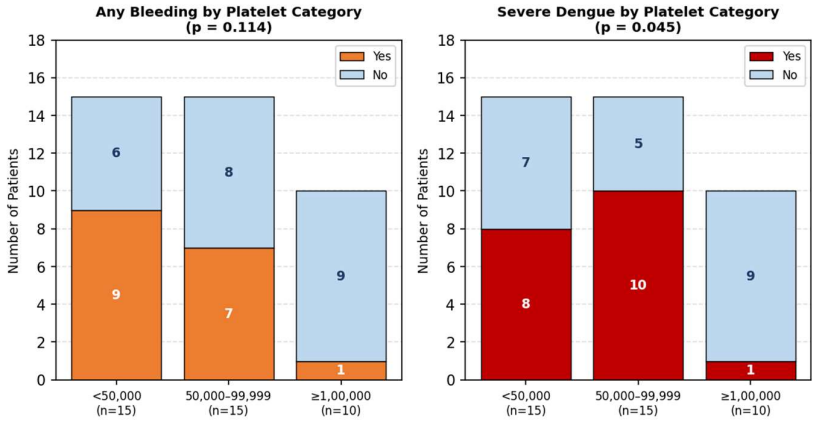

Figure 5: Stacked bar charts showing distribution of (a) any bleeding and (b) severe dengue across platelet count categories

DISCUSSION

This cross-sectional study had a statistically significant correlation between the severity of dengue in adult patients with both bleeding symptoms and extended aPTT at admission. An NPV of 95% for significant bleeding, which established aPTT as a trustworthy rule-out test at the bedside, was the study's most clinically significant discovery.

In the present study, 50% of patients exhibited prolonged aPTT, which is in close agreement with the pooled estimate of 44.9% published by Adane and Getawa (2021) in their comprehensive evaluation of 22 studies and the 40.9% reported by Thomas RS et al. (2024) from Christian Medical College, Vellore [6,5]. Confidence in the occurrence of intrinsic coagulopathy in dengue is strengthened by this stability across geographically different institutions.

The present study's relative risk for severe dengue (RR=3.75) and any bleeding with extended aPTT (RR=3.25) is directionally comparable with the RR values of 2.52–4.03 and 3.14 reported by Thomas RS et al., respectively [5]. The smaller research sample or variations in dengue serotype distribution and presentation time may be the cause of our study's somewhat higher RR for severe dengue.

Since a normal aPTT at admission consistently identifies dengue patients at low risk of major hemorrhage, the NPV of 95% for serious bleeding has direct clinical utility. This is especially helpful in settings with limited resources, such as district and teaching hospitals in South India, since it can direct admission decisions, monitoring intensity, and resource allocation. This mirrors the NPV of 93.1% reported by Thomas RS et al. and the high sensitivity rates (84–92%) for day-4 and day-5 aPTT reported by Kulasinghe et al. from Sri Lanka [5,7].

The proposed pathophysiological mechanism involves dengue-virus-induced IL-6 secretion downregulating Factor XII synthesis in the intrinsic coagulation pathway. Studies have also identified deficiencies of Factors VIII, IX, and XI in dengue patients, suggesting that coagulopathy extends beyond Factor XII alone and represents a broader intrinsic pathway failure. This explains why PT often remains normal in dengue – since the extrinsic pathway (Factor VII) is comparatively spared.

Platelet count showed no statistically significant correlation with bleeding manifestations (p=0.114 for any bleeding; p=0.822 for major bleeding). This replicates the findings of Jain et al. (2017), Hamsa et al. (2018), Lum et al. (2002), and Thomas RS et al. (2024). [8-10,5] The therapeutic implication is significant: prophylactic platelet transfusion in dengue patients with thrombocytopenia but no active bleeding may not prevent hemorrhage and could expose patients to transfusion-related risks.

Limitations of this study include modest sample size (n=40), single-center design, absence of factor assays (VIII, IX, XI, XII), no serial aPTT measurements, and non-assessment of fibrinogen, D-dimer, and ADAMTS-13. Future studies should incorporate these parameters and be conducted across multiple centers with larger cohorts.

CONCLUSION

Derangement of aPTT at admission is significantly and independently associated with both bleeding manifestations and severity of dengue in adult patients. With a negative predictive value of 95% for major bleeding, a normal aPTT reliably identifies patients at low risk of hemorrhage, making it a valuable rule-out screening tool in dengue management. Platelet count alone was not a reliable predictor of bleeding in this cohort. Routine aPTT estimation at admission should be incorporated into dengue management protocols to supplement conventional monitoring. Larger multicenter studies with serial aPTT measurements and factor assays are warranted to further characterize dengue-associated coagulopathy.

ACKNOWLEDGEMENTS

The authors acknowledge the Department of General Medicine, SVMCH & RC, Puducherry, for institutional support, the laboratory staff for assistance with sample processing and all patients who consented to participate in this study.

REFERENCES

1. Centers for Disease Control and Prevention. Dengue Virus Infections – Case Definition 2015. Available from: https://nndss.cdc.gov/conditions/dengue-virus-infections/case-definition/2015/. [Accessed 2024 Oct 15].

2. Mutheneni SR, Morse AP, Caminade C, Upadhyayula SM. Dengue burden in India: Recent trends and importance of climatic parameters. Emerg Microbes Infect. 2017;6(8):e70.

3. Kannan A, Narayanan K, Sasikumar S, Philipose J, Surendran S. Coagulopathy in dengue fever patients. Int J Res Med Sci. 2014;2:1070–2.

4. Kavitha R, Clarin JD. Study of coagulation profile in dengue fever. Natl J Lab Med. 2020;9(3):PO01–PO05.

5. Thomas RS, Lenin A, Sathyendra S, Hansdak SG, George T, Zachariah A, et al. Activated partial thromboplastin time (aPTT) as a screening test for predicting bleeding manifestations in adult patients with dengue infection – A diagnostic accuracy study. J Clin Infect Dis Soc. 2024;2:6–11.

6. Adane T, Getawa S. Coagulation abnormalities in dengue fever infection: A systematic review and meta-analysis. PLoS Negl Trop Dis. 2021;15:e0009666.

7. Kulasinghe S, Ediriweera R, Kumara P. Association of abnormal coagulation tests with dengue virus infection and their significance as early predictors of fluid leakage and bleeding. Sri Lanka J Child Health. 2016;45:184.

8. Jain S, Mittal A, Sharma SK, Upadhyay AD, Pandey RM, Sinha S, et al. Predictors of dengue-related mortality and disease severity in a tertiary care center in North India. Open Forum Infect Dis. 2017;4:ofx056

9. Hamsa BT, Srinivasa SV, Prabhakar K, Raveesha A, Manoj AG. Significance of APTT as early predictor of bleeding in comparison to thrombocytopenia in dengue virus infection. Int J Res Med Sci. 2018;7:67–70.

10. Lum LC, Goh AY, Chan PW, El-Amin AL, Lam SK. Risk factors for hemorrhage in severe dengue infections. J Pediatr. 2002;140:629–31.