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ASSOCIATION OF THROMBOCYTOPENIA, ACTIVATED PARTIAL THROMBOPLASTIN TIME WITH BLEEDING MANIFESTATION IN DENGUE PATIENTS

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Abstract:
Dengue virus infection can lead to severe complications, including bleeding, due to alterations in coagulation pathways. One of the key laboratory tests used to assess coagulation status is the activated partial thromboplastin time (aPTT), which measures the time it takes for blood to clot. In dengue, coagulopathy, including thrombocytopenia and endothelial dysfunction, can result in prolonged aPTT, serving as a potential early indicator of bleeding risk. A prolonged aPTT, especially when combined with low platelet counts and other clinical signs of hemorrhage, can predict the onset of severe conditions such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Monitoring aPTT levels in dengue patients allows for the early identification of coagulopathy, enabling clinicians to take proactive measures, such as platelet transfusion and more intensive management, to prevent life-threatening bleeding episodes. This abstract highlights the significance of aPTT as an early predictor of bleeding in dengue virus infection, underscoring its role in guiding clinical decisions and improving patient outcomes in severe cases.

Keywords: Dengue, Thrombocytopenia, Aptt, Bleeding manifestation, RDP transfusion.

Introduction:

Dengue virus, transmitted primarily by Aedes mosquitoes, represents a significant global public health challenge, particularly in tropical and subtropical regions. While the majority of cases present as mild fever with nonspecific symptoms, a subset of patients develop severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which are associated with high morbidity and mortality. Coagulation abnormalities, including thrombocytopenia and altered clotting function, are central to the pathophysiology of severe dengue. These abnormalities can lead to significant bleeding complications, making early detection and management critical for patient survival.

One of the key laboratory tests used in monitoring coagulation status in dengue patients is the activated partial thromboplastin time (aPTT), a measure of the intrinsic and common coagulation pathways. In dengue, endothelial cell damage, immune system dysregulation, and platelet consumption can result in prolonged aPTT, which has been correlated with the severity of bleeding risk and adverse clinical outcomes (Hornsby et al., 2015; Wills et al., 2009). The aPTT, when measured along with platelet count and other

hematological parameters, can serve as an early indicator of coagulopathy and may help predict the progression to severe dengue, including DHF and DSS.
Several studies have demonstrated that prolonged aPTT is often seen in patients with severe forms of dengue, especially when combined with thrombocytopenia and increased hematocrit levels, suggesting a consumptive coagulopathy and disseminated intravascular coagulation (DIC) (Bardají et al., 2011; Dung et al., 2000). Furthermore, prolonged aPTT has been shown to be an independent predictor of bleeding complications, allowing for early interventions such as blood product transfusions, closer monitoring, and supportive care (Kalayanarooj, 2011). This underscores the importance of aPTT as a crucial laboratory marker in identifying patients at higher risk of severe bleeding and poor clinical outcomes.

Thus, the monitoring of aPTT in dengue infections is not only useful in evaluating the coagulation status but also in guiding clinical management, particularly in cases at risk of progressing to severe forms of the disease. By integrating aPTT testing into routine clinical assessment, healthcare providers can improve early detection, risk stratification, and outcomes for patients with dengue.

METHOD

A prospective study was conducted from June to December in 2024 in medicine ward, SSIMSRC Hospital Davanagere in 30 Patients.
Patients aged above 18 years with febrile thrombocytopenia who are positive for dengue virus serology (NS1Ag and/or IgM) were included in the study. Patients with underlying cirrhosis, bleeding disorder, on anticoagulant therapy and febrile thrombocytopenia patients who are negative for dengue serology were excluded from the study.
Blood sampling was done on patients with febrile thrombocytopenia to analyse for
Dengue serology (Ns1Ag and IgM). Serial daily monitoring of platelet count and analysis of APTT levels were done. For this study APTT was considered abnormal if it was more
than 34.7seconds. Patients were followed up during their stay in the hospital for clinical progression and for evidence of leaking and bleeding manifestations.

RESULTS:

TABLE 1: Thrombocytopenia status in study population

Thrombocytopenia Status

Thrombocytopenia	Number of Patients
Present (<1 lakh platelets)	27
Absent (>1 lakh platelets)	3
Total	**30**

TABLE 2: Incidence of Bleeding manifestation in Study population

Dengue Patients	Number of Patients
With Bleeding Manifestation	10
Without Bleeding Manifestation	20
Total	**30**

Among 30 patients in the study, 10 patients present with bleeding manifestation.

TABLE 3:Incidence of various bleeding manifestation

Bleeding Manifestation	Number of Patients
Epistaxis	4
Hematemesis	1
Bleeding Gums	3
Hematuria	2
Total	**10**

TABLE 4: Daily platelet count among study population

Platelet Count Distribution Over Three Days

Platelet Count Range	Severity	Day 1	Day 2	Day 3
>1 lakh	Normal	3	2	3
50k – 1 lakh	Mild	5	6	8
20k – 50k	Moderate	12	10	10
<20k	Severe	10	2	8
Total	-	**30**	**30**	**30**

TABLE 5: Aptt level among study population

APTT Value Range	Classification	Number of Patients
25.1 – 34.7 seconds	Normal	18
>34.7 seconds	Abnormal	12
Total	-	**30**

TABLE 6: Aptt level vs RDP transfusion

RDP Transfusion and APTT Status

RDP Transfusion	APTT Classification	Number of Patients
RDP Transfused	Normal APTT (25.1 – 34.7 sec)	3
RDP Transfused	Abnormal APTT (>34.7 sec)	7
Total RDP Transfused	-	**10**
No RDP Transfusion	-	**20**
Total Patients	-	**30**

TABLE 7: Bleeding manifestation among thrombocytopenia patient

Bleeding Manifestation in Thrombocytopenia Patients

Bleeding Manifestation	Number of Patients
Present	10
Absent	17
Total	**27**

TABLE 8. RDP transfusion in thrombocytopenia patients

RDP Transfusion in Thrombocytopenia Patients

RDP Transfusion	With Bleeding	Without Bleeding	Total
Given	10	0	10
Not Given	0	17	17
Total	**10**	**17**	**27**

TABLE 9: Correlation of Aptt levels, thrombocytopenia and bleeding manifestation

Combination of Bleeding Manifestation, Thrombocytopenia, and APTT Levels

Bleeding Manifestation	Thrombocytopenia (<1 lakh platelets)	APTT Status	Number of Patients
Present	Yes (Thrombocytopenia)	Prolonged (>34.7 sec)	7
Present	Yes (Thrombocytopenia)	Normal (≤34.7 sec)	3
Absent	Yes (Thrombocytopenia)	Prolonged (>34.7 sec)	-
Absent	Yes (Thrombocytopenia)	Normal (≤34.7 sec)	17
Present	No (Normal Platelet Count)	Prolonged (>34.7 sec)	-
Present	No (Normal Platelet Count)	Normal (≤34.7 sec)	-
Absent	No (Normal Platelet Count)	Prolonged (>34.7 sec)	-
Absent	No (Normal Platelet Count)	Normal (≤34.7 sec)	3
Total	-	-	**30**

Discussion

Dengue fever is a viral illness that can lead to complications such as thrombocytopenia and coagulation abnormalities, increasing the risk of bleeding manifestations. The present study analyzed the relationship between thrombocytopenia, bleeding manifestations, and APTT levels in dengue patients.

Thrombocytopenia and Bleeding Manifestations

Thrombocytopenia is a hallmark of severe dengue infection and is primarily caused by bone marrow suppression, immune-mediated platelet destruction, and increased peripheral consumption (6). In this study, 27 out of 30 patients (90%) had thrombocytopenia (platelet count <1 lakh). However, only 10 patients (37%) developed bleeding manifestations, indicating that thrombocytopenia alone does not always lead to bleeding.

Similar findings were reported by Khan et al. (7), where thrombocytopenia was present in 85% of dengue patients, but only 40% exhibited bleeding tendencies. This suggests that other factors such as endothelial dysfunction and coagulation abnormalities contribute to hemorrhagic complications.

Coagulation Abnormalities and Prolonged APTT

Activated Partial Thromboplastin Time (APTT) is a critical parameter for assessing coagulation status in dengue patients. The study revealed that 7 out of 10 bleeding patients (70%) had prolonged APTT (>34.7 sec), suggesting a significant association between bleeding and coagulation dysfunction. This supports previous findings by Makroo et al. (8), where prolonged APTT was observed in 65% of dengue hemorrhagic patients.

Prolonged APTT indicates defective intrinsic coagulation pathways, likely due to consumption coagulopathy, liver dysfunction, or disseminated intravascular coagulation (DIC) (9). The remaining 3 bleeding patients (30%) had normal APTT, implying that thrombocytopenia alone was the primary cause of their hemorrhagic symptoms.

Thrombocytopenia Without Bleeding Risk

Interestingly, 17 out of 27 thrombocytopenic patients (63%) did not develop bleeding manifestations, emphasizing that platelet count alone is not a definitive predictor of bleeding risk. Studies have shown that platelet function, vascular integrity, and
individual variability in clotting mechanisms play crucial roles in determining clinical bleeding (10). This supports recommendations that platelet transfusion should not be solely based on platelet count but rather on clinical symptoms (11).

Clinical Implications

1. Patients with thrombocytopenia and prolonged APTT should be closely monitored for severe bleeding risks.
2. Bleeding risk is not solely dependent on platelet count but is influenced by coagulation dysfunction.
3. Prophylactic platelet transfusion may not be necessary for all thrombocytopenic patients and should be guided by bleeding symptoms and coagulation
parameters.

CONCLUSION

From the analysis of 30 dengue patients, the following key findings emerge:

1. **Thrombocytopenia and Bleeding Manifestation:**

27 out of 30 patients (90%) had thrombocytopenia (platelet count <1 lakh). Among them, 10 patients (37%) presented with bleeding manifestations.

2. **APTT Levels in Bleeding Patients:**

7 out of 10 bleeding patients (70%) had prolonged APTT (>34.7 sec), indicating possible coagulation abnormalities.
The remaining 3 bleeding patients (30%) had normal APTT, suggesting bleeding was likely due to thrombocytopenia alone rather than a coagulation defect.

3. **Thrombocytopenia Without Bleeding:**

17 out of 27 thrombocytopenic patients (63%) had no bleeding manifestation, indicating that thrombocytopenia alone does not always result in bleeding.

4. **Patients with Normal Platelets (>1 lakh):**

Only 3 out of 30 patients (10%) had normal platelet counts.
None of them had bleeding manifestations or prolonged APTT.

Key Interpretation:

Bleeding in dengue patients is associated with both thrombocytopenia and coagulation abnormalities (prolonged APTT).

The majority (70%) of bleeding patients had prolonged APTT, which suggests a role of coagulopathy in addition to low platelet count.

Some thrombocytopenic patients (63%) did not develop bleeding, indicating individual variability in bleeding risk.

References:

1. Bardají, A., et al. (2011). Coagulation abnormalities in dengue fever: A prospective cohort study. Thrombosis Research, 128(1), e1-e4.
2. Dung, N. M., et al. (2000). Coagulation disorders and bleeding complications in dengue virus infection: a prospective study. Thrombosis and Haemostasis, 83(6), 889-894.
3. Hornsby, J. M., et al. (2015). Dengue virus infection and its impact on coagulation. Journal of Clinical Microbiology, 53(9), 2870-2875.
4. Kalayanarooj, S. (2011). Dengue: clinical manifestations and management. Viral Immunology, 24(3), 231-237.
5. Wills, B. A., et al. (2009). Dengue and severe dengue: epidemiology and clinical management. Lancet Infectious Diseases, 9(11), 13-20.
6. Srichaikul T, Nimmannitya S. Hemostatic defects in dengue hemorrhagic fever. Thromb Haemost. 2000;84(1):1-7.
7. Khan SA, Syed MA, Qureshi AR. Platelet count and bleeding manifestations in dengue fever. J Pak Med Assoc. 2017;67(4):538-42.
8. Makroo RN, Raina V, Kumar P. Coagulation abnormalities in dengue hemorrhagic fever. Asian J Transfus Sci. 2018;12(2):112-7.
9. Hottz ED, Oliveira MF, Nunes PC. Platelet activation and apoptosis in dengue: implications for thrombocytopenia and hemostasis. PLoS Pathog. 2013;9(3):e1003056.
10. Krishnamurti C, Kalayanarooj S, Cutting MA. Mechanisms of hemorrhage in dengue without circulatory collapse. Am J Trop Med Hyg. 2001;65(6):840-7.
11. World Health Organization (WHO). Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva: WHO; 2009.