

TO EVALUATE THE PROPENSITY FOR BLEEDING IN INDIVIDUALS DIAGNOSED WITH DENGUE FEVER

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Abstract

Background: Aim: To evaluate the propensity for bleeding in individuals diagnosed with dengue fever. **Materials and Methods:** A cohort study was done on a sample of 120 patients who were diagnosed with Dengue. All patients diagnosed with platelet abnormalities such as ITP, drug-induced disorders, cirrhosis, DIC, etc., were not included in this research. Every hospitalised patient had preliminary diagnostic testing to confirm the diagnosis, including a complete blood count and platelet count. The patients were monitored for the occurrence of any bleeding symptoms, including rash/petechiae, bleeding gums, conjunctival suffusion, epistaxis, hematuria, melena, and rectal bleeding. **Results:** Out of the entire 120 patients, a bleeding incidence was seen in just 40 individuals, accounting for 33.33% of the study group. Table 2 shows that 66.67% of the 120 patients, specifically 80 individuals, did not exhibit any signs of bleeding. The analysis of platelet count values revealed that 35 patients (29.17%) exhibited severe thrombocytopenia, 55 patients (45.83%) displayed moderate thrombocytopenia, and 30 patients (25%) demonstrated mild or normal platelet count. There were 40 individuals who had bleeding symptoms, either as a single symptom or in combination. 38 patients (95%) exhibited a rash or petechiae; 2 patients (5%) experienced hematuria, 3 patients (7.5%) had melena, 3 patients (7.5%) had PR bleeding, 11 patients (27.5%) had gum bleeding, 9 patients (22.5%) had conjunctival suffusion, and 5 patients (12.5%) had epistaxis. **Conclusions:** Dengue is a prevalent cause of febrile illness that often manifests with thrombocytopenia in the majority of patients. Thrombocytopenia is a significant factor in the death of patients who experience bleeding symptoms.

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INTRODUCTION

Dengue fever is a viral illness transmitted by mosquitoes. It is caused by the dengue virus (DENV), which is a kind of RNA virus that belongs to the Flavivirus genus. There are four distinct types of dengue virus, namely DENV 1-4, which are mostly transmitted to humans by the *Aedes Aegypti* mosquito. These mosquitoes often reproduce in stagnant water, such as water that has accumulated in containers, water-based air coolers, and tyre dumps. Dengue fever often experiences an epidemic surge during the post-monsoon season in tropical and subtropical countries worldwide. Around 50-100 million individuals worldwide are afflicted with the dengue virus, with around 50,000 cases progressing to dengue hemorrhagic fever. Among them, 2000 individuals die each year as a result of its consequences. The mortality rate for individuals with treated dengue hemorrhagic fever or dengue shock syndrome is 1%, but it rises to 20% if left untreated.^[2]

Dengue is prevalent across India and is a significant public health issue. The National Vector Borne Diseases Control Programme has documented an average of 20,474 cases of dengue and 132 fatalities year from 2006 to 2012. Regional comparisons indicate that the official figures only capture a tiny portion of the complete effect of the illness. The causative agents of dengue fever are all four dengue serotypes, which are classified under the genus flaviviruses in the Flaviviridae family.^[3] The dengue virus is a member of the Flaviviridae family and consists of four serotypes, known as DENV-1, DENV-2, DENV-3, and DENV-4.^[4] The Dengue virus is an RNA virus with a positive strand that is enclosed in a protective capsule. It consists of three genes that encode the structural proteins: the nucleocapsid or core protein, the membrane-associated (M) protein, and the enveloped glycoprotein. Additionally, it has seven non-structural proteins. There is a temporary cross protection across the four kinds, which diminishes

and vanishes over the course of many months after infection.^[4] Dengue fever is generally a self-limiting illness, with symptoms typically appearing after an incubation period of 8-10 days and lasting for around 2-7 days. The condition might be asymptomatic or exhibit a wide array of clinical signs, ranging from moderate fever to a potentially fatal shock syndrome.^[4] Additional symptoms that may be present in individuals with dengue include fever, headache, discomfort behind the eyes, muscle and joint pain, nausea, vomiting, overall weakness, fatigue, sore throat, and different forms of bleeding. The many hemorrhagic symptoms found in dengue fever include rash, petechiae, gum bleeding, conjunctival suffusion, hematuria, PR bleeding, melena, and others. These symptoms may be attributed to a reduction in platelet count during dengue fever. The dengue virus has been extracted from many types of white blood cells, including polymorphonuclear leukocytes, monocyte/macrophages, and dendritic cells. Furthermore, it has been identified in megakaryocyte progenitors and platelets that are present in the bloodstream. These results indicate that the dengue virus may cause a decrease in platelet count by directly interacting with megakaryocytes and platelets.^[5] Studies have shown that the dengue virus may decrease the number of platelets in the bloodstream, regardless of whether the virus attaches to or enters platelets or their early forms. Therefore, it is likely that two processes contribute to the development of thrombocytopenia in dengue: hindered production of platelets and destruction of platelets in the peripheral regions.^[5] The diagnosis of dengue virus infection may be confirmed via laboratory testing, either by directly detecting viral components in the patient's serum or indirectly through serology. The detection of viral nucleic acid or viral antigen has a high level of specificity, but it is labor-intensive and expensive. On the other hand, serology has a lower level of specificity, but it is less expensive and more readily available. Thrombocytopenia may be linked to several illnesses, with risks that can vary from severe bleeding or blood clotting to no risk at all. Thrombocytopenia is characterised by a platelet count that falls below the lower threshold of the normal range, namely less than 150,000 platelets per microliter (μl).^[7] Megakaryocytes are the specific kind of blood cell responsible for the production of platelets. James Homer Wright originally established this link in 1906. He discovered that circulating platelets and a large bone marrow cell, today referred to as a megakaryocyte, had similar staining qualities when exposed to a modified Romanowsky stain.^[8] A single megakaryocyte generates a range of 1000 to 3000 platelets.^[8,9] Thrombopoietin has significant influence on almost every stage of megakaryocyte development and maturation, and it is synthesised by the Liver. An inverse correlation exists between the standard platelet count and the average platelet volume, leading to a rather consistent amount of

platelets in circulation. The body safeguards the overall mass of platelets, rather than the count of individual platelets. Roughly 33% of the overall platelet mass is typically stored in a splenic pool that may be readily exchanged. Platelets have a typical lifespan of 7-10 days as they move through the bloodstream.

Hemostasis relies on a sufficient quantity of operational platelets, together with an intact coagulation (clotting factor) system.

Degree of Thrombocytopenia: Mild: platelet count of 100,000 to 150,000/ μl , **Moderate:** platelet count of 50,000 to <1,00,000/ μl and **Severe:** platelet count of <50,000/ μl . Patients who are actively bleeding and have thrombocytopenia should get an urgent platelet transfusion to maintain platelet counts over 50,000/ μl in most bleeding conditions, including disseminated intravascular coagulation (DIC). If there is bleeding in the central nervous system, the platelet counts should be kept above 1,00,000/ μl . Transfusion used as a prophylactic measure against uncontrolled bleeding. Prophylactic platelet transfusion is used to avoid spontaneous bleeding in a majority of patients who have platelet counts below 10,000/ μl owing to bone marrow suppression. However, for patients who are feverish or septic, higher thresholds (specifically, 20,000 to 30,000/ μl) are used.

MATERIALS AND METHODS

A cohort study was done on a sample of 120 patients who were diagnosed with Dengue and were hospitalised to the Department of General Medicine. This research included only individuals who were diagnosed with dengue fever and were aged 18 years or older. All patients diagnosed with platelet abnormalities such as ITP, drug-induced disorders, cirrhosis, DIC, etc., were not included in this research. Every hospitalised patient had preliminary diagnostic testing to confirm the diagnosis, including a complete blood count and platelet count. The patients were monitored for the occurrence of any bleeding symptoms, including rash/petechiae, bleeding gums, conjunctival suffusion, epistaxis, hematuria, melena, and rectal bleeding. The observations were systematically observed and recorded, including the platelet count, and then subjected to statistical analysis.

RESULTS

During this research period, we monitored 120 patients who were diagnosed with dengue fever and met the study criteria. The research observed a majority of men, with 75 male patients (62.5%), while the female patients accounted for 45 (37.5%) out of a total of 120 patients. The male-to-female ratio was 1.36:1, as seen in Table 1. The largest proportion of patients, including 33.33%, fell within the age range of 25-35 years. This was followed by 19.17% of patients who were between 45-55 years

old. Patients aged 35-45 years accounted for 16.67% of the total, while those under 25 years made up 15%. The age group of 55-65 years had 10.83% of patients, and the lowest frequency was seen in patients beyond 65 years, with just 5%. Out of the entire 120 patients, a bleeding incidence was seen in just 40 individuals, accounting for 33.33% of the study group. Table 2 shows that 66.67% of the 120 patients, specifically 80 individuals, did not exhibit any signs of bleeding. The analysis of platelet count values revealed that 35 patients (29.17%) exhibited severe thrombocytopenia, 55 patients (45.83%) displayed moderate thrombocytopenia, and 30 patients (25%) demonstrated mild or normal platelet count, as shown in Table 3.

There were 40 individuals who had bleeding symptoms, either as a single symptom or in combination. 38 patients (95%) exhibited a rash or petechiae; 2 patients (5%) experienced hematuria, 3 patients (7.5%) had malena, 3 patients (7.5%) had PR bleeding, 11 patients (27.5%) had gum bleeding, 9 patients (22.5%) had conjunctival suffusion, and 5

patients (12.5%) had epistaxis. The analysis of platelet count values revealed that 30 patients (25%) with severe thrombocytopenia and 8 patients (6.67%) with moderate thrombocytopenia had rash/petechiae, indicating bleeding tendencies. In the same vein, a mere 2 individuals (1.67%) had hematuria in the presence of severe thrombocytopenia, whereas 3 patients (2.5%) experienced malena with severe thrombocytopenia. Three patients (2.5%) had gastrointestinal bleeding due to severe thrombocytopenia. Ten patients (8.33%) experienced gum bleeding due to severe thrombocytopenia, while one patient (0.83%) experienced gum bleeding due to moderate thrombocytopenia. Out of the total number of patients, 8 individuals (6.67%) had conjunctival suffusion in cases of severe thrombocytopenia, whereas 1 patient (0.83%) had conjunctival suffusion in cases of moderate thrombocytopenia. Out of the total number of patients, 5 individuals (4.17%) had nosebleeds due to a condition of low blood platelet count. No signs of bleeding were found in cases with mild thrombocytopenia.

Table 1: Age and gender of the participants

Age	Number of Patients=120	Percentage
Below 25	18	15
25-35	40	33.33
35-45	20	16.67
45-55	23	19.17
55-65	13	10.83
Above 65	6	5
Mean age	43.25±3.68	
Gender		
Males	75	62.5
Females	45	37.5

Table 2: Bleeding incidence

	Number of Patients=120	Percentage
Bleeding manifestations	40	33.33
No Bleeding manifestations	80	66.67

Table 3: Platelet count

Platelet Count (µl)	Number of Patients=120	Percentage
≥1Lakh (Mild)	30	25
50 Thousand to 1lakh (Moderate)	55	45.83
<50 Thousand (Severe)	35	29.17

Table 4: Bleeding tendencies

Bleeding tendencies	Number of Patients=40	Percentage
Rash/Petechiae	38	95
Hematuria	2	5
Malena	3	7.5
PR Bleed	3	7.5
Gum Bleed	11	27.5
Conjunctiva suffusion	9	22.5
Epistaxis	5	12.5

Table 5: Platelet count relation with bleeding tendencies

Bleeding Tendencies	<50,000/µl		50,000/µl to 1Lakh/µl		>1Lakh/µl	
	Number of Patients	Percentage	Number of Patients	Percentage	Number of Patients	Percentage
Rash/Petechiae	30	25	8	6.67		
Hematuria	2	1.67				
Malena	3	2.5				
PR Bleed	3	2.5				

Gum Bleed	10	8.33	1	0.83		
Conjunctival suffusion	8	6.67	1	0.83		
Epistaxis	5	4.17				

DISCUSSION

The wide spectrum of symptoms associated with dengue poses a challenge for physicians in accurately diagnosing the disease. Some folks are asymptomatic. Infants and toddlers who are infected often exhibit mild skin rashes and have fever, without any other symptoms. Older children and adults may also experience these mild symptoms, or they may exhibit typical dengue symptoms such as prolonged high fever lasting 2-7 days, intense muscle and bone pain, discomfort in the eyes, fatigue, headaches, minor bleeding, skin rashes, and feelings of nausea and vomiting. Dengue sickness has a bimodal fever response. During the first phase of the sickness, the patient has an elevated body temperature, which later decreases and then increases once again. Additional indications of dengue fever include reduced leukocyte count and thrombocytopenia. In individuals with dengue fever, skin haemorrhages may manifest as red or purple regions on the body. The recuperation period for dengue fever may last for several weeks, during which patients may have symptoms of weariness and depression.^[11-13]

Dengue is a prevalent illness that occurs often throughout the monsoon and winter seasons. Additionally, it is a prevalent factor in fever cases linked to thrombocytopenia. Thrombocytopenia is commonly found in varying degrees and often manifests with a severe form (platelet count < 50,000/ μ l). This severe form is associated with bleeding symptoms and may require platelet transfusion, either as a treatment or as a preventive measure. Platelets may be transfused for therapeutic purposes, such as treating acute bleeding or preparing for an invasive operation that may induce bleeding, or for preventive purposes, to avoid spontaneous bleeding.^[14]

After receiving a platelet transfusion, the number of platelets in the blood should increase, reaching its highest point within 10 minutes to one hour, and then gradually decreasing over a period of 72 hours. Typically, the transfusion of six units of pooled platelets or one apheresis unit is expected to raise the platelet count by about 30,000/ μ l in an average-sized adult.^[15] Platelet transfusion is the only effective method to quickly raise the platelet count in a bleeding patient.^[16] Therefore, it is recommended to provide platelet transfusion to patients with low platelet count and bleeding symptoms in order to reduce and avoid bleeding presentations, ultimately leading to a drop in death rate among individuals with dengue fever.

In the study conducted by Radhika B.V. et al,^[17] and Jacob K. Jacob,^[18] it was found that dengue is the main cause of thrombocytopenia in patients with fever. Our study also showed a higher number of male patients, which aligns with the findings of

Radhika B.V. et al,^[17] and Jacob K. Jacob.^[18] The manifestation was most prevalent among individuals aged 25-35, with the highest incidence occurring between the ages of 18 and 50. This finding aligns with a study conducted by Radhika B.V. et al,^[17] which reported that the majority of patients (92.5%) fell within the 18-40 age group. In contrast, a study by Jacob K. Jacob,^[18] found that the 40-49 age group was most affected (21.95%), followed by the 20-29 age group (21.14%). Our investigation revealed that the majority of patients had a moderate degree of thrombocytopenia, which aligns with the findings of previous studies done by Radhika B.V. et al,^[17] and Jacob K. Jacob.^[18] Out of the 120 patients included in our research, 40 of them, accounting for 33.33% of the total, had bleeding symptoms. Our investigation revealed that a significant proportion of patients had cutaneous bleeding, namely in the form of rash or petechiae. This finding aligns with the research conducted by Radhika B.V. et al,^[17]

CONCLUSION

Dengue is a prevalent cause of febrile illness that often manifests with thrombocytopenia in the majority of patients. Thrombocytopenia is a significant factor in the death of patients who experience bleeding symptoms. These symptoms act as a warning sign during clinical examination and prompt the evaluation of platelet count at regular intervals. They also assist in determining the necessity of platelet transfusion. Administering platelet transfusion promptly to these individuals can effectively mitigate bleeding symptoms and maintain platelet count within acceptable levels. This intervention will facilitate the management of individuals afflicted with dengue and concurrently contribute to the reduction of fatality rates.

REFERENCES

1. World Health Organization. Dengue and severe dengue; 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/dengue-andsevere-dengue>. [accessed on: Mar 17 2023].
2. Shastri PS, Taneja S. Dengue and other viral hemorrhagic fevers. *Indian J Crit Care Med.* 2021;25; Suppl 2: S130-3. doi: 10.5005/jp-journals-10071-23814, PMID 34345126.
3. Ganeshkumar P, Murhekar MV, Poornima V, Saravanakumar V, Sukumaran K, Anandaselvasankar A, et al. Dengue infection in India: A systematic review and meta-analysis. *PLOS Negl Trop Dis.* 2018;12(7): e0006618. doi: 10.1371/journal.pntd.0006618, PMID 30011275.
4. Pawar A, Chafekar N. Clinical study of diagnosed cases of dengue fever in tertiary Care Hospital in North Maharashtra. *MVP J Med Sci.* 2018;5(1):58-63. doi: 10.18311/mvpjms/2018/v5/i1/11018.
5. Wilder-Smith A, Ooi EE, Horstick O, Wills B. Dengue. *Lancet.* 2019;393(10169):350-63. doi: 10.1016/S0140-6736(18)32560-1, PMID 30696575.
6. Scheres J, Kuszewski K. The ten threats to global health in 2018 and 2019. A welcome and informative communication

- of WHO to everybody. *OZ*. 2019;17(1):2-8. doi: 10.4467/20842627OZ.19.001.11297.
7. Javed S, Singh P, Paliwal SK. Correlation of severity of dengue with serum aminotransferase levels. *Int J Adv Med*. 2021;8(3):415-9. doi: 10.18203/2349-3933.ijam20210599.
 8. Khan KU, Khan MI, Uddin A, Imran M, Khan MS, Khalid R et al. Frequency of Bleeding Diathesis amongst patients presenting with dengue fever in Tertiary Care Hospital. *PJMHS* 2021.3915-3917;15(12):3915-7. doi: 10.53350/pjmhs2115123915.
 9. Raza MA, Khan MA, Ejaz K, Haider MA, Rasheed F. A case of dengue fever with hemorrhagic manifestations. *Cureus*. 2020 June 12;12(6): e8581. doi: 10.7759/cureus.8581, PMID 32670716, PMCID PMC7358921.
 10. Logia P, Selvam V, Parasuraman V, Renuka MK, Rajagopalan RE. Predictors of clinically significant bleeding in thrombocytopenic dengue patients admitted to Intensive Care Unit: A retrospective Study. *Indian J Crit Care Med*. 2023;27(12):888-94. doi: 10.5005/jp-journals-10071-24574, PMID 38074960.
 11. Sureshkumar VK, Vijayan D, Kunhu S, Mohamed Z, Thomas S, Raman M. Thromboelastographic analysis of hemostatic abnormalities in dengue patients admitted in a multidisciplinary intensive care unit: A cross-sectional study. *Indian J Crit Care Med*. 2018;22(4):238-42. doi: 10.4103/ijccm.IJCCM_486_17, PMID 29743762.
 12. Adane T, Getawa S. Coagulation abnormalities in dengue fever infection: A systematic review and meta-analysis. *PLOS Negl Trop Dis*. 2021;15(8): e0009666. doi: 10.1371/journal.pntd.0009666. PMID 34407078.
 13. Lee IK, Liu JW, Yang KD. Fatal dengue hemorrhagic fever in adults: emphasizing the evolutionary pre-fatal clinical and laboratory manifestations. *PLOS Negl Trop Dis*. 2012;6(2): e1532. doi: 10.1371/journal.pntd.0001532, PMID 22363829.
 14. Lee VJ, Lye DCB, Sun Y, Fernandez G, Ong A, Leo YS. Predictive value of simple clinical and laboratory variables for dengue hemorrhagic fever in adults. *J Clin Virol*. 2008;42(1):34-9. doi: 10.1016/j.jcv.2007.12.017, PMID 18282738.
 15. Laoprasopwattana K, Binsaii J, Pruekprasert P, Geater A. Prothrombin time prolongation was the most important indicator of severe bleeding in children with severe dengue viral infection. *J Trop Pediatr*. 2017;63(4):314-20. doi: 10.1093/tropej/fmw097, PMID 28177091.
 16. Radhika BV, Sooraj CS, Kamath V. A study of febrile thrombocytopenia *International Journal of Contemporary Medical Research*. 2019;6(9):1.
 17. Jacob JK, Ranjith PS, Aswathyraj S, Asaraf BK, Praveen GS, Shiji K. Haemorrhagic Tendencies in Patients Presenting with Fever and thrombocytopenia in a hospital setting – A Cross Sectional Study *JMSCR*. 2017;5(10):29325-31.