ORIGINAL ARTICLE

Effect of papaya leaf extract on thrombocytopenia in children with dengue fever at a tertiary care center in Karachi

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ABSTRACT

Background: Dengue fever causes thrombocytopenia in children and may lead to serious complications. This study assessed the efficacy of Carica papaya leaf extract in improving platelet counts among pediatric patients with dengue-associated thrombocytopenia.

Material and Methods: A randomized controlled trial was conducted at the Pediatric Department, Dr. Ziauddin Hospital, Karachi (1st June to 30th August 2025). 107 children aged 2–12 years with dengue associated thrombocytopenia were enrolled and randomized into intervention group (n = 55), receiving Carica papaya leaf extract syrup plus standard therapy, and a control group (n = 52), receiving standard therapy only. Platelet counts were recorded on Day 1 and Day 3. Secondary outcomes included hemoglobin, WBC count, packed cell volume, platelet transfusion requirement, and PICU admissions. Statistical analysis was performed using SPSS version 20 with $p < 0.05$ considered significant.

Results: Among 107 pediatric dengue patients (55 intervention, 52 control), baseline platelet counts were similar (median 109 ×10⁹/L, IQR 88). By Day 3, counts increased slightly in both groups (median 115 ×10⁹/L, IQR 81) with no significant difference ($p = 0.968$). PICU admissions were higher in the intervention group (16.4% vs. 3.8%), and more patients required platelet transfusions (3 vs. 1). Overall, *Carica papaya* leaf extract did not significantly improve platelet counts or clinical outcomes.

Conclusion: Short-term use of Carica papaya leaf extract did not significantly improve platelet counts or clinical outcomes in pediatric dengue patients. Larger, long-term studies are needed to confirm its efficacy.

Keywords: *Carica papaya* leaf extract, Dengue, Randomized controlled trial, Thrombocytopenia

BACKGROUND

Dengue fever is an outstanding example of one of the fastest-spreading arboviral mosquito-transmitted diseases worldwide, posing an emerging public health threat in tropical and subtropical areas including Pakistan. The dengue virus (DENV) that causes this disease has four serotypes (DENV-1 to DENV-4) and is primarily spread to humans by the virus manifests with a wide variety of clinical manifestations from mild febrile illness, severe dengue hemorrhagic fever to dengue shock syndrome, thrombocytopenia being a common hematological sign among patients.[1,2] Dengue incidence globally has sharply increased in recent decades. World Health Organization (WHO) reports that 129 countries with nearly 3.9 billion population are threatened with dengue, and about 70% of the disease's burden is in Asia.[3] However, since 1982 dengue fever in Pakistan has become endemic. Seasonal peaks in dengue activity is usually witnessed after the monsoon following the turn of events in urban settings such as Karachi since the levels of humidity is increased and the drainage systems are not sufficient enough thus creating room for mosquitoes procreation.[4,5] The thrombocytopenia in those who have dengue is a result of a bone marrow suppression with the destruction of platelets by the immune system, and increased peripheral sequestration of platelets. Severe thrombocytopenia can cause a bleeding problem which should be addressed immediately by healthcare providers.[6,7] Currently, the keyway of dealing with dengue is supportive care. On the other hand, there is an appearance of Carica papaya leaf extract (CPLE) as a promising therapy given the fact that it enhances platelet counts and reduces levels of bleeding.[8] Papaya or Carica papaya is a tropical plant found in the family of Salicaceae. The extract from the leaf is distinguished by flavonoids, glycosides, and alkaloids content which has

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shown anti-inflammatory, antiviral and antioxidant properties. Numerous experimental and clinical studies have reported that CPLE stimulates thrombopoiesis and promotes platelet count recovery in dengue fever patients.[9,10] Recent literature has continued to explore the potential role of Carica papaya leaf extract in improving dengue-associated thrombocytopenia, particularly in resource-limited settings.[16,17,18] Research conducted in India has shown that CPLE significantly increased platelet count among pediatric dengue patients when combined with standard therapy [11]. Similar findings have been reported in studies from investigations in Malaysia, Sri Lanka, and Bangladesh.[12-14] Despite supportive international evidence, there is limited data regarding the use of CPLE in Pakistani children with dengue. Given the significant burden of dengue in Pakistan and the limited treatment options available, evaluating the effects of CPLE in the local populations is both relevant and essesntial.[15]

MATERIAL AND METHODS

A randomized controlled trial was carried out during three months at Department of Pediatrics, Dr. Ziauddin Hospital, Clifton campus, Karachi. The intent was to establish whether Carica papaya leaf extract could improve the platelet levels in children with dengue fever diagnosed with low platelet levels. Overall, a total of 107 patients aged between 2-12 years old who met the inclusion and exclusion criteria were enrolled in the study. The sample size was calculated using OpenEpi software based on the mean difference and standard deviation between platelet in the intervention and placebo groups, obtained from the pilot data. The calculated sample size was 5 individuals in each group. To increase reliability and validity of our study we enrolled 107 participants (55 in intervention, 52 in control group) in our study. Participants were diagnosed with dengue fever based on positive NS1 antigen results and/or IgM ELISA results. Patients with platelet counts less than 150,000/µL were enrolled in the study. Patients were excluded if parental consent was refused, they were hypersensitive to papaya, any of its parts, or they had a bleeding disorder. Selection was made by probability random sampling using the lottery method. The participating children were randomly allocated to one of two groups after having written informed consent from parents or guardians. All laboratory investigations, including platelet count, hemoglobin level, white blood cell (WBC) count, and packed cell volume (PCV), were part of routine clinical management for dengue fever and were not performed solely for the purpose of the clinical trial. The study utilized results from these routinely indicated investigations for data analysis. Patients in the intervention set (n=55) were given standard supportive treatment plus 10 ml of Carica papaya leaf extract syrup, administered three times daily, while patients in the control set (n=52) only received standard treatment. Each 10 ml of the syrup contained 1000 mg of Carica papaya leaf extract. Age, gender, weight, clinical signs, laboratory results, site admitted (ward or PICU) and the need for transfusion were recorded using a standardized form. All study participants had blood tests conducted to measure platelet count, hemoglobin and total leukocyte count on Day 1 and Day 3. The primary endpoint was assessed on Day 3 because thrombocytopenia in dengue fever typically reaches its nadir during the early critical phase of illness, which commonly occurs within the first 3–5 days. Evaluating platelet counts on Day 3 allowed assessment of the early therapeutic response to *Carica papaya* leaf extract during the period of greatest clinical concern. Additionally, most patients with uncomplicated dengue show hematological improvement within this timeframe, making Day 3 a clinically relevant and practical endpoint for short-term efficacy assessment. The data was analyzed using Statistical package for social sciences (SPSS) v. 20. Platelet count, a continuous variable, was represented as mean ± standard deviation and subjected to differences analysis through paired t-tests. Required categorical data were presented using number and proportions of participants. In all analyses, a p-value <0.05 indicated a statistically significant result. The institution's review board and CPSP approved the study, and a strict habit of patient confidentiality was adhered to during the research

Ethical approval was obtained from the Institutional Review Board of Ziauddin University (ERC reference code 6600223GMPED). This randomized controlled trial was registered at ClinicalTrials.gov (NCT07172100) with Unique Protocol ID 6600223GMPED.

RESULTS

This study was carried out in 107 pediatric patients diagnosed with dengue with thrombocytopenia. In the intervention group (n = 55, CPLE syrup + standard therapy), 34 (61.8%) were males and 21 (38.2%) were females, while in the control group (n = 52, standard therapy only), 25 (48.1%) were males and 27 (51.9%) were females. The results indicated that there was no statistically significant difference in platelet counts between the intervention and control groups. On Day 1, the intervention group had a median platelet count of 109 ×10⁹/L (IQR 88) and the control group also had a median of 109 ×10⁹/L (IQR 88), with p = 0.03. On Day 3, the intervention group had a median platelet count of 115 ×10⁹/L (IQR 81), and the control group had a median of 115 ×10⁹/L (IQR 81), with p = 0.968 (Table-I).

As a part of secondary assessment, mean increase in hemoglobin count and WBC count was analyzed in both intervention and control groups. The comparison of biochemical parameters between the groups were made (Table-II). Normality of all the numeric variable- age, hemoglobin level, platelet count, packed cell volume and total leucocyte count was checked using Shapiro wilk test. Only Hemoglobin level day 1 showed a normal distribution (p= .458). Median and interquartile range was used to summarize rest of the numeric variables. Frequency and percentages were calculated for categorical variable like gender and sign and symptoms. Independent sample Mann-Whitney U test was used to find difference in median between platelet count in intervention and control group. P value of ≤ .05 was considered statistically significant.

In the intervention group (n = 55), 46 patients were admitted to the ward and 9 to the PICU, whereas in the control group (n = 52), 50 patients were admitted to the ward and 2 to the PICU. The data suggest that a higher proportion of patients in the intervention group required intensive care compared to the control group. Specifically, 16.4% of patients in the intervention group required PICU care, compared to only 3.8% in the control group (Figure-I).

Platelet transfusions were given per institutional guidelines (<10,000/µL, or <20,000/µL with bleeding), applied uniformly to both groups, with decisions made by treating pediatricians independent of the study, and transfusion was analyzed as a secondary outcome to minimize bias. In the intervention group, three patients were transfused platelets whereas, in the control group only one patient was transfused platelets. Although the study hypothesized that *Carica papaya* leaf extract could boost platelet counts and reduce the need for transfusions, these findings suggest that the extract did not significantly alter the clinical course of thrombocytopenia in dengue patients during the study period (Figure-II).

Table-I: Comparison of platelet count before and after papaya leaf extract

	Papaya leaf extract given	N	Median	Inter Quartile range	p value
Platelet Count before papaya leaf extract-Day 1(10^9/L)	Intervention group	55	109	88	0.03
	Control group	52			
Platelet Count after papaya leaf extract-Day 3 (10^9/L)	Intervention group	55	115	81	0.968
	Control group	52			

Table-II: Comparison of biochemical parameters between two groups.

	Papaya leaf extract given	N	Median	Inter Quartile range	p value
Hemoglobin day 1(mg/dl)	Intervention Group	55	11.15	2.13	0.407
	Control Group	52			
Hemoglobin day 3(mg/dl)	Intervention Group	55	11.4	2.15	0.713
	Control Group	52			
Packed cell volume day 1 (%)	Intervention Group	55	32	2.25	0.088
	Control Group	52			
Packed cell volume day 3 (%)	Intervention Group	55	32.5	4	0.746
	Control Group	52			
Total leucocyte count day 1 (10^9/L)	Intervention Group	55	5.35	2.9	0.661
	Control Group	52			
Total leucocyte count day 3 (10^9/L)	Intervention Group	55	6.1	3.4	0.323
	Control Group	52			

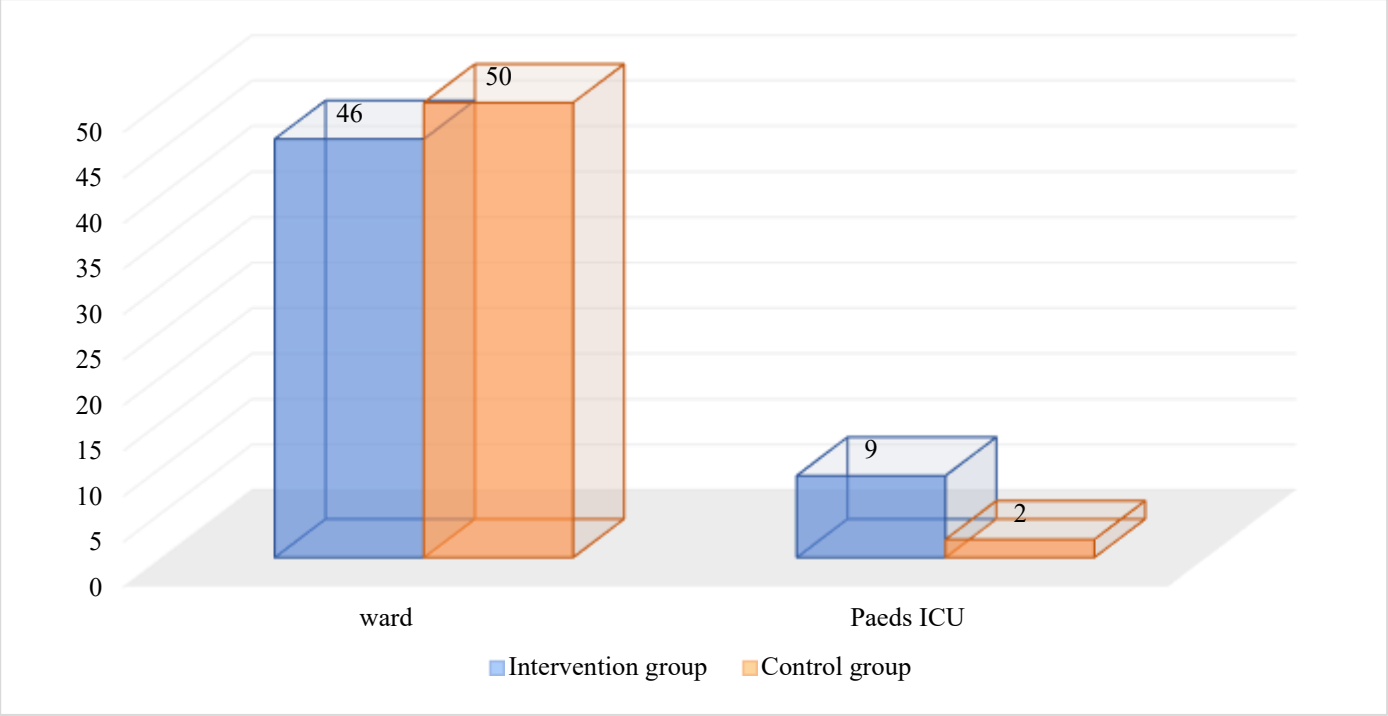

Figure-I: Location of admission.

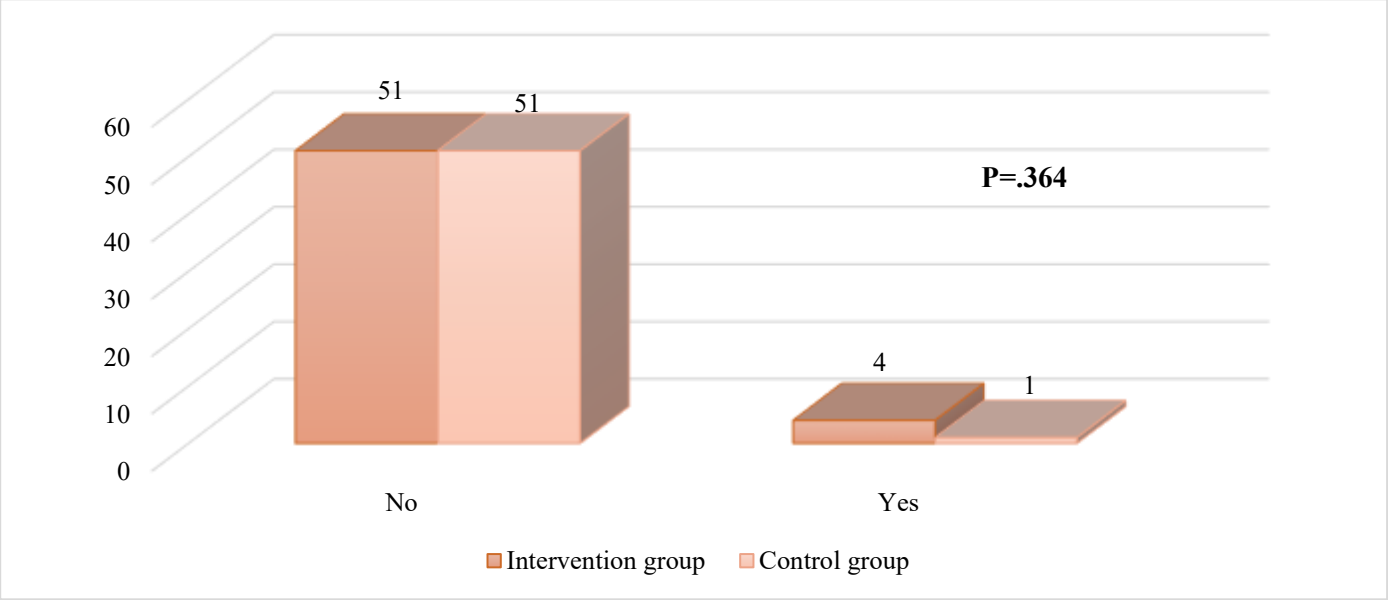

Figure-II: Platelet transfusion given.

DISCUSSION

In this randomized controlled trial, we evaluated the effect of *Carica papaya* leaf extract (CPLE) on platelet recovery in children with dengue-associated thrombocytopenia. Overall, CPLE did not demonstrate a clinically meaningful improvement in platelet counts or other hematological parameters compared with standard therapy.

Pakistan, like many dengue-endemic regions, faces significant seasonal outbreaks, and thrombocytopenia is one of the most serious complications, potentially leading to hemorrhagic manifestations and the need for hospital care or platelet transfusion. CPLE has recently gained attention as a potential platelet recovery agent, with studies suggesting it may enhance thrombopoiesis through improved megakaryocyte activity and bone marrow support. However, evidence remains inconsistent, particularly in pediatric populations.

Our findings differ from studies in India, Malaysia, and Sri Lanka, where more pronounced improvements in platelet counts were reported following CPLE administration. Recent reports and reviews have

similarly highlighted ongoing interest in papaya leaf extract, while also emphasizing the need for more robust and well-designed clinical trials before routine recommendation can be made.[16-18] The divergence may be explained by differences in study populations, extract preparation and concentration, duration of therapy, and dosing regimens. In our study, a fixed pediatric dose was administered over three days, whereas other studies often employed longer treatment periods or higher doses.

There were no clinically meaningful differences between groups in secondary outcomes such as hemoglobin, white blood cell count, or packed cell volume. The higher proportion of PICU admissions and platelet transfusions observed in the intervention group, while not statistically significant, warrants careful interpretation and suggests the possibility of more severe underlying disease in this group or a lack of effect of CPLE during the acute phase.

A key limitation of our study is that platelet counts were measured only on Day 1 and Day 3, which may be insufficient to capture the full trajectory of platelet recovery in dengue. Additionally, the three-day hospitalization period common in our setting limited longer follow-up. Future studies should consider extended monitoring and varied dosing regimens to better evaluate the potential role of CPLE in pediatric dengue.

In summary, CPLE did not show clinically significant benefits in platelet recovery or other hematological outcomes in our pediatric population, and the observed higher rates of transfusion and PICU admission underscore the need for cautious interpretation and further research.

CONCLUSION

This study shows that the use of Carica papaya leaf extract to augment common therapy had no statistically significant increase in platelet counts in children with dengue fever and thrombocytopenia. There is no evidence to support this study that short term papaya leaf extract supplementation results in superior clinical outcome compared with established supportive care during the acute period of dengue. There were no noticeable variations in related results such as hemoglobin levels, white blood count and the need for platelet transfusion. As the current evidence does not demonstrate high clinical benefit, Carica papaya should not be a universal option for platelet support in the pediatric dengue until the results of a good enough clinical study.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Guzel Maxood: Contributed significantly to the development of the article, study design, and analysis and interpretation of the data, final approval, accountable for all aspects of the work.

Shaista Ehsan: Contributed significantly to the concept of the article, critically reviewed it for important intellectual content, final approval, accountable for all aspects of the work.

Bina Fawad: Made substantial contributions to the analysis and interpretation of data, performed critical revision of the manuscript, final approval, accountable for all aspects of the work.

REFERENCES

1. Schaefer TJ, Panda PK, Wolford RW. Dengue fever. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2025 May 11]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430732/
2. Durrance-Bagale A, Hoe N, Lai J, Liew JW, Clapham H, Howard N. Dengue vector control in high-income, city settings: A scoping review. PLoS Negl Trop Dis. 2024; 18(4): e0012081. DOI: https://doi.org/10.1371/journal.pntd.0012081
3. WHO. Dengue and severe dengue. Geneva: World Health Organization; 2022 [cited 2025 May 11]. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue
4. Awan UA, Shahbaz H, Raza F, Iqbal M, Saleem M, Sadiq A. Current situation and control strategies of dengue outbreak in Pakistan. Infect Dis Rep. 2023;15(2):139–46. DOI: https://doi.org/10.1016/j.amsu.2022.103670
5. Gadhwal AK, Ankit BS, Chahar C, Tantia P, Sirohi P, Agrawal RP. Effect of carica papaya leaf extract capsule on platelet count in patients of dengue fever with thrombocytopenia. J Assoc Physicians India. 2016. Available from: https://pubmed.ncbi.nlm.nih.gov/27739263/
6. Srikanth BK, Reddy L, Biradar S, Shamanna M, Mariguddi DD, Krishnakumar M. An open-label, randomized prospective study to evaluate the efficacy and safety of Carica papaya leaf extract for thrombocytopenia associated with dengue fever in pediatric subjects. Pediatr Health Med Ther. 2019; 10: 5-11. DOI: https://doi.org/10.2147/phmt.s176712
7. Charan J, Saxena D, Goyal JP, Yasobant S. Efficacy and safety of Carica papaya leaf extract in the dengue: A

systematic review and meta-analysis. Int J Clin Pharmacol Ther. 2016; 54(12) :962-970.
DOI: https://doi.org/10.2147/phmt.s176712

8. Hasani SJ, Sgroi G, Esmaeilnejad B, Nofouzi K, Mahmoudi SS, Shams N, *et al*. Recent advances in the control of dengue fever using herbal and synthetic drugs. Heliyon. 2025; 11(3): e41939
DOI: https://doi.org/10.1016/j.heliyon.2025.e41939
9. Subenthiran S, Choon TC, Cheong KC, Thayan R, Teck MB, Muniandy PK, *et al*. Carica papaya leaves juice significantly increases platelet count in patients with dengue fever. Evid Based Complement Alternat Med. 2020; 2020: 1-7.
DOI: https://doi.org/10.1155/2013/616737
10. Rajapakse S, Rodrigo C, Maduranga S, Rajapakse A. Carica papaya extract in dengue: a systematic review and meta-analysis. BMC Complement Altern Med. 2019; 19 (1): 265. DOI: https://doi.org/10.1186/s12906-019-2678-2
11. Srikanth BK, Reddy L, Biradar S, Shamanna M, Mariguddi DD, Krishnakumar M. An open-label, randomized prospective study to evaluate the efficacy and safety of Carica papaya leaf extract for thrombocytopenia associated with dengue fever in pediatric subjects. Pediatr Health Med Ther. 2019; 10: 5–11.
DOI: https://doi.org/10.2147/phmt.s176712
12. Ahmed S, Arif F, Yahya Y, Rehman A, Abbas K, Ashraf S, *et al*. Dengue fever outbreak in Karachi 2006--a study of profile and outcome of children under 15 years of age. J Pak Med Assoc. 2008. Available from: https://pubmed.ncbi.nlm.nih.gov/18297966/
13. Ali N, Usman M, Syed N, Khurshid M. Hemorrhagic manifestations and utility of haematological parameters in dengue fever: a tertiary care centre experience at Karachi. Scand J Infect Dis. 2007;39(11-12):1025-8. DOI: https://doi.org/10.1080/00365540701411492
14. Farooq A, Aurangzeb B, Sheikh TK, Bashir H, Ghuncha M, Mustafa T. Successful outpatient management of children at a secondary care hospital in Pakistan in a dengue fever epidemic and their clinical outcomes. J Trop Med. 2021; 2021: 3296448.
DOI: https://doi.org/10.1155/2021/3296448
15. Hussain W, Karim A, Khan MA, Jalbani IK, Kamal M, Ali M, *et al*. Pattern and outcome of dengue fever in a pediatric tertiary care hospital: A retrospective report. Cureus. 2021; 13(4): e14164. DOI: https://doi.org/10.7759/cureus.14164
16. Khalid M, Khan MS, Siddiqui E, Waafira A. Exploring the potential of Carica papaya leaf extract: a perspective on its effectiveness in ameliorating thrombocytopenia in dengue patients. Infect Ecol Epidemiol. 2025; 15(1): 2456055. DOI: https://doi.org/10.1080/20008686.2025.2456055
17. Jaggernauth S, Ramoutar SR, Ramoutar R, Piaralal N. Is papaya leaf extract the sweet remedy for dengue-induced thrombocytopenia? Cureus. 2024; 16(10): e71852. DOI: https://doi.org/10.7759/cureus.71852
18. Siddiqui MN, Khan MU, Ali A, Samadi A. Papaya leaf extract: A potential ally against dengue-induced thrombocytopenia in low-resource settings. Next Res. 2025; 2(3): 100742.
DOI: https://doi.org/10.1016/j.nexres.2025.100742