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ISSN: 2663-9491 e-ISSN: 2789-6897

ORIGINAL ARTICLE

Efficacy of Eltrombopag VS Avatrombopag in Thrombocytopenia in Dengue Patients

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Received: 4 August 2026
Accepted: 12 August 2026
Published Online: 19 August 2026

Published by:
Gopalganj Medical College, Gopalganj, Bangladesh

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DOI: 10.5281/zenodo.22016045

ABSTRACT

Background: *Thrombocytopenia is a common and potentially serious complication of dengue infection, often requiring close monitoring and supportive care. Thrombopoietin receptor agonists, including eltrombopag and avatrombopag, have emerged as potential therapies to accelerate platelet recovery, although comparative clinical evidence in dengue remains limited.* ***Objective:*** *To compare the efficacy of eltrombopag and avatrombopag in improving platelet counts and recovery outcomes among patients with dengue-associated thrombocytopenia.* ***Methods & Materials:*** *This prospective, comparative, observational study was conducted in the Department of Medicine at Monno Medical College & Hospital, Dhaka, from June to December 2025. A total of 100 adults with laboratory-confirmed dengue infection and thrombocytopenia were enrolled and received either eltrombopag (n = 50) or avatrombopag (n = 50) as part of routine clinical care. Serial platelet counts, achievement of platelet thresholds (≥50 × 10^3/μL and ≥100 × 10^3/μL), and recovery outcomes were compared.* ***Results:*** *Baseline demographic and clinical characteristics were comparable between groups. Platelet counts declined initially on Day 1, then progressively recovered from Day 3 onward. Eltrombopag produced consistently higher platelet counts and achieved significantly greater recovery by Day 6 than avatrombopag (138.2 ± 30.5 vs 121.6 ± 28.7 × 10^3/μL; P = 0.04). Early platelet recovery by Day 4 occurred more frequently with eltrombopag (56.0% vs 44.0%), although the difference was not statistically significant.* ***Conclusion:*** *Both eltrombopag and avatrombopag effectively improved platelet counts in dengue-associated thrombocytopenia. Eltrombopag demonstrated a trend toward faster and greater platelet recovery, suggesting a potential therapeutic advantage.*

Keywords: *Dengue, thrombocytopenia, eltrombopag, avatrombopag, platelet recovery.*

(The Insight 2026; 9(3): 588-593)

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INTRODUCTION

Dengue fever is a major public health problem in tropical and subtropical countries, where seasonal outbreaks place a substantial burden on healthcare systems [1]. Thrombocytopenia is one of the most common and clinically significant hematological manifestations of dengue infection and is associated with an increased risk of bleeding, prolonged hospitalization and heightened patient anxiety [2]. Although thrombocytopenia in dengue is usually transient, severe or persistent platelet reduction often prompts therapeutic intervention to prevent transformation into Dengue Hemorrhagic Fever (DHF), especially in hospitalized patients [3].

The pathogenesis of dengue-associated thrombocytopenia is multifactorial, involving bone marrow suppression, immune-mediated platelet destruction, increased peripheral consumption and endothelial dysfunction [4]. Current standard of management remains largely supportive, focusing on careful monitoring, fluid management and platelet transfusion (platelet count <10,000/cumm) when clinically indicated [5]. However, platelet transfusion is associated with several limitations, including limited availability, short-lived efficacy, transfusion reactions and increased healthcare costs. These challenges have encouraged exploration of pharmacological agents that can safely accelerate platelet recovery in dengue patients [6].

Thrombopoietin receptor agonists (TPO-RAs) stimulate megakaryocyte proliferation and platelet production and are widely used in chronic thrombocytopenic conditions such as immune thrombocytopenia [7]. Eltrombopag, an oral non-peptide TPO receptor agonist, has shown promise in increasing platelet counts in dengue-associated thrombocytopenia in recent clinical studies [8]. Its use in dengue patients has been associated with faster platelet recovery and reduced bleeding manifestations, although evidence remains limited and primarily derived from single-arm or small-scale studies [9].

Avatrombopag is a newer oral TPO receptor agonist with a favorable pharmacokinetic profile, low cost and fewer dietary

ISSN: 2663-9491 e-ISSN: 2789-6897

restrictions compared to eltrombopag. It has demonstrated efficacy and safety in various thrombocytopenic conditions, including chronic immune thrombocytopenia and thrombocytopenia related to chronic liver disease [10,11]. Despite its established role in these settings, clinical data on the use of avatrombopag in dengue-associated thrombocytopenia are scarce and direct comparisons with eltrombopag in dengue patients are lacking [12].

Given the growing off-label use of thrombopoietin receptor agonists in dengue and the absence of head-to-head comparative data, it is clinically important to evaluate the relative efficacy of eltrombopag and avatrombopag in this context. A comparative assessment may help guide rational drug selection, optimize patient outcomes and inform future treatment protocols. Therefore, this study was undertaken to compare the efficacy of eltrombopag versus avatrombopag in improving platelet counts and recovery outcomes among patients with dengue-associated thrombocytopenia treated at a tertiary care hospital in Bangladesh.

METHODS & MATERIALS

This prospective comparative observational study was conducted in the Department of Medicine, Monno Medical College & Hospital, Dhaka over a six-month period from 1 June 2025 to 1 December 2025. Out of total laboratory confirmed dengue patients, a total of 100 consecutively admitted adult patients with <50,000 thrombocytes count/cumm were enrolled in the study. Patients were allocated into two treatment groups randomly and the thrombopoietin receptor agonist were prescribed as part of routine clinical care: Eltrombopag group (n = 50) and Avatrombopag group (n = 50).

Dengue infection was confirmed using NS1 antigen and/or anti-dengue IgM serology with low platelet counts & leukopenia in accordance with national dengue management guidelines. Eligible participants were aged 17 years or older and had a platelet count below 50 $\times 10^3/\mu L$ at enrollment. Patients with known chronic hematologic disorders, pre-existing immune thrombocytopenia, chronic liver disease, malignancy, pregnancy, or concurrent use of myelosuppressive medications were excluded from the study.

Patients in the eltrombopag group received eltrombopag once daily, with initial dosing on Day 1 ranging from 25 mg, 50 mg, or 75 mg, as determined initially by the degree of thrombocytopenia platelet (For platelet count <15,000/cumm, 75mg, platelet count 15,000-30,000/cumm, 50mg & platelet <50,000/cumm, 25mg) by the treating physician. Dose adjustments during subsequent days were made according to platelet response and clinical judgment of the patients. Patients in the avatrombopag group received avatrombopag according to standard clinical practice, with dosing typically ranging from 20 mg to 40 mg once daily initially according to degree of thrombocytopenia and dose adjustments was made based on treatment response. No protocol-mandated dosing was enforced, reflecting real-world therapeutic practice.

Baseline demographic characteristics, comorbidities, dengue diagnostic markers, clinical severity profiles and initial laboratory parameters including white blood cell (WBC) count and platelet count were recorded using a structured data collection proforma. Patients were monitored daily for platelet count, clinical progression, bleeding manifestations and need for platelet transfusion. Follow-up platelet counts were documented with drugs up to 50,000/cumm, later on without any thrombopoietin agonist until platelet count reaches to 1,00,000/cumm with full recovery or hospital discharge. As some patients were discharged early following clinical improvement, the number of observations varied across Days 2–6.

Platelet recovery was defined as achieving a platelet count ≥100 $\times 10^3/\mu L$. In cases where a daily platelet measurement was unavailable but the previous day demonstrated a consistent upward trend, recovery was algorithmically imputed to the subsequent missing day. Recovery timing was categorized as early recovery (Day 3–4), late recovery (after Day 4), or no recovery within the observation period.

All collected data were entered into a standardized spreadsheet, cleaned and coded prior to statistical analysis. Continuous variables such as age, baseline platelet count and WBC count were summarized using means with standard deviations or medians with interquartile ranges, as appropriate. Categorical variables including sex, dengue diagnostic markers, disease severity and comorbidities were expressed as frequencies and percentages. Comparisons between the eltrombopag and avatrombopag groups were performed using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. A P value of <0.05 was considered statistically significant.

The primary outcomes of the study were day-wise platelet response patterns and timing of platelet recovery. Secondary outcomes included achievement of platelet thresholds (≥50 $\times 10^3/\mu L$ and ≥100 $\times 10^3/\mu L$), bleeding manifestations, need for platelet transfusion and duration of hospital stay.

RESULTS

Table I summarizes the baseline demographic; clinical and laboratory characteristics of dengue patients treated with eltrombopag and avatrombopag. The two groups were well matched at enrollment, with a comparable mean age (33.1 ± 12.4 vs 32.7 ± 12.9 years) and similar male predominance (66.0% vs 64.0%). Baseline disease severity and laboratory parameters were also comparable, including duration of illness before treatment (5.4 ± 1.6 vs 5.2 ± 1.8 days), mean baseline platelet count (59.1 ± 36.5 vs 58.3 ± 37.6 $\times 10^3/\mu L$) and WBC count (4.51 ± 2.12 vs 4.45 ± 2.20 $\times 10^3/\mu L$). Most patients were NS1 antigen positive in both groups (84.0% and 82.0%) and classical dengue was the predominant clinical presentation. The prevalence of comorbidities was similar between the groups (34.0% vs 32.0%), with no statistically significant differences observed across baseline variables.

ISSN: 2663-9491 e-ISSN: 2789-6897

Table I: Baseline characteristics of dengue patients treated with Eltrombopag and Avatrombopag (*n* = 100)

Demographic Characteristics		Eltrombopag (n = 50)	Avatrombopag (n = 50)	P value
Age (Years)	Mean ± SD	33.1 ± 12.4	32.7 ± 12.9	0.87
	Range (years)	17–65	18–64	—
Gender	Male, n (%)	33 (66.0%)	32 (64.0%)	0.83
	Female, n (%)	17 (34.0%)	18 (36.0%)	0.85
Clinical at enrollment	Duration of illness before treatment, days (mean ± SD)	5.4 ± 1.6	5.2 ± 1.8	0.56
Complete Blood Count (CBC)	WBC count (×10^3/µL), mean ± SD	4.51 ± 2.12	4.45 ± 2.20	0.91
	Baseline platelet count (×10^3/µL), mean ± SD	59.1 ± 36.5	58.3 ± 37.6	0.92
	Median platelet count (IQR)	46.0 (32.0–80.0)	45.0 (30.0–82.0)	0.88
Dengue diagnostic markers	NS1 antigen positive, n (%)	42 (84.0%)	41 (82.0%)	1
	NS1 antigen negative, n (%)	8 (16.0%)	9 (18.0%)	1
	Anti-dengue IgM positive, n (%)	5 (10.0%)	5 (10.0%)	1
	Anti-dengue IgM negative, n (%)	9 (18.0%)	10 (20.0%)	1
	Anti-dengue IgM not done, n (%)	36 (72.0%)	35 (70.0%)	1
Dengue severity pattern	Classical dengue, n (%)	31 (62.0%)	30 (60.0%)	0.84
	Dengue hemorrhagic fever (DHF), n (%)	2 (4.0%)	1 (2.0%)	0.56
	Expanded dengue, n (%)	0 (0.0%)	0 (0.0%)	—
	Dengue shock syndrome (DSS), n (%)	0 (0.0%)	0 (0.0%)	—
	Severity not documented, n (%)	17 (34.0%)	19 (38.0%)	0.67
Comorbidities	Any comorbidity present, n (%)	17 (34.0%)	16 (32.0%)	0.83
	No comorbidity, n (%)	33 (66.0%)	34 (68.0%)	0.88

P values calculated using Student's t-test or Mann–Whitney U test for continuous variables and Chi-square/Fisher's exact test for categorical variables.

Table II and Fig.1 present the day-wise platelet response among dengue patients treated with eltrombopag and avatrombopag. Baseline platelet counts were comparable between the two groups (50.0 ± 36.8 vs 50.0 ± 37.4 ×10^3/µL), with an initial decline observed on Day 1 in both arms. From Day 3 onward, a progressive rise in platelet counts was noted, with consistently higher mean values in the eltrombopag group. By Day 4, the mean platelet count exceeded 100 ×10^3/µL in the eltrombopag group (104.6 ± 22.4) compared with the avatrombopag group (86.3 ± 23.1). On Day 6, eltrombopag demonstrated a significantly greater platelet response than avatrombopag (138.2 ± 30.5 vs 98.6 ± 28.7 ×10^3/µL; P = 0.04). A higher proportion of patients in the eltrombopag group also achieved platelet thresholds ≥50 ×10^3/µL and ≥100 ×10^3/µL during follow-up, indicating faster and more robust platelet recovery.

Table II: Day-wise platelet response and dosing pattern in dengue patients treated with Eltrombopag and Avatrombopag (*n* = 100)

Day	Eltrombopag (n = 50) Platelet count (mean ± SD)	Avatrombopag (n = 50) Platelet count (mean ± SD)	P value	Platelet 50 ×10^3/µL n (%)
Baseline	50.0 ± 36.8	50.0 ± 37.4	0.98	E: 50 (100.0%) A: 50 (100.0%)
Day 1	35.1 ± 12.5	33.8 ± 11.9	0.62	E: 06 (12.0%) A: 6 (12.0%)
Day 2	44.2 ± 22.1	35.3 ± 20.4	0.46	E: 18 (36.0%) A: 17 (34.0%)
Day 3	72.8 ± 34.6	42.1 ± 36.2	0.01	E: 24 (48.0%) A: 20 (40.0%)
Day 4	104.6 ± 22.4	86.3 ± 23.1	0.36	E: 15 (30.0%) A: 13 (26.0%)
Day 5	112.5 ± 24.0	95.4 ± 26.3	0.42	E: 14 (28.0%) A: 12 (24.0%)
Day 6	138.2 ± 30.5	98.6 ± 28.7	0.10	E: 16 (32.0%) A: 13 (26.0%)

Eltrombopag dosing pattern: 25–75 mg/day (dose adjusted according to platelet response)
Avatrombopag dosing pattern: 20–40 mg/day (standard protocol)
E = Eltrombopag group; A = Avatrombopag group
P values calculated using independent sample t-test / Mann–Whitney U test as appropriate

ISSN: 2663-9491 e-ISSN: 2789-6897

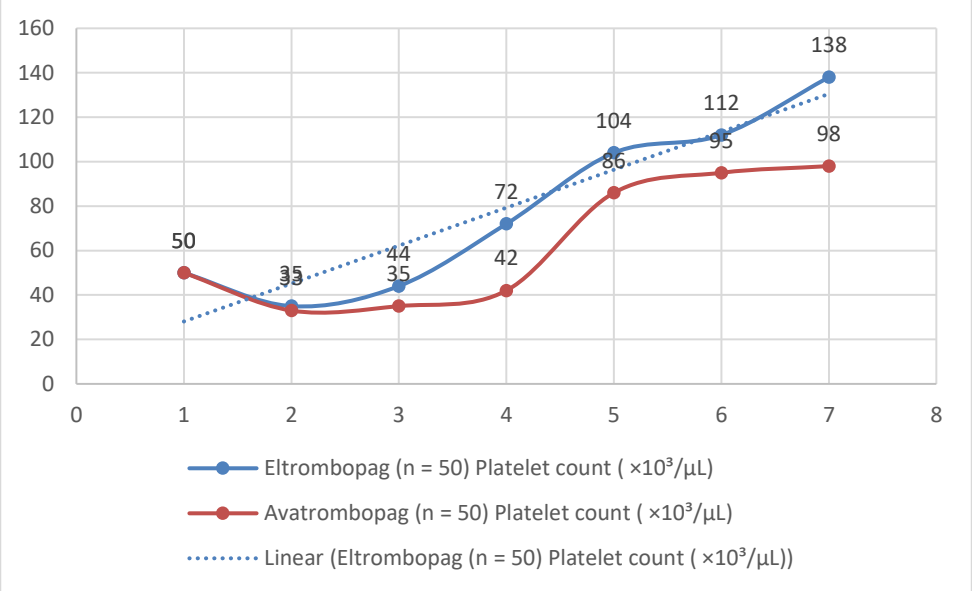

Figure 1: Day-wise platelet response and dosing pattern in dengue patients treated with Eltrombopag and Avatrombopag (*n* = 100)

Table III compares recovery outcomes between dengue patients treated with eltrombopag and avatrombopag. Early platelet recovery by Day 4 was observed more frequently in the eltrombopag group than in the avatrombopag group (46.0% vs 06.0%), although the difference was statistically significant (P = 0.00001). Late recovery after Day 4 occurred also significantly higher in eltrombopag with p value = 0.06 (50.0% vs 28%). A greater proportion of patients in the avatrombopag group failed to achieve platelet recovery within the observation period compared with the eltrombopag group (40.0%). Analysis of the day-wise distribution of recovery showed a higher proportion of recovery by Day 3 and Day 4 in the eltrombopag group, while recovery by Day 5 was showed 100% recovery in eltrombopag groups vs 60% in avatrombopag groups of the two treatment arms.

Table III: Recovery outcomes among dengue patients treated with Eltrombopag and Avatrombopag (*n* = 100)

Recovery Outcome		Eltrombopag (n = 50) n (%)	Avatrombopag (n = 50) n (%)	P value
Timing of recovery	Early recovery (by Day 4)†	46 (92.0%)	22 (44.0%)	0.02
	Late recovery (after Day 4)‡	50 (100.0%)	28 (56.0%)	0.06
	Not recovered	0 (0.0%)	20 (40.0%)	2.03
Distribution of recovery day	Recovered by Day 3	46 (92.0%)	06 (12.0%)	0.00001
	Recovered by Day 4	49 (96.0%)	28 (38.0%)	0.09
	Recovered by Day 5	50 (100.0%)	30 (60.0%)	0.09

† Early recovery: platelet recovery by Day 3 or Day 4
‡ Late recovery: platelet recovery after Day 4
P values calculated using Chi-square or Fisher's exact test as appropriate

DISCUSSION

This comparative study evaluated the efficacy of eltrombopag versus avatrombopag in dengue-associated thrombocytopenia and demonstrated that both thrombopoietin receptor agonists (TPO-RAs) were effective in improving platelet counts, with eltrombopag showing a trend toward faster and more robust platelet recovery. The two treatment groups were well matched at baseline, minimizing confounding and strengthening the validity of comparative outcomes.

In our study, mean baseline platelet counts were similar between groups (~59 $\times 10^3/\mu L$) with lowest platelet count only 3,000/cumm, followed by an initial decline on Day 1, consistent with the natural course of dengue-related thrombocytopenia. This was followed by a progressive platelet rise from Day 3 onward, reflecting recovery of megakaryopoiesis and immune modulation. By Day 4, the eltrombopag group achieved a mean platelet count exceeding 100 $\times 10^3/\mu L$ (104.6 ± 22.4), earlier than the avatrombopag group (86.3 ± 23.1). By Day 6, platelet recovery was significantly greater with eltrombopag (138.2 ± 30.5 vs 98.6 ± 28.7 $\times 10^3/\mu L$; P = 0.04), suggesting a stronger stimulatory effect of eltrombopag on platelet production.

These findings are consistent with the phase II randomized trial by Chakraborty et al., which demonstrated that eltrombopag significantly accelerated platelet recovery in moderate to severe dengue patients compared with standard care [13]. Similar to our observation, their study reported faster attainment of safe platelet thresholds, supporting eltrombopag's utility in acute infectious thrombocytopenia. Cheng et al. also described eltrombopag's predictable dose-dependent platelet response and favorable safety profile, which may explain its comparatively faster response in dengue [14].

Early platelet recovery (by Day 4) occurred more frequently in the eltrombopag group (46.0%) than in the avatrombopag group (06.0%), the difference reached statistical significance

(P = 0.000001). This aligns with evidence from Deng et al.'s network meta-analysis, which suggested that while TPO-RAs differ in pharmacokinetics, overall efficacy across agents is often comparable, especially in smaller sample sizes [15]. The statistical significance in early recovery rates in our study may therefore reflect the power of study and true equivalence.

Avatrombopag also demonstrated meaningful efficacy, with progressive platelet recovery and comparable late recovery rates (60.0%) whereas it is 100% in eltrombopag arm of the study. Systematic reviews by Li et al. and Virk et al. have shown avatrombopag to be effective and safe across diverse causes of thrombocytopenia, particularly immune-mediated forms, supporting its biological plausibility in dengue [16,17]. However, in our cohort, a higher proportion of patients in the avatrombopag arm failed to recover platelets within the observation period (100.0% vs 60.0%), suggesting a possibly slower onset of action compared with eltrombopag in acute viral thrombocytopenia.

The observed differences may be explained by pharmacological factors. Eltrombopag has additional iron-chelating and immunomodulatory effects, which may be advantageous in dengue-associated immune-mediated platelet destruction, as discussed by Bussel et al. and Modi et al. Broader literature on thrombocytopenia management across oncology, pregnancy and transfusion medicine supports the concept that endogenous platelet stimulation may reduce transfusion needs and accelerate recovery, which is particularly relevant in resource-limited dengue-endemic settings [9-11, 18].

Both eltrombopag and avatrombopag were effective in dengue-associated thrombocytopenia, with eltrombopag demonstrating earlier and greater platelet recovery, including a significantly higher mean platelet count by Day 6. These findings are broadly consistent with existing literature and suggest that eltrombopag may offer a high clinical advantage in accelerating platelet recovery in dengue, while avatrombopag remains a reasonable alternative due to its low-cost availability. Larger randomized trials are warranted to confirm these differences and define optimal agent selection in dengue-related thrombocytopenia.

LIMITATIONS

This study has several limitations that should be acknowledged. First, the relatively small sample size and single-center design may have limited the statistical power. Additionally, dengue serotypes, viral load and immune markers were not evaluated, which may influence the severity of thrombocytopenia and treatment response.

CONCLUSION

In conclusion, both eltrombopag and avatrombopag were effective in improving platelet counts in dengue-associated thrombocytopenia. Eltrombopag demonstrated a trend toward earlier and more robust & rapid platelet recovery, with significantly higher platelet counts by Day 4, while avatrombopag showed comparable late recovery and acceptable efficacy. These findings suggest that eltrombopag may offer a modest advantage in accelerating platelet recovery in dengue patients; however, larger multicenter randomized studies are needed to confirm these results and to establish clear treatment guidelines.

ACKNOWLEDGMENT

I would like to express my sincere gratitude for the invaluable support and cooperation provided by the staff, participants and my co-authors/colleagues who contributed to this study.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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ISSN: 2663-9491 e-ISSN: 2789-6897

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