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Research Article

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Persistent Thrombocytopenia Beyond Convalescent Phase of Dengue – ITP in disguise: Evidence of Dengue-Associated Secondary Immune Thrombocytopenia and Steroid Responsiveness

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ABSTRACT

Background: In classical dengue, thrombocytopenia peaks during the critical phase and normalizes spontaneously in convalescence usually by10th day of illness. A minority of patients, however, remain profoundly thrombocytopenic after convalescent phase. Whether dengue can precipitate secondary immune thrombocytopenia (ITP) is under-recognized.

Methods: We conducted a single-center, prospective case–control study (July 2024 – May 2025) at Ad-din Women's Medical College & Hospital, Dhaka. Among NS1 and/or RT-PCR-confirmed adults, cases had platelet counts < 50,000 μL^{-1} persisting ≥ 10 days after illness onset, while controls showed no spontaneous recovery by day 14. We excluded common secondary causes of ITP (HBV, HCV, HIV, SLE, drugs, pregnancy). Cases received high-dose dexamethasone 40 mg daily for 4 days; controls received standard supportive care only. The primary end-points were platelet counts on days 11 and 15.

Results: Fifty patients (34 cases, 16 controls) were enrolled. Baseline characteristics were comparable. On day 11, mean platelet counts were similarly low (cases 40 471 ± 4775 vs controls 37 063 ± 6598 μL^{-1}; P = 0.043). By day 15, cases had risen to 319 353 ± 93 717 μL^{-1} while controls remained at 48 438 ± 7908 μL^{-1} (P < 0.001). All 34 cases achieved a clinically meaningful platelet response; no serious adverse events attributable to steroids were observed.

Conclusions: Persistent isolated thrombocytopenia after defervescence in convalescent phase dengue is uncommon but clinically important. In carefully phenotyped patients, a short course of high-dose corticosteroids—after exclusion of other secondary causes—produced rapid, sustained platelet recovery. These data support the concept of dengue-associated secondary ITP and justify larger multicenter trials.

Keywords: Dengue, immune thrombocytopenic purpura, persistent thrombocytopenia, convalescent phase, dexamethasone.

Introduction

Dengue is a systemic arboviral illness classically divided into febrile, critical/ leakage and convalescent phases. Thrombocytopenia usually peaks around defervescence and resolves spontaneously thereafter [1]. A subset of patients, however, remain thrombocytopenic beyond day 10 despite clinical improvement, raising the possibility of an immune-mediated process analogous to secondary ITP [2].

Randomized trials of early corticosteroids during the viraemic phase have shown no benefit and possible harm; consequently, current guidelines advise against their routine use [3, 4]. The pathobiology of dengue thrombocytopenia is multifactorial: direct viral effects (NS1-mediated endothelial activation), immune-complex clearance, complement activation and aberrant megakaryopoiesis all contribute, and their relative importance evolves across illness phases [5,6].

In the convalescent phase, ongoing isolated thrombocytopenia without plasma leakage, disseminated intravascular coagulation (DIC) or marrow suppression suggests a different mechanism

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from the consumption-dominant coagulopathy seen in the critical phase [7]. Case series have described rapid platelet recovery after corticosteroids instituted after defervescence [8, 9], but prospective, controlled data are lacking.

Prophylactic platelet transfusion for isolated low counts is ineffective and potentially harmful; a restrictive, symptom-guided strategy is now recommended [10-12]. Contemporary ITP guidelines endorse short, high-dose dexamethasone (40 mg daily × 4 days) as first-line therapy for adults, a regimen that is safe, inexpensive and feasible in resource-limited settings [13, 14].

We hypothesized that patients with persistent isolated thrombocytopenia ≥ 10 days after dengue onset have a form of secondary ITP, and that a brief corticosteroid course would accelerate platelet recovery without excess adverse effects.

Methods

Study Design and Place

Prospective, single-center case–control study conducted at Addin Women's Medical College & Hospital, Dhaka, Bangladesh, during two consecutive dengue seasons (July 2024 – May 2025). The protocol was approved by the institutional review board; all participants gave written informed consent.

Participants

Adults ≥ 18 years with laboratory-confirmed dengue (positive NS1 antigen, RT-PCR, or IgM seroconversion) were screened daily among them who were afebrile for ≥ 48 h, ≥ 10 day of illness, platelet count < 50,000 μL^{-1} were taken as participants. Among them causes of secondary thrombocytopenia (HBV, HCV, HIV, SLE, pregnancy, drugs, aplasia, DIC, haemophagocytic syndrome) were excluded. 50 such patients were enrolled in this study. 34 patients were taken as case and 16 were taken as control.

Interventions

All participants received WHO-recommended supportive care [15]. Cases received dexamethasone 40 mg orally daily for 4 days together with omeprazole and blood-glucose monitoring. Controls were kept in close observation and only received supportive care. Platelet count was measure at day 11 of illness while enrolling the patients into this study and at day 15 of illness.

Statistical Analysis

Continuous variables are summarized as mean ± SD. Categorical variables were compared with χ^2 or Fisher's exact test. All tests were two-sided; $P < 0.05$ was considered significant. Analyses were performed with using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Fifty adults were enrolled: 34 cases, 16 controls. Mean age was 37.0 ± 14.2 years; 64% were male. Comorbidities were balanced (Table 1). NS1 antigen positivity was present in 74% and IgM in 26%, with no between-group difference (Table 2).

On day 11, mean platelet counts were similarly low (cases 40 471 ± 4775 vs controls 37 063 ± 6598 μL^{-1}; $P = 0.043$). By day 15, cases had risen to 319 353 ± 93 717 μL^{-1} while controls remained at 48 438 ± 7908 μL^{-1} ($P < 0.001$) – an absolute difference of ≈ 271000 μL^{-1} (Table 3).

All 34 cases achieved a hematologic response (platelet 1,00,000 μL^{-1} or doubling from baseline) within 5 days of starting steroids. No patient required rescue therapy or prophylactic platelet transfusion.

No serious adverse events occurred. Transient hyperglycemia requiring short-acting insulin occurred in two cases; mild dyspepsia responded to omeprazole. No GI bleeding, infections or psychiatric disturbances were observed.

Table 1: Baseline demographic and comorbidities (N = 50)

Variable	Total (N=50)	Cases (n=34)	Controls (n=16)
Age, years (mean ± SD)	37.02 ± 14.24	37.55 ± 14.94	35.87 ± 13.02
Sex — male, n (%)	32 (64)	19 (55.9)	13 (81.3)
Sex — female, n (%)	18 (36)	15 (44.1)	3 (18.8)
Diabetes mellitus, n (%)	7 (14)	4 (11.8)	3 (18.8)
Hypertension, n (%)	5 (10)	4 (11.8)	1 (6.3)
Bronchial asthma, n (%)	6 (12)	3 (8.8)	3 (18.8)
Multiple comorbidities*	6 (12)	3 (8.8)	3 (18.8)

Table 2: Virologic profile (N = 50)

Variable	Total (N=50)	Cases (n=34)	Controls (n=16)
NS1 antigen positive, n (%)	37 (74)	27 (79.4)	10 (62.5)
Dengue IgM positive, n (%)	13 (26)	7 (20.6)	6 (37.5)

Table 3: Platelet counts at day 11 and day 15 (primary endpoint)

Timepoint	Cases (n=34) mean ± SD	Controls (n=16) mean ± SD	p-value
Day 11 (cells/μL)	40 470.58 ± 4 775.15	37 062.50 ± 6 597.66	0.043
Day 15 (cells/μL)	319 352.94 ± 93 717.13	48 437.50 ± 7 907.53	<0.001

Discussion

The present study provides prospective, controlled clinical evidence that persistent isolated thrombocytopenia beyond defervescence in convalescent phase of dengue represents a steroid-responsive, immune-mediated process, consistent with secondary immune thrombocytopenia (ITP). While transient thrombocytopenia during the febrile and critical phases of dengue is well documented, spontaneous platelet recovery is expected during convalescence in nearly all patients [1]. Our findings challenge this dogma by identifying a distinct subset of

patients in whom severe thrombocytopenia persists beyond day 10, despite clinical stabilization.

Dengue-associated thrombocytopenia is classically attributed to a combination of bone marrow suppression, immune-mediated platelet destruction, endothelial activation, and consumptive coagulopathy [5, 14 –15]. During the acute phase, direct viral invasion of megakaryocytes and immune-complex–mediated platelet clearance dominates [6]. However, in the convalescent phase, viremia has typically resolved, and coagulation parameters normalize [14]. Therefore, persistent isolated thrombocytopenia without DIC, marrow suppression, or hemophagocytic features strongly suggests an immune mechanism, analogous to secondary ITP. Recent molecular studies have demonstrated NS1-driven immune dysregulation, macrophage activation, complement fixation, and platelet desialylation, all of which may persist beyond the critical phase and perpetuate immune platelet destruction [6, 7]. These findings provide strong biological plausibility for dengue-triggered secondary ITP, as observed in our cohort.

Although corticosteroids are contraindicated in early dengue viremic phases, several case-based and cohort studies have documented dramatic platelet responses when steroids were initiated after defervescence, similar to our observations. Verma et al. reported a classic case of steroid-responsive thrombocytopenia developing after dengue defervescence, with platelet normalization within 72 hours of dexamethasone administration [2]. Likewise, Lim et al. described immune-mediated thrombocytopenia following dengue that responded promptly to corticosteroids once viral clearance was complete [1]. A large Vietnamese cohort demonstrated that coagulation abnormalities typically normalize by day 10, supporting our choice of day 11 as the biological transition point to evaluate immune-mediated thrombocytopenia [14]. This temporal distinction is critical, as early steroid use during the viremic phase has shown no benefit and potential harm, including delayed viral clearance and secondary infections [3, 4]. In contrast to early-phase trials, our intervention was administered strictly during the post-viremic immune phase, fully explaining the striking platelet recovery observed in the steroid-treated group.

In our study, mean platelet counts increased from ~40,000/µL on day 11 to >3,10,000/µL by day 15 following dexamethasone, whereas untreated controls remained severely thrombocytopenic. This rapid rise parallels the expected response kinetics of classic immune thrombocytopenia treated with high-dose dexamethasone, as demonstrated in the GIMEMA and subsequent ITP trials [13]. Notably, 100% of treated patients in our cohort achieved a clinically meaningful platelet response, strongly supporting immune responsiveness rather than delayed spontaneous recovery. This response rate exceeds that reported in primary ITP trials, possibly reflecting the acute trigger–driven nature of dengue-associated autoimmunity.

WHO and major dengue guidelines strongly discourage corticosteroids based on negative trials conducted entirely in early dengue infection [3, 4]. However, these trials assessed steroids during the viraemic inflammatory phase, not during the immune-dominant convalescent phase. Our study fundamentally differs by demonstrating that:

- Steroids were started only after fever resolution
- Secondary thrombocytopenia causes were excluded
- Rapid, sustained platelet correction followed
- No serious steroid-related complications occurred

This phase-specific therapeutic window aligns with biological immune dynamics and should not be conflated with early-phase steroid failure.

Numerous studies have demonstrated that prophylactic platelet transfusion in dengue does not prevent bleeding and may worsen outcomes [8 – 10]. In our cohort, no patient required platelet transfusion, reinforcing the role of immune-targeted therapy over consumptive correction strategies. This is particularly relevant for resource-limited settings such as Bangladesh, where platelet availability is constrained and transfusion risks remain substantial.

Current ITP classification systems list viral infections such as HIV and hepatitis C as recognized secondary causes, but dengue is rarely acknowledged [12]. Our prospective controlled data now provide convincing clinical evidence that Dengue can act as a trigger for secondary immune thrombocytopenia during the convalescent phase. This aligns with emerging immunological concepts of post-infectious autoimmunity, increasingly recognized across viral illnesses.

This study is among the first prospective controlled investigations to:

- Clearly define post-dengue secondary ITP
- Apply immune-targeted therapy after viral clearance
- Demonstrate dramatic therapeutic platelet recovery
- Provide a biological explanation for steroid responsiveness
- Offer a transfusion-sparing therapeutic alternative

Limitations

The single-center design and modest sample size limit statistical power. Anti-platelet antibody testing was not available. Marrow failure was not excluded by bone marrow examination as all the cases were below 65 years of age. Long-term relapse risk could not be evaluated. Larger multicenter randomized trials with immune profiling are required.

Conclusion

Persistent isolated thrombocytopenia after defervescence during convalescent stage in dengue represents an under-recognized immune-mediated complication. In carefully selected patients, a short course of high-dose corticosteroids instituted after the viraemic phase accelerates platelet recovery without apparent harm. A phase-specific, restrictive transfusion-sparing approach is biologically coherent and clinically feasible in resource-constrained settings. Multicenter trials using harmonized immune-phenotype criteria are warranted.

References

1. Low JG, Ong A, Tan LK, Chaterji S, Chow A, et.al. The early clinical features of dengue in adults. PLoS Negl Trop Dis. 2011. 5: 1191.
2. Verma SP, Hamide A, Wadhwa J, Sivamani K. Corticosteroid-responsive thrombocytopenia in dengue fever: a case report. BMJ Case Rep. 2013. 26: 200249

3. Tam DTH, Ngoc TV, Tien NTM. Effects of short-course oral prednisolone in early dengue infection: a randomized, placebo-controlled trial. Clin Infect Dis. 2012. 55: 1216-1224.
4. Bandara SR, Herath HM. Effectiveness of corticosteroid in the treatment of dengue – a systematic review. Heliyon. 2018. 4: 00816.
5. Azeredo EL, Monteiro RQ, de-Oliveira Pinto, LM. Thrombocytopenia in dengue: interrelationship between virus and the imbalance between coagulation and fibrinolysis and inflammatory mediators. Mediators Inflamm. 2015. 313842.
6. Chen HR, Chuang YC, Lin YS, Liu HS, Liu CC, et al. Dengue virus nonstructural protein 1 induces vascular leakage through macrophage migration inhibitory factor and autophagy. PLoS Negl Trop Dis. 2016. 10: 0004828.
7. Riswari SF, Tunjungputri RN, Kullaya V, Garishah FM, Utari GS, et al. Desialylation of platelets induced by von Willebrand factor is a novel mechanism of platelet clearance in dengue. PLoS Pathog. 2019. 15: 1007500.
8. Lee TH, Wong JG, Leo YS, Thein TL, Ng EL, et al. Potential harm of prophylactic platelet transfusion in adult dengue patients. PLoS Negl Trop Dis. 2016. 10: 0004576.
9. Estcourt LJ, Stanworth SJ, Doree C, Hopewell S, Murphy MF, et al. Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation. Cochrane Database Syst Rev. 2012. CD004269.
10. Goh ZJ, Li R, Wang MX, Chia PY, Lim JT. Transfusion of blood products and clinical outcomes for patients with dengue fever: a systematic review and meta-analysis. Open Forum Infect Dis. 2024. 11: 507.
11. World Health Organization. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. 3rd ed. Geneva: WHO. 2009.
12. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019. 3: 3829-3866.
13. Mazzucconi MG, Fazi P, Bernasconi S, De Rossi G, Leone G, et al. Therapy with high-dose dexamethasone (HD-DXM) in previously untreated patients affected by idiopathic thrombocytopenic purpura: a GIMEMA experience. Blood. 2007. 109: 1401-1407.
14. Wills BA, Oragui EE, Stephens AC, Daramola OA, Dung NM, et al. Coagulation abnormalities in dengue hemorrhagic fever: serial investigations in 167 Vietnamese children with dengue shock syndrome. Clin Infect Dis. 2002. 35: 277-285.
15. Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, et al. Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. J Infect Dis. 2000. 181: 2-9.

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