



INFLUENCE OF DIABETES MELLITUS ON DISEASE OUTCOMES AND COMPLICATIONS IN DENGUE FEVER: A PROSPECTIVE OBSERVATIONAL STUDY.

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ABSTRACT

Background: Diabetes mellitus is increasingly recognized as a host-level risk factor that may worsen the clinical trajectory of dengue infection by amplifying inflammatory and endothelial dysfunction, thereby predisposing to complications and severe disease.

Objectives: To compare disease outcomes, complication rates, transfusion requirements, and hospital stay between dengue patients with and without diabetes mellitus.

Methods: This prospective observational study included 100 serologically confirmed dengue patients admitted to a tertiary care center in Mumbai from June 2023 to June 2024. Patients were categorized into diabetic (n=25) and non-diabetic (n=75) groups. Clinical severity was classified according to the WHO 2009 criteria. Outcome variables included development of complications (shock, bleeding, fluid accumulation, hepatic/renal involvement), transfusion requirement, level of care (ward vs. HDU/ICU), duration of hospitalization, and final clinical outcome. Statistical significance was set at $p < 0.05$.

Results: Diabetic patients exhibited a higher proportion of warning signs (56.0% vs. 29.3%) and severe dengue (16.0% vs. 5.3%) than non-diabetics. Shock (12.0% vs. 2.7%) and hepatic involvement (40.0% vs. 24.0%) were more frequent in the diabetic subgroup. Transfusion requirement (32.0% vs. 9.3%) and HDU/ICU admission (20.0% vs. 4.0%) were also significantly higher among people with diabetes. Length of hospital stay was longer in diabetics (mean 5.8 vs. 4.6 days), and the only fatality occurred in this group.

Conclusion: Diabetes mellitus meaningfully worsened prognostic outcomes in dengue, as reflected by higher complication rates, greater need for escalated care, and prolonged hospitalization. These findings highlight diabetes as an early risk marker requiring intensified monitoring and proactive management to prevent deterioration.

Keywords: Dengue; Diabetes mellitus; Severe dengue; Complications; Transfusion; ICU admission; Prognosis

INTRODUCTION

Dengue fever continues to pose a significant clinical challenge in endemic regions because of its unpredictable course and potential to progress from a mild illness to a life-threatening disease. Outcomes in dengue are not determined solely by viral virulence but also by host-related factors that modulate immune, metabolic, and vascular responses to infection. In recent years, the increasing burden of non-communicable diseases has introduced new layers of complexity in the clinical management of dengue, particularly in adults with metabolic comorbidities.^{1,2}

Among these comorbidities, diabetes mellitus has received particular attention due to its established association with endothelial damage, impaired microcirculation, and dysregulated inflammatory pathways. These mechanisms can amplify the consequences of dengue-associated plasma leakage, capillary fragility, and organ stress, thereby predisposing diabetic individuals to more unfavorable clinical trajectories.^{3,4} In several hospital-based studies, the presence of diabetes has been linked to worse outcomes, including higher rates of warning signs, prolonged hospitalization, and increased need for supportive interventions such as transfusion or intensive monitoring.^{5,6,7}

The interplay between hyperglycemia and dengue infection may also influence the severity of complications such as hepatic dysfunction, fluid overload, bleeding manifestations, and hemodynamic instability.⁸

Evidence remains heterogeneous, with most existing data being retrospective or restricted to limited endpoints. Robust prospective comparisons of dengue outcomes in people with diabetes versus non-diabetics are still lacking, particularly in India, where both conditions are highly prevalent. This study prospectively evaluates whether diabetes mellitus alters complication rates, transfusion requirements, hospital stay, and overall outcomes in dengue, aiming to clarify its prognostic impact and improve risk stratification in this high-risk subgroup.

MATERIALS AND METHODS

Study Setting, Design, and Duration: This prospective observational study was conducted in the Department of General Medicine at a tertiary healthcare institute. Data were collected over one year from June 2023 to June 2024, encompassing the peak dengue transmission season. The study was designed to assess the influence of pre-existing diabetes mellitus on the clinical course and outcomes of dengue infection.

Study Population: All individuals aged 15–75 years with serologically confirmed dengue infection (NS1 antigen or IgM/IgG ELISA positivity) were assessed for eligibility and subsequently stratified according to glycemic status into two cohorts: a diabetic group comprising previously diagnosed diabetics or newly detected cases with HbA1c $\geq$ 6.5%, and a non-diabetic group consisting of patients without known diabetes and HbA1c $<$ 6.5%. Cases presenting with other concomitant infections (including malaria, scrub typhus, enteric fever, leptospirosis, or COVID-19), chronic liver or kidney disease, pregnancy, sepsis, or HIV/AIDS were excluded to minimize confounding influences on clinical outcomes.

Sample Size and Sampling Technique: A total of 100 patients fulfilling the inclusion criteria were enrolled consecutively using purposive sampling. Of these, 25 were in the diabetic group and 75 were non-diabetic. The sample size had been estimated a priori based on anticipated differences in clinical outcomes between the two cohorts.

Outcome Assessment and Definitions: Data were recorded at the time of admission and continuously monitored throughout the hospital stay to evaluate the following clinical outcomes: the development of disease-related complications such as plasma leakage, hemodynamic shock, hemorrhagic manifestations, or hepatic dysfunction; the need for blood or platelet transfusion; the total duration of hospitalization (in days); the requirement for escalation of care from the general ward to a high-dependency unit or intensive care unit; and the final clinical outcome in terms of recovery or mortality. Disease severity was categorized according to the WHO 2009 criteria into dengue without warning signs, dengue with warning signs, and severe dengue. Prolonged hospital

stay was defined as >5 days. Transfusion requirement was determined based on clinical judgment and institutional protocol.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee before commencement. Written informed consent was obtained from all study participants. Data confidentiality was maintained throughout the study.

Data Analysis: Data were entered and analyzed using Epi Info 7 software. Continuous variables were summarized as mean $\pm$ standard deviation, while categorical variables were expressed as proportions. Group comparisons were performed using a *t*-test or Chi-square/Fisher's exact test as appropriate. A *p*-value <0.05 was considered statistically significant.

RESULTS

Table 1. Clinico-demographic profile, selected WHO warning signs, and WHO 2009 severity classification

Variable	Non-diabetic (n=75)	Diabetic (n=25)
Age (years)		
• <20	10 (13.3%)	1 (4.0%)
• 21–40	25 (33.3%)	7 (28.0%)
• 41–60	37 (49.3%)	17 (68.0%)
• >60	3 (4.0%)	0 (0.0%)
Sex		
• Male	53 (70.7%)	18 (72.0%)
• Female	22 (29.3%)	7 (28.0%)
WHO warning signs		
• Abdominal pain/tenderness	23 (30.7%)	17 (68.0%)
• Persistent vomiting	26 (34.7%)	10 (40.0%)
• Mucosal bleeding	1 (1.3%)	0 (0.0%)
• Clinical fluid accumulation (ascites/effusion)	2 (2.7%)	1 (4.0%)
WHO 2009 severity classification		
• Dengue without warning signs	49 (65.3%)	7 (28.0%)
• Dengue with warning signs	22 (29.3%)	14 (56.0%)
• Severe dengue	4 (5.3%)	4 (16.0%)

Table 1 shows that diabetic dengue patients were concentrated in the older age group (41–60 years), whereas non-diabetic patients were more evenly distributed across younger age groups. Although the sex distribution was similar across both groups, the burden of WHO warning signs at presentation was markedly higher in diabetics, especially abdominal pain and persistent vomiting, indicating early clinical instability. This translated into a significantly larger proportion of diabetics progressing to either "dengue with warning signs" or "severe dengue," suggesting that underlying metabolic disease may predispose to a more aggressive disease trajectory from the outset.

Table 2. In-hospital complications and organ involvement

Complications	Non-diabetic (n=75)	Diabetic (n=25)	p-value
Shock	2 (2.7%)	3 (12.0%)	0.04
Clinically significant bleeding	2 (2.7%)	2 (8.0%)	0.18
Fluid accumulation (ascites/pleural effusion)	5 (6.7%)	4 (16.0%)	0.11
Hepatic involvement	18 (24.0%)	10 (40.0%)	0.10
AKI	3 (4.0%)	2 (8.0%)	0.36

Table 2 shows that complications during the course of illness were more frequent among diabetic patients. Shock occurred nearly fourfold more often in the diabetic group, and fluid accumulation was also higher, reflecting more pronounced capillary leak. Hepatic involvement was substantially more common in people with diabetes, consistent with their heightened metabolic vulnerability. Although bleeding events were numerically higher among people with diabetes as well, the difference was not statistically significant. Overall, diabetics exhibited a broader spectrum of organ involvement once complications began to evolve.

Table 3. Interventions and level of care

Intervention / Level of care	Non-diabetic (n=75)	Diabetic (n=25)	p-value
Platelet transfusion (any)	7 (9.3%)	8 (32.0%)	0.006
Packed RBC / FFP	1 (1.3%)	1 (4.0%)	0.38
HDU/ICU admission	3 (4.0%)	5 (20.0%)	0.01

Table 3 highlights that diabetics required more therapeutic interventions and escalation of care compared to non-diabetics. Platelet transfusion requirements were disproportionately higher in the diabetic subgroup, and a greater share of diabetic patients required HDU/ICU admission, reflecting greater clinical complexity. These findings suggest that comorbid diabetes not only modifies disease progression but also increases the overall resource burden in terms of transfusion support and level of inpatient monitoring.

Table 4. Length of stay and disposition

Outcome	Non-diabetic (n=75)	Diabetic (n=25)	p-value
Length of stay, days — mean ± SD	4.6 ± 1.8	5.8 ± 2.1	0.002
Hospital stay >5 days	12 (16.0%)	10 (40.0%)	0.01
In-hospital death	0 (0.0%)	1 (4.0%)	0.08

Table 4 describes differences in clinical outcomes and hospital stay duration. Diabetic patients required significantly longer hospitalization, with a higher proportion staying beyond five days, indicating slower clinical recovery. Furthermore, the only in-hospital death observed in this study occurred in the diabetic group, whereas all non-diabetic patients were discharged successfully. These differences reinforce the observation that diabetes serves as an adverse prognostic marker in dengue infection, contributing to prolonged illness and less favorable outcomes.

DISCUSSION

In this cohort, diabetes mellitus (DM) was associated with a higher burden of WHO warning signs at presentation and a larger proportion classified as severe dengue, alongside more frequent shock, greater need for transfusion and HDU/ICU care, longer hospitalization, and one in-hospital death. These directions align with a robust body of evidence showing that diabetes independently increases the odds of severe clinical presentation in dengue. A landmark meta-analysis reported that pre-existing DM approximately doubles the risk of severe dengue (OR ~1.75), underscoring the consistency of our findings with pooled estimates across diverse settings.¹⁰ Recent updates further reinforce this association, including a 2024 synthesis that again found DM significantly elevates the risk of severe disease across arboviral infections, with dengue contributing the bulk of events.¹¹

The complication profile in our study—particularly the excess of shock and clinically relevant fluid accumulation among diabetics—echoes observations from adult cohorts. In a Taiwanese series, DM was linked to increased risk of dengue shock syndrome/severe dengue, and the effect appeared stronger with co-morbid conditions or poorer glycemic control.¹² Beyond hemodynamics, our diabetics showed greater hepatic involvement; this is biologically plausible and supported by cohort studies suggesting that metabolic inflammation and endothelial dysfunction lower hepatic resilience during dengue, thereby potentiating transaminase elevations and clinical decompensation.¹² Our

results also mirror broader prognostic literature that identifies DM among the key host comorbidities predicting progression to severe dengue.¹³

Greater resource utilization in the DM group in our cohort—more platelet transfusions and higher rates of HDU/ICU admission—aligns with contemporary analyses highlighting DM as a risk factor for escalation of care.¹² Multi-country work has emphasized that DM modifies the microvascular and inflammatory response to dengue, lowering physiological reserve and increasing the likelihood of organ dysfunction and severe outcomes; our higher rates of shock and prolonged hospitalization in diabetics are directionally consistent with those observations.¹³ While ICU outcome studies in severe dengue are heterogeneous, they consistently show that once intensive care is required, mortality rises steeply—underscoring the clinical importance of early risk stratification in diabetics to prevent late deterioration.¹⁵

Finally, our longer length of stay among people with diabetes coheres with the cumulative picture: more warning signs, more severe classifications, and more complications translate into extended recovery times. The totality of evidence—from systematic reviews and prediction meta-analyses to country-level cohorts—supports treating diabetes as a prognostic modifier in dengue rather than a coincidental comorbidity. Early identification of diabetic status, vigilant monitoring for warning signs, and a lower threshold for escalation (e.g., timely observation in higher-dependency settings) are practical implications directly supported by our data and by external literature.^{10,12,13}

CONCLUSION

This study demonstrates that diabetes mellitus significantly alters the clinical course and outcomes of dengue infection, with a higher frequency of WHO warning signs, greater progression to severe dengue, and increased rates of shock and organ involvement. Diabetic patients required more transfusion support, more frequent escalation to HDU/ICU-level care, and experienced longer hospitalization compared with non-diabetics. These findings are consistent with international evidence showing that diabetes acts as an independent prognostic modifier in dengue by reducing physiological reserve and amplifying vascular and inflammatory stress responses. Early identification of diabetic status, vigilant monitoring for evolving warning signs, and timely escalation of supportive care should therefore be considered key components of management to mitigate severe outcomes in this high-risk subgroup.

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