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A study on the new onset of diabetes mellitus in patients with dengue fever

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Abstract
Background: Dengue, the most widespread arboviral illness globally, has seen a 4.5-fold increase in incidence from 1990 to 2017. The primary vector, Aedes aegypti, thrives in tropical and subtropical regions, impacting over 100 countries. Dengue has four serotypes, causing symptoms from mild fever to severe dengue hemorrhagic fever (DHF). Diabetes mellitus (DM), prevalent in dengue-endemic areas, exacerbates dengue symptoms due to compromised immunity and chronic inflammation. Understanding the link between severe dengue and diabetes is critical amid rising prevalence.
Aim of the study: This study reports the findings of newly diagnosed Type 2 diabetes mellitus among patients previously diagnosed with dengue fever.
Methods: The study conducted at North Bengal Medical College Hospital, Sirajganj, from June to November 2023, observed 320 hospital-admitted patients with confirmed dengue and diabetes. It involved both descriptive and analytic elements, utilizing purposive sampling. Participants met inclusion criteria of fever, positive NS1 and/or IgM antibodies for dengue, and confirmed diabetes mellitus. Random fasting blood glucose levels were checked for all patients, and confirmed by oral glucose tolerance test.
Result: The majority of patients were aged 30-59 (73.75%), with more males (65%) than females (35%). Service holders made up 47.5%, housewives 20%, and unemployed individuals 15%. Half were low-income, 45% middle-income, and 5% high-income. Most had Type 2 diabetes (92.5%). Fever was the most common symptom (91.25%), followed by petechiae, bone pain, headache, and rashes. Hypertension was the most frequent comorbidity (51.25%). Recovery within three days was seen in 33.33% of Type 1 and 16.22% of Type 2 diabetes patients. Recovery beyond three days occurred in 66.67% of Type 1 and 78.38% of Type 2 diabetes patients.
Conclusion: This study finds a notable prevalence of Type 2 diabetes among dengue fever patients, especially middle-aged to older males. Common symptoms include fever, bone pain, and petechiae. Hypertension worsens severity. Dengue may trigger diabetes, emphasizing the need for rigorous glycemic monitoring in these patients to reduce complications.

Keywords: Diabetes mellitus, dengue fever, and dengue virus

1. Introduction
Dengue is the world's most prevalent arboviral illness [1]. The incidence of Dengue has risen 4.5-fold over the past three decades, from 1990 to 2017 [2]. The primary vector for Dengue globally is *Aedes aegypti*, commonly found in tropical and subtropical regions, causing infections in over 100 countries [1, 3]. The broad habitat preferences of *A. aegypti* give it an advantage, enabling it to invade larger areas more rapidly. Kraemer *et al.* (2019) projected that over the next 30 years, 19.96 million km^2 of land will become suitable for *A. aegypti*, potentially putting 49.13% of the global population at risk of Dengue fever, considering factors like climate change, population growth, and urbanization [4]. The Dengue virus has four serotypes: Den 1, Den 2, Den 3, and Den 4. Each serotype can cause a wide range of clinical symptoms, from mild, nonspecific febrile illness and classic dengue fever (DF) to dengue hemorrhagic fever (DHF). DF is usually self-limiting, with patients typically experiencing fever, joint pain, muscle pain, and headache. In contrast, DHF is marked by thrombocytopenia, bleeding, and plasma leakage due to increased vascular permeability [5]. Infection with a single serotype provides lifelong immunity to that specific type but only temporary immunity to others.

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If subsequently infected with a different serotype, the risk of severe complications increases. When infected, cells initially respond by producing interferon, a cytokine that boosts various defenses against viral infections via the innate immune system [6, 7]. Certain dengue virus serotypes seem to have mechanisms to slow down this process. It has been suggested that pre-existing chronic conditions, such as diabetes, may increase the risk of developing severe dengue [8]. Diabetes mellitus (DM) is an endocrine disorder characterized by abnormal glucose metabolism. Patients with DM typically have elevated blood glucose levels, leading to various complications associated with hyperglycemia [9]. In dengue-endemic areas, the prevalence of DM is also high, and previous studies revealed that dengue and DM can co-occur [10, 11]. Hyperglycemia affects the structural and functional integrity of the endothelium, leading to chronic inflammation through T-lymphocyte activation and the production of proinflammatory cytokines like gamma interferon (IFN) and TNF. These factors significantly contribute to the primary symptoms of severe dengue fever. Additionally, diabetes mellitus negatively impacts the immune system by reducing chemotaxis, leukocyte adhesion, and phagocytosis of infections, thereby increasing susceptibility to infections [12-14]. Due to weakened immunity, fragile blood vessels, and an increased risk of hemorrhage, symptoms of dengue often exacerbate in individuals with diabetes. Given the rising prevalence of both conditions, it's crucial to comprehend the association between severe dengue and diabetes mellitus [14]. This study reports the findings of newly diagnosed Type 2 diabetes mellitus among patients previously diagnosed with dengue fever.

Methodology and Materials

This study employed a hospital-based observational approach with both descriptive and analytic components. The participants were hospital-admitted patients (both male and female) in the Department of Medicine at North Bengal Medical College Hospital, Sirajganj, from June 2023 to November 2023. The present study involved 320 patients. The study group was selected from all adult dengue patients with laboratory-confirmed diagnoses. Additionally, Random fasting blood glucose levels were checked for all patients and confirmed by oral glucose tolerance test (OGTT). Purposive sampling was used. The study protocol was approved by Ethics Committee of the Institution.

Inclusion criteria

All included patients exhibited fever, tested positive for NS1 and/or IgM antibodies against dengue, and had confirmed diabetes mellitus.

Exclusion criteria

Among 320 patients, 120 known nondiabetic patients and patients with negative IgM antibodies (120 patients) were excluded.

Data Collection and Analysis

Data was gathered according to patients' records. The results are presented subsequently in tables and graphs and their significance is discussed. All data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (Version 26.0). For the quantitative and qualitative variables, the mean±standard deviation and the frequency and rate, respectively, were measured.

Result

The demographic characteristics of the 80 patients included in the study are presented in Table 1. The majority of patients were in the age range of 30-59 years (73.75%), followed by those aged 60-80 years (18.75%), with a smaller proportion falling in the 15-29 age group (7.5%). In terms of gender distribution, there were more male patients (65%) than female patients (35%). 47.5% of patients were service holders, followed by 20% housewives, and 15% unemployed individuals. Businesspersons, laborers, and cultivators constituted smaller percentages at 8.75%, 3.75%, and 5%, respectively. Half of the patients fell into the low-income category (50%), while 45% were classified as middle-income and 5% as high-income group (Table 1). Among all, 92.5% had Type 2 diabetes and 7.5% had Type 1 diabetes (Figure 1). The results indicate that fever (91.25%) was the most common symptom/sign observed at hospital presentation among patients. Other frequently reported symptoms included bone pain (45.00%), petechiae (56.25%), headache (38.75%), and rashes (36.25%). Abdominal pain, myalgia, vomiting/nausea, and gastrointestinal bleeding were also reported by a notable proportion of patients, with percentages ranging from 16.25% to 33.75%. Orbital pain, hemoptysis, and gum bleeding were less commonly observed, with percentages ranging from 6.25% to 23.75% (Table 2). Table 3 shows that associated comorbid conditions include hypertension (51.25%), chronic kidney disease (1.25%), end-stage renal disease (2.5%), previous stroke (1.25%) and ischemic heart disease (3.75%). Among patients with Type 1 diabetes (N=6), 33.33% recovered within 3 days, and 66.67% recovered in more than 3 days. For patients with Type 2 diabetes (N=74), 16.22% recovered within 3 days, and 78.38% recovered in more than 3 days (Table 4).

Table 1: Demographic characteristics of patients (N=80).

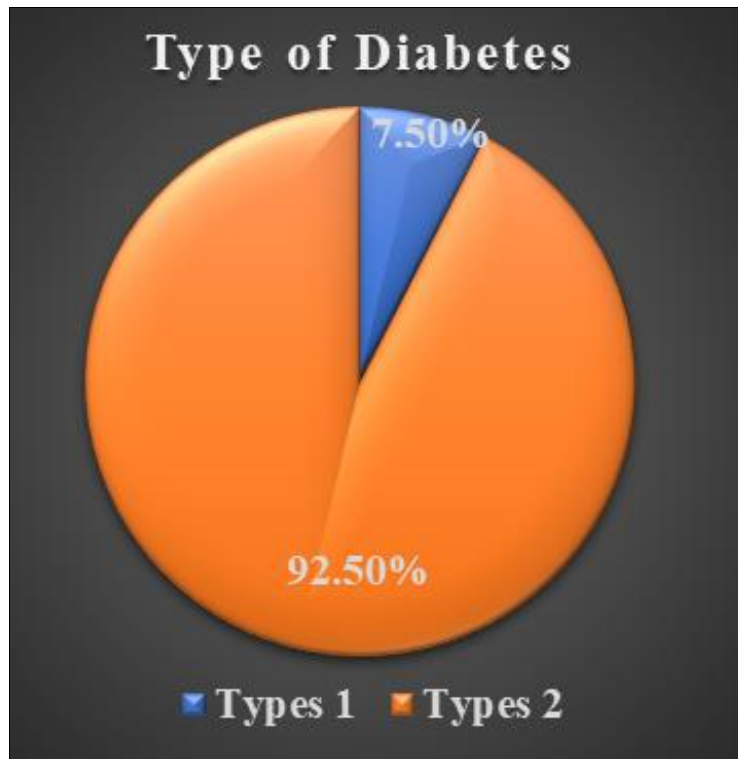| Variables	No. of patients	Percentage
Age (in years)		
15-29	6	7.5
30-59	59	73.75
60-80	15	18.75
Gender		
Female	28	35
Male	52	65
Occupation		
Service holder	38	47.5
Business	7	8.75
Labour	3	3.75
Cultivator	4	5
Housewife	16	20
Unemployed	12	15
Economic status (Per year)		
Low (<60,000 Tk.)	40	50
Middle (60,000-1,80,000 Tk.)	36	45
High (>180,000 Tk.)	4	5

Fig 1: Type of diabetes mellitus (N=80).

Table 2: Symptoms/signs at hospital presentation among patients.

Sign and symptom	No. of patients	Percentage
Fever	73	91.25
Abdominal pain	27	33.75
Orbital pain	9	11.25
Bone pain	36	45.00
Myalgia	22	27.5
Headache	31	38.75
Rashes	29	36.25
Vomiting/nausea	25	31.25
Diarrhea	13	16.25
Petechiae	45	56.25
Gastrointestinal bleeding	19	23.75
Gum bleeding	19	23.75
Hemoptysis	5	6.25

Table 3: Associated comorbidity of the study population (N=80).

Comorbid condition	No. of patients	Percentage
Hypertension	41	51.25
Chronic kidney disease	1	1.25
End-stage renal disease	2	2.5
Previous stroke	1	1.25
Ischemic heart disease	3	3.75

Table 4: General outcome of the study patients based on diabetic type.

Variables	Type 1 (N=6)		Type 2 (N=74)	
	n	%	n	%
Recovery within ≤3days	2	33.33	12	16.22
Recovery within >3 days	4	66.67	58	78.38
Death	0	0.00	0	0.00

Discussion

The prevalence and frequency of diabetes and dengue is increasing internationally. However, it is critical to determine the relationship between dengue and diabetes mellitus. Moreover, if the severity of dengue keeps on rising in uncontrolled or poorly controlled diabetes patients then it would result in higher morbidity and mortality in comparison to the diabetic and non-diabetic populations [15-17]. The author hereby assesses the effect of the glycosylation process in poor glycemic control cases on the course of dengue infection. In this study, 80 patients were enrolled as per the inclusion and exclusion criteria. Among the study population, the maximum number of patients with both diabetes and dengue infection were found to be in the 30-59 years age group (73.75%), followed by the 60-80 years age group (18.75%). Other similar studies also found that the most affected age group was 30-60 years [12,13]. This suggests that individuals in their middle to late adulthood are more susceptible to diabetes and dengue infection. Gender distribution indicates a higher prevalence of diabetes linked to dengue among males, constituting 65% of the patients. Conversely, other studies reported the increased prevalence of female than male [18, 19]. These disparities can be due to differences in exposure or behavioral patterns. Occupationally, service holders represent the largest proportion of patients, followed by housewives. This finding aligns with a previous study [18]. Economic status also emerges as a significant factor, with half of the patients belonging to the low-income category. This highlights the potential role of socio-economic factors in dengue infection, including access to healthcare, living conditions, and preventive measures against mosquito breeding. The prevalence of diabetes among the patients in this study is notable, with a substantial majority (92.5%) having Type 2 diabetes, while a smaller proportion (7.5%) had Type 1 diabetes. Lee *et al*. also observed the linkage between dengue fever and Type 2 diabetes [19]. This finding highlights the significant association between dengue fever and Type 2 diabetes, indicating a potential link between the two conditions. Fever is the most commonly reported symptom, observed in 91.25% of patients, which aligns with the characteristic fever associated with dengue infection.

Additionally, bone pain and myalgia are prevalent, reported by 45% and 27.5% of patients, respectively, reflecting the musculoskeletal manifestations commonly seen in dengue fever. Headache, abdominal pain, rashes gastrointestinal symptoms, and hemorrhagic manifestations are also frequently reported. Regarding signs and symptoms, our findings are comparable with the study of Lee *et al*. and Latt *et al* [18, 19]. Diabetic dengue patients with significantly higher incidences of severe bleeding suggest that they should be target candidates for strict monitoring of the emergence of warning signs that require urgent treatment. Besides diabetes, the comorbidities (i.e., HTN, CKD, ESRD, stroke, and IHD) in our patients are also reported to cause damaged vasculature in major organs. HTN was the predominant comorbidity (91.25%). Dengue patients with a coexisting DM and HTN were previously reported to be at higher risk for developing dengue hemorrhagic fever (DHF) [20]. Previous studies found an association between comorbidities like hypertension, ischemic heart disease, bronchial asthma, cardiac disorder, renal disorder, and skin allergy with the severity of dengue [21-24].

Limitations of the study: The study is limited by its observational design and reliance on purposive sampling, which may introduce selection bias and limit the generalizability of the findings. The sample size is relatively small, encompassing only 80 patients, and the study is conducted in a single hospital, further restricting the applicability of the results to broader populations.

Conclusion and Recommendations
This study concludes that there is a notable prevalence of newly diagnosed Type 2 diabetes mellitus among patients previously diagnosed with dengue fever. The majority of affected individuals are in their middle to late adulthood, with a higher incidence observed in males. Fever, bone pain, and petechiae are the most common symptoms, and comorbid conditions, particularly hypertension, significantly contribute to disease severity. The findings suggest that dengue fever may serve as a trigger for the onset of diabetes mellitus, particularly Type 2, highlighting the need for rigorous monitoring and management of glycemic control in dengue patients to reduce morbidity and potential complications.

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Ethical approval: The study was approved by the Institutional Ethics Committee.

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