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# Association of dysglycemia with severity of COVID-19 disease in Bangladeshi patients

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## Abstract

**Background:** The coronavirus disease 2019 (COVID-19) pandemic has had a significant global impact. While pre-existing diabetes is a known risk factor for severe COVID-19, recent evidence suggests that severe COVID-19 may also significantly contribute to the development of new-onset dysglycemia.

**Objective:** To determine the association between COVID-19 severity and the development of new-onset dysglycemia (diabetes and prediabetes) among Bangladeshi patients and to identify clinical factors associated with this relationship.

**Methods:** This cross-sectional study enrolled 88 participants without a pre-existing diagnosis of diabetes mellitus within 6 months of COVID-19 infection from the post-COVID outpatient clinic and the Department of Endocrinology of Bangabandhu Sheikh Mujib Medical University, Dhaka, from July 2021 to June 2022 by convenient sampling. Patients were categorized based on COVID-19 severity (mild/moderate vs. severe) and assessed by oral glucose tolerance tests (OGTT) and hemoglobin A1c (HbA1c). Glucose levels were measured by glucose oxidase method and HbA1c through ion-exchange high-performance liquid chromatography.

**Results:** Among 88 participants, 11 had severe COVID-19, and 77 had mild-to-moderate. The severe group had a lower frequency of urban residence than rural (63.6% vs. 92.2%, p=0.02), lower vaccination rates (63.6% vs. 92.2%, p=0.02), and lower lymphocyte count than the mild to moderate group (35.0% vs. 19.3%, p=0.03). At 6 months, severe COVID-19 cases had higher fasting (p=0.05) and plasma glucose 2-hour after 75-gm oral glucose (p=0.01) but no significant differences in HbA1c (5.6 vs. 5.8%, p=0.11) than the mild to moderate group. Dysglycemia was more prevalent in severe cases than mild to moderate cases (63.6% vs. 31.2%, p=0.04; prediabetes 54.5% vs. 22.1%, diabetes 9.1% in both), with an odds ratio for dysglycemia 3.68 (95% CI: 1.03-14.88, p=0.04).

**Conclusion:** Severe COVID-19 is observed to be associated with the development of new-onset dysglycemia, particularly prediabetes, in Bangladeshi patients. *[J Assoc Clin Endocrinol Diabetol Bangladesh, January 2025; 4 (1): 04-08]*

**Keywords:** Severe COVID-19, New onset dysglycemia, Prediabetes

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## Introduction

The emergence of Coronavirus disease 2019 (COVID-19) in late 2019 triggered a global health crisis, with the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leading to a wide range of symptoms and disease severities. While most cases

presented with mild to moderate illness, a considerable number of patients progressed to severe disease requiring hospitalization, oxygen therapy, and intensive care.[1] Understanding the factors influencing COVID-19 severity is crucial for optimizing patient care and developing effective strategies to combat the virus.

One concerning aspect of COVID-19 infection is its potential to exacerbate existing chronic conditions, particularly diabetes. Studies have shown that pre-existing diabetes significantly increases the risk of severe COVID-19 complications and mortality.[2] However, a growing body of evidence suggests a more complex relationship, with COVID-19 itself potentially triggering the development of new-onset dysglycemia.[3] Recent research indicates a potential link between the severity of COVID-19 infection and the development of new-onset dysglycemia.[4] This newfound association necessitates further investigation, particularly in regions like Bangladesh, where the prevalence of both COVID-19 and diabetes is high.[5]

Bangladesh has emerged as a global hotspot for both COVID-19 and diabetes. According to the International Diabetes Federation (IDF), in 2021, the estimated national diabetes prevalence of Bangladesh was 14.2%, highlighting the vulnerability of the population.[6] Furthermore, research revealed a significant burden of COVID-19 cases in Bangladesh, with potential underreporting.[7] Given this context, investigating the interplay between COVID-19 severity and new onset dysglycemia in Bangladesh holds significant public health implications.

COVID-19 may trigger new-onset diabetes through multiple mechanisms, including direct viral damage to pancreatic beta cells, leading to beta-cell dysfunction and systemic inflammation, causing insulin resistance. Additionally, the use of corticosteroids in severe cases may exacerbate hyperglycemia.[8] Unveiling the potential link between COVID-19 and new onset dysglycemia can contribute to a more comprehensive understanding of the virus's long-term effects. It can also inform the development of targeted interventions for high-risk individuals, particularly those with severe COVID-19. Our study aimed to investigate whether patients with severe COVID-19 are more likely to develop new-onset dysglycemia compared to those with mild/moderate illness and to identify clinical characteristics associated with COVID-19 severity and dysglycemia. By exploring these questions, this study sought to contribute to the growing body of knowledge surrounding COVID-19 and its potential to trigger new-onset diabetes.

## Methods

**Study design and participants:** This cross-sectional, observational study was conducted at the Post-COVID Outpatient Department (OPD) and the Department of Endocrinology of Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2021 to June 2022. A total of 88 patients were selected by convenient sampling technique based on inclusion and exclusion criteria, with patients classified into two groups: mild/moderate or severe COVID-19 based on clinical severity.[9]

**Selection criteria:** Patients were included if they had: (1) a COVID-19 diagnosis confirmed via reverse transcription polymerase chain reaction (RT-PCR) within 6 months prior to enrollment and (2) aged 18 years or more. Those with (1) pre-existing diagnosis of diabetes mellitus, (2) history of taking drugs like steroids or cancer chemotherapy before (3) pregnancy and lactation were excluded.

**Data collection:** Data were collected using a semi-structured questionnaire that included demographics (age, sex, residence), COVID-19 severity, and pre-existing medical conditions. Lymphocyte counts, C-reactive protein (CRP), and D-dimer level during infection were obtained from medical records. COVID-19 severity was classified based on clinical criteria, including hospitalization, oxygen therapy, and intensive care unit (ICU) admission.[9]

**Glycemic measurements:** Glycemic assessments were performed using the oral glucose tolerance test (OGTT) and glycated hemoglobin level (HbA1c). Fasting plasma glucose (FPG) and 2-hour post-glucose plasma glucose (2h PG) levels were measured using the glucose-oxidase method. HbA1c was measured using ion-exchange high-performance liquid chromatography (HPLC).

**Statistical analysis:** Descriptive statistics were used to summarize patient characteristics, including age, body mass index (BMI), vaccination status, and COVID-19 severity. Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR), while categorical variables were presented as frequencies and percentages. To compare groups (mild/moderate

vs. severe COVID-19), the Chi-square or Fisher's exact test was applied for categorical data, and the independent t-test or Mann-Whitney U test was used for continuous variables. The association between COVID-19 severity and the development of new-onset dysglycemia was evaluated using odds ratios (OR) with a 95% confidence interval (CI). A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

**Ethical Considerations:** This study adhered to the principles of the Declaration of Helsinki. Approval from the Institutional Review Board (IRB) of BSMMU (Reg: No: 3749; BSMMU/2022/219) was obtained before study initiation. Patient confidentiality and anonymity were maintained throughout the study, and informed consent was taken from all participants.

## Results

A total of 88 patients were included in the study, with 11 categorized as having severe COVID-19 and 77 as mild-to-moderate cases. The mean age was slightly higher in the severe group (37 years vs. 33.89 years), but this difference was not statistically significant (p=0.11). The groups had no significant differences in body mass index (BMI) or the prevalence of pre-existing hypertension. However, rural residence (p=0.02) and lower vaccination rates (p=0.00) were significantly more common in the severe COVID-19 group. Lymphocyte levels were significantly lower in the severe group (p=0.03). At the same time, other inflammatory markers, such as CRP and D-dimer, showed non-significant trends toward being higher in the severe group [Table-I].

At the 6-month follow-up, the severe COVID-19 group had significantly higher FPG (p=0.05) and 2h PG levels (p=0.01) than the mild-to-moderate group. However, the two groups had no significant difference in HbA1c levels (p=0.55) [Table-II].

**Table-II:** Glycemic outcomes of the participants at 6 months (n=88)

| Variables | Severity of COVID-19 | | P |
|---|---|---|---|
| | Mild to moderate (n=77) | Severe (n=11) | |
| FPG [mmol/L; median (IQR)] | 5.2 (4.4, 7.4) | 5.7 (5.2, 5.9) | **0.05*** |
| 2h PG [mmol/L; median (IQR)] | 6.6 (3.5,15.5) | 8.3(6.4, 10.8) | **0.01†** |
| HbA1c [%; median (IQR)] | 5.6 (4.5, 7.9) | 5.8(5.2, 6.1) | 0.11† |

* calculated using the Independent t-test
†calculated using the Mann-Whitney U test
FPG: fasting plasma glucose 2h PG: plasma glucose 2h after 75 gm oral glucose
HbA1c: Hemoglobin A1c IQR: interquartile range

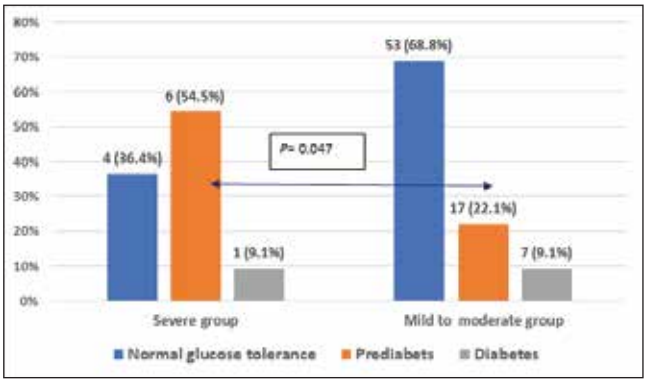
The overall prevalence of dysglycemia was significantly higher in the severe COVID-19 group (63.6%) compared to the mild-to-moderate group

**Table-I:** Baseline characteristics of study participants (n=88)

| Variables | | Severity of COVID-19 | | p |
|---|---|---|---|---|
| | | Mild to moderate (n=77) | Severe (n=11) | 0.11* |
| Age [years; median (IQR)] | | 33.9 (19, 57) | 37.0 (20, 60) | |
| Age category | <30 | 32 (41.6) | 1(9.1) | 0.07† |
| (years) | 31-50 | 38 (49.4) | 9 (81.8) | |
| | >51 | 7 (9.1) | 1 (9.1) | |
| BMI [kg/m$^2$; median (IQR)] | | 24.6 (16.4, 31.6) | 24.5 (21.5, 28.3) | 0.94† |
| Residence | Urban | 71 (92.2) | 7 (63.6) | **0.02*** |
| | Rural | 6 (7.8) | 4 (36.7) | |
| Vaccinated against COVID-19 | | 71 (92.2) | 7 (63.6) | **0.00*** |
| Hypertensive | | 19 (24.7) | 1 (9.1) | 0.44* |
| Lymphocyte [%, median (IQR)] | | 35.0% (22.5, 36) | 19.3% (7,28) | **0.03†** |
| CRP [mg/dL, median (IQR)] | | 6.2 (2.0, 61.7) | 44.0 (11.5, 178.0) | 0.11† |
| D-dimer [mg/L, median (IQR)] | | 0.11 (0.1,140.6) | 0.38 (0.2, 314.8) | 0.20† |

Within parenthesis values are percentages over column total if not mentioned otherwise
*calculated using the Mann-Whitney U test †calculated using Fisher's exact test
IQR: interquartile range BMI: body mass index CRP: C-reactive protein

(31.2%) (p=0.047). The severe group had a higher prevalence of prediabetes (54.5% vs. 22.1%), while the prevalence of diabetes was similar between the two groups (9.1% in both) [Figure-1]. Severe COVID-19 was associated with a 3.68 times higher risk of developing new-onset dysglycemia compared to mild to moderate cases (95% CI: 1.03-14.88).




P-value calculated by the Fisher Exact Test
Percentages are over group total

**Figure-1:** Prevalence of dysglycemia types in mild to moderate vs. severe COVID-19 cases

## Discussion

Our study found a significant association between COVID-19 severity and the development of new-onset dysglycemia, particularly prediabetes, in a Bangladeshi population. Those who suffered from severe COVID-19 had a 3.68 times higher risk of developing new-onset dysglycemia compared to mild-to-moderate cases within 6 months. This has a similar trend to the Keerthi BY et al. study, which has shown a higher prevalence of diabetes and prediabetes at 3 months after COVID-19 infection (30% and 5%).[10] Another study by Li J. found that new-onset diabetes and hyperglycemia were 1.75 times higher in COVID-19 patients than in non-COVID-19 patients.[4] The underlying mechanisms remain unclear, but potential factors include viral-induced pancreatic beta-cell dysfunction and systemic inflammation.

Interestingly, the occurrence of overt diabetes was similar in both severe and mild/moderate COVID-19 groups in the current study (around 9.1%). This is somewhat unexpected, considering the established association between diabetes and severe COVID-19 outcomes. A possible explanation could be the relatively small sample size of the study. Larger studies might be needed to confirm this finding.

This analysis of COVID-19 cases also revealed some interesting trends. While age, BMI, and pre-existing conditions (except vaccination) showed no major differences between mild/moderate and severe cases, vaccination status and residence played a role. Those who were unvaccinated and from rural areas were more likely to have severe illness. This analysis of COVID-19 cases aligns with existing research on the critical role of vaccination in reducing disease severity.[11] However, findings on age, BMI, and pre-existing conditions (except vaccination) warrant further exploration in larger studies, as established knowledge suggests these factors are often linked to worse outcomes.[12,13] The study aligns with the established association between inflammation markers and severity.[14,15] Further investigation in larger cohorts is needed to solidify these findings.

This study acknowledges the limitations inherent to its cross-sectional design. Additionally, the sample size may limit the generalizability of the findings. Future prospective studies with larger cohorts are warranted to explore this potential association further.

In summary, our study demonstrates a significant association between severe COVID-19 and new-onset dysglycemia, particularly prediabetes, highlighting the potential role of glucose dysregulation in disease severity. While overt diabetes rates were similar across groups, the higher prevalence of dysglycemia in severe cases suggests the need for further exploration of this link. Secondary findings emphasize the protective effect of vaccination, while lower lymphocyte counts align with immune dysregulation in severe COVID-19.

## Conclusions

Severe COVID-19 is significantly associated with the development of new-onset dysglycemia in Bangladeshi patients. The findings suggest that severe illness may precipitate impaired glycemic control, especially prediabetes. Rural living, lack of vaccination and lower lymphocyte count further contribute to this risk. Longitudinal studies are necessary to explore the underlying mechanisms in greater detail.

**Conflict of interest**

The authors have no conflicts of interest to disclose.

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**Financial Disclosure**
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**Data Availability**
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author upon reasonable request.

**Ethical Approval and Consent to Participate**
This study was approved by the Institutional Review Board (IRB) of BSMMU, Reg: No: 3749; BSMMU/2022/219. Informed written consent was obtained from each participant in the study.



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