Characteristics of patients with diabetes and prediabetes admitted for covid-19 treatment in Khulna: Single-centre cross-sectional study

**Syed Didarul Haque¹,
Prithwy Shankar Biswas²,
Purabi Sarkar³**

1. Syed Didarul Haque, Associate Professor, Department of Pharmacology & Therapeutics, Gazi Medical College, Khulna, Bangladesh.
2. Prithwy Shankar Biswas, Associate Professor, Department of Biochemistry, Gazi Medical College, Khulna, Bangladesh.
3. Purabi Sarkar, Assistant Professor & Head, Department of Pathology, Ad-din Akij Medical College, Khulna, Bangladesh.

Correspondence

Dr. Syed Didarul Haque, Associate Professor, Department of Pharmacology & Therapeutics, Gazi Medical College, Khulna, Bangladesh.
Mobile: +880-1720661978
e-mail: bappy.dmc.k64@gmail.com

Abstract

Background: The coronavirus disease 2019 (COVID-19) outbreak has become a significant threat to global health due to its highly contagious nature and varied mortality. Recent studies have shown that diabetes is an important risk factor contributing to the severity of COVID-19 and resulting mortality. Poor glycemic control is also associated with poor patient outcomes (e.g., hospitalisation and death). **Objectives:** This study aims to investigate the clinical characteristics of patients with diabetes and prediabetes admitted for COVID-19 treatment in Gazi Medical College Hospital (GMCH), Khulna, Bangladesh. **Materials and Methods:** This was a cross-sectional observational study on patients with diabetes and prediabetes who were diagnosed with COVID-19 based on laboratory and radiological findings and admitted to Gazi Medical College Hospital, Khulna, Bangladesh, from July 1 to July 31, 2021. In that timeframe, overall, 215 patients with COVID-19 were admitted. Among them, 47 patients having diabetes or prediabetes fulfilled the inclusion criteria for the study. Demographic, clinical, laboratory, and radiological data of those 47 patients were recorded and analysed. **Results:** Among 47 study subjects, 61.7% were male. The mean age of the patients was 55.5±12.9 years. Hypertension (44.7%) among the study subjects was the most common comorbidity. Regarding laboratory parameters, the mean HbA1c of the patients was 7.9±1.4%. In addition, the mean random blood sugar (RBS) level was 15.3±2.5 mmol/l. Neutrophilia and lymphocytopenia were observed in 93.6% and 95.7% of cases, respectively. The mean D-dimer (4.1 mg/l) and CRP (71.1 mg/l) levels were well above their normal limits. In a high-resolution chest CT scan (HRCT chest), bilateral lung involvement was present in 91.5% of cases. The ground-glass appearance was the most frequent (95.7%) radiologic pattern. Out of the 47 diabetic patients, 2 (4.3%) patients had type 1 diabetes, and 35 (74.5%) patients had type 2 diabetes. Moreover, 10 of 47 (21.2%) patients were prediabetic. Regular insulin was the most prescribed parenteral antidiabetic medication (63.9%). Among oral antidiabetic drugs, DPP-4 inhibitors were the most frequently used ones (21.3%). A total of 15 (31.9%) patients were severely affected by COVID-19 and admitted to the ICU, requiring mechanical ventilation. Six (6) patients (12.8%) died during our study due to multiple organ dysfunction syndrome or cardio-respiratory failure. **Conclusion:** The study provides critical information to understand better the clinical characteristics of patients with diabetes and prediabetes admitted for COVID-19 treatment, which may help physicians to identify the factors associated with adverse outcomes in this disease.

Keywords: Diabetes, Prediabetes, COVID-19, Gazi Medical College

Introduction

Towards the end of December 2019, pneumonia cases with no identifiable cause began to appear in Wuhan and quickly spread to most of China. The genetic makeup of the virus isolated from these patients revealed that it is one of the members of the Coronaviridae family; as a result, it was given the names "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" and "coronavirus disease 2019" (COVID-19) to describe the illness it causes (1). Since the World Health Organization (WHO) designated this sickness a pandemic in early March 2020, it has already spread to several nations worldwide (2). Managing COVID-19 patients is extremely difficult in countries like Bangladesh since the few medical resources are soon exhausted. IEDCR, the nation's epidemiology institute, released information about the first three instances on March 8th, 2020. Since then, the epidemic has progressively spread over the entire country, and the number of victims has risen (3). Bangladesh has experienced a threefold increase in coronavirus incidence during the previous several months. The specialised beds in many other hospitals are likewise filled, as are all COVID-19 hospitals in the capital and other cities (4). As of June 2021, it has been noted that Sylhet has the lowest confirmed cases rate (9.75%) out of all eight divisions in Bangladesh, while Khulna division possesses the highest known cases rate (19.94%) (5).

According to new studies, hyperglycemia is a key risk factor that influences the severity and mortality of COVID-19 (6). As documented in 20% to 30% of these individuals, diabetes is also an essential risk indicator for diagnosing severe pneumonia and the clinical course brought on by COVID-19 (7). It is also known that poor glycemic control, whether brought on by diabetes or stress hyperglycemia, is associated with unfavourable patient outcomes, including hospitalisation and death (8).

In this study, we sought to understand better the clinical characteristics of patients with diabetes and prediabetes who were admitted to Gazi Medical College Hospital in Khulna, Bangladesh, for COVID-19 management.

Materials and Methods

Study design

This was a cross-sectional, observational study of patients with diabetes diagnosed with COVID-19 based on laboratory or radiological findings and admitted to Gazi Medical College Hospital, Khulna, Bangladesh, from July 1 to July 31, 2021. In that timeframe, overall, 215 patients with COVID-19 were admitted. Among them, 56 patients had diabetes or prediabetes. Thus, 26.1% (56/215) of all patients admitted with COVID-19 had coexistent diabetes or prediabetes (9). Among them, 47 patients who fulfilled the inclusion criteria were selected for the study. This study was approved by the Ethical Review Board of the concerned institute (Ethical Clearance No: GMC/IER-B/2021/01).

Inclusion criteria

- Patients of either sex aged ≥18 years
- COVID-19-positive patients who were either diabetic or prediabetic
- Patients who gave consent to be included in the study

Exclusion criteria

- Pregnant women having gestational diabetes
- Patients who had incomplete data regarding clinical and laboratory profile

Case definitions (9)

- A positive reverse transcription-polymerase chain reaction (RT-PCR) test for COVID-19 and consistent imaging results from chest radiography or chest high-resolution computed tomography (HRCT), that is, radiological features of COVID-19 that are pathognomonic (for example, ground-glass opacity), were required to confirm a diagnosis of COVID-19.

- Hemoglobin A1c (HbA1c) levels ≥ 6.5% upon admission or a prior diagnosis of diabetes served as confirmation.

- HbA1c 5.7%–6.4% upon admission and prior diagnosis both supported the presence of prediabetes.

- Laboratory tests ordered within 24 hours after hospital admission were referred to as initial tests.

- When patients were clinically healthy and were negative on two consecutive nasopharyngeal swab tests (laboratory tests) for COVID-19 RT-PCR, they were released from the hospital.

Data collection

We reviewed each study participant's medical records, nursing notes, test results, and HRCT chest report. The demographic, clinical, biochemical, and radiological characteristics, treatments, and outcomes information was collected and then put into standardised data-collecting forms from patients' case files and electronic medical records. Up to July 31, 2021, clinical effects (such as discharges, death, and readmission) were monitored.

Data analysis

For descriptive explanations, the clinical and demographic parameters of the patients were collated. According to the situation, continuous variables were reported as means ± standard deviations (SDs) or medians (with interquartile ranges, IQR). We computed the frequencies and proportions of patients in each group for categorical variables. Microsoft Excel and SPSS Version 21.0 for Windows (SPSS Inc., Chicago, IL, USA) were used for all analyses.

Results

The demographic characteristics, laboratory findings, information about comorbidities, and HRCT chest reports of the 47 study subjects are described below.

Demographic characteristics:

We included 47 patients in this study, with 29 (61.7%) male and 18 (38.3%) female (Table-1). The age of the patients ranged from 21 to 79 years; the mean age was 55.5±12.9 years. Among the study subjects, 30 (63.8%) came from urban a,reas and 17 (36.2%) came from rural areas.

Laboratory findings

The first results of the laboratory tests after admission were analysed. The mean HbA1c of the patients was 7.9±1.4% **(Table 2)**. In addition, the mean random blood sugar (RBS) level was 15.3±2.5 mmol/l. The routine blood tests showed that the mean Hb concentration of the study subjects was 12.1±1.9 g/dl. The blood counts of 44 patients out of 47 (93.6%) showed neutrophilia (neutrophil count >70%), and 45 patients (95.7%) showed lymphocytopenia (lymphocyte count <20%). Also, 3 (6.4%) patients had thrombocytopenia (platelet count <1,50,000/cm). The mean D-dimer level of the study subjects was 4.1±3.7 mg/l. In addition, the mean plasma CRP and serum creatinine levels were

71.1±20.7 mg/l and 1.5±1.2 mg/dl, respectively. The median oxygen saturation level (SpO2) was 84 (IQR, 62 to 96) **(Table 2).**

Comorbidities

Among the study subjects, 32 patients had either one or more comorbidities. The most common comorbid condition was hypertension (HTN) [21 (44.7%)], followed by ischemic heart disease [6 (12.8%)], and bronchial asthma [4 (8.5%)]. Coexisting cerebrovascular disease, chronic kidney disease and chronic liver disease were found in 1 (2.1%) patient each **(Table 3).**

HRCT of chest

All 47 patients had abnormal findings on HRCT; bilateral lung field involvement was observed in 43 (91.5%), and unilateral lung field involvement was observed in 4 (8.5%) patients (Figure 1). Ground-glass opacity, the predominant CT imaging pattern, was observed in 45 (95.7%) patients, followed by patchy consolidation shadow in 22 (46.8%) patients. Interstitial abnormalities, including reticular appearance and interlobular septal thickening, were found in 9 (19.2%) patients (Figure 2).

Table 1: Demographic characteristics of the study subjects

Demographic characteristics	Patients (N = 47)
Sex	
Male	29 (61.7%)
Female	18 (38.3%)
Locality	
Urban	30 (63.8%)
Rural	17 (36.2%)

Table 2: Laboratory findings of the study subjects

Laboratory findings	Frequency (percentage)
HbA1c (%)	7.9±1.4*
RBS (mmol/l)	15.3±2.5*
Hb concentration (g/dl)	11.2±1.9*
Neutrophilia (neutrophil count >70%)	44 (93.6)
Lymphopenia (lymphocyte count <20%)	45 (95.7)
Thrombocytopenia (platelet count <1,50,000/cm)	3 (6.4)
D-dimer (mg/l)	4.1±3.7*
Plasma CRP (mg/l)	71.1±20.7*
Serum creatinine (mg/dl)	1.5±1.2*
Finger oxygen saturation level (SpO2)	84 (62 to 96) **

Table 3: Comorbidities of the study subjects

Comorbidities*	Frequency (percentage) n = 32
Hypertension	21 (44.7)
Ischemic heart disease	6 (12.8)
Bronchial asthma	4 (8.5)
Cerebrovascular disease	1 (2.1)
Chronic kidney disease	1 (2.1)
Chronic liver disease	1 (2.1)

*More than one comorbidity was reported in some patients

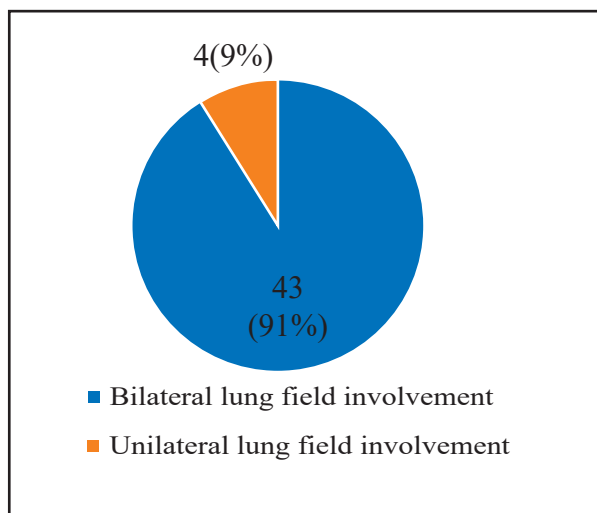**Fig 1.** Lung field involvement of the study subjects reported by HRCT of chest
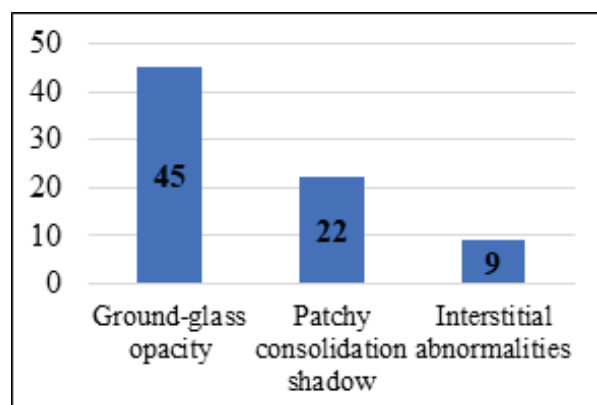

Fig 2. Imaging pattern found in HRCT of chest

The diabetes status of study subjects, information regarding antidiabetic drug use and clinical outcome are described below.

Status of diabetes

Out of the 47 diabetic patients, 2 (4.3%) patients had type 1 diabetes and 35 (74.5%) patients had type 2 diabetes. Moreover, 10 of 47 (21.2%) patients were prediabetic **(Table 4).**

The pattern of antidiabetic drugs used

A survey of the treatment regimen of the patients showed that, among parenteral drugs, regular insulin was the most prescribed medication [30 (63.9%], followed by long-acting insulin [8 (17.1%]. The premixed drug in the form of (regular+intermediate-acting) insulin was administered in 2 (4.3%) patients, and (rapid+intermediate-acting) insulin was given to 1 (2.1%) patient.

Among oral antidiabetic drugs, DPP-4 inhibitors were the most frequently used ones [10 (21.3%], followed by metformin in 6 (12.8%), sulfonylureas in 3 (6.4%) and SGLT-2 inhibitors in 2 (4.3%) patients **(Table 5).**

Table 4: Diabetes status of the study subjects

Type of diabetes	Frequency (percentage)
Type 1	2 (4.3%)
Type 2	35 (74.5%)
Prediabetes	10 (21.2%)

Table 5: Pattern of antidiabetic drug use among study subjects

Antidiabetic drugs*	Frequency (percentage)
Regular insulin	30 (63.9)
Long-acting insulin	8 (17.1)
(Regular+intermediate) insulin	2 (4.3)
(Rapid+intermediate) insulin	1 (2.1)
DPP-4 inhibitors**	10 (21.3)
Metformin	6 (12.8)
Sulfonylureas	3 (6.4)
SGLT-2 inhibitors***	2 (4.3)

* **The same patient could have received more than one drug**
** **DDP-4 inhibitors: dipeptidyl peptidase-4 inhibitors**
*** **SGLT-2 inhibitors: sodium-glucose co-transporter-2 inhibitors**

Clinical outcome

Among the study subjects, 15 (31.9%) patients were severely affected by COVID-19 and admitted to the ICU due to moderate or severe ARDS, requiring noninvasive mechanical ventilation therapy. The median PaO2 level of ICU-admitted patients was 72 mmHg (54 to 86). During the study period, six patients (12.8%) died either due to multiple organ dysfunction syndrome or cardio-respiratory failure-all of whom were in the ICU **(Table 6)**.

Table 6: Clinical outcome of the study subjects

Clinical outcome	Frequency (percentage)
ICU admission	15 (31.9)
PaO2 level (mmHg)	72 (54 to 86) *
Mortality	6 (12.8)

*Median (IQR)

Discussion

This single-centre study was conducted at Gazi Medical College Hospital, Khulna, Bangladesh, on patients with COVID-19 with diabetes mellitus (DM) or prediabetes. In our study, 26.1% of the patients had DM or prediabetes. A previous study shows that the overall prevalence of DM and prediabetes in Bangladesh is 9.2% and 13.3%, respectively (10). The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is widely recognised for attacking the pancreas, damaging both exocrine and endocrine cells. It is a member of the SARS coronavirus family (11). According to earlier research, diabetes was linked to worse patient outcomes during the SARS-CoV and Middle East Respiratory Syndrome (MERS) coronavirus epidemics (12, 13). So, the hypothesis put out was that diabetes contributes to an immunological response that is dysfunctional, which results in a damaging state of the lungs (14, 15).

Patients in our study were predominantly male (61.7%) compared to female (38.3%). This data is consistent with recent research showing that males with COVID-19 are more likely than women to experience catastrophic effects, including death (6, 16, 17).

Additionally, a substantial number of the people in our group who had COVID-19 and diabetes or prediabetes also had other severe comorbidities (32/47, 68.1%), which is consistent with another study's results (76/103, 73.8%) (9). This result reflects that the metabolic syndrome's main contributors are cardiovascular disease and diabetes (18). Proinflammatory and prothrombotic states are also linked to metabolic syndrome, which may have significant repercussions for COVID-19 patients, where these consequences are more prevalent and problematic (19).

In our study, 63.9% of patients received regular insulin, and 17.1% received long-acting insulin. Also, DPP-4 inhibitors were the most used oral antidiabetic medication (21.3%). These findings differ from the study conducted by Bhatti et al. (9). 7.8% of patients received long-acting insulin, 5.8% of patients received a basal-bolus insulin regimen, and metformin was the most used oral medication for diabetes (62.1%).

In this study, patients with DM and COVID had increased HbA1c, RBS, D-dimer and CRP levels. These findings align with the results of another study and indicate the increased cytokine response that occurs in COVID-19 cases (20).

Moreover, 31.9% of patients (15/47) needed ICU support due to a marked decrease in O2 saturation. This finding is consistent with a previous study, where 28.2% of patients (29/103) required ICU admission (9). Acute hyperglycemia causes the ACE2 gene to be upregulated, which makes it easier for the SARS-CoV-2 virus to enter cells. Long-term hyperglycemia reduces the expression of ACE2, leaving cells more susceptible to the inflammatory properties of the SARS-CoV-2 virus (21). Therefore, doing biochemical investigations at the time of admission to the hospital may help estimate disease severity and assess the required degree of patient care.

Limitations and conclusion

It is essential to consider the present study's limitations. First, our sample size was small because we conducted the study at just one centre. Therefore, the current study does not accurately reflect the COVID-19 burden in the Khulna area. Our study's lack of a control group of individuals without diabetes to compare the outcomes to is another drawback. Additionally, most of our patients lacked information on how accurately they might be classified as overweight or obese, even though obesity is associated with more severe disease and higher death risk. This is because, during a short period, a rising number of new patients presented to our healthcare institution with COVID-19 symptoms.

Despite these drawbacks, our study offers essential insights into the characteristics of diabetic and prediabetic patients hospitalised for COVID-19 management. This study may aid medical professionals in determining the causes of unfavourable outcomes in diabetic individuals hospitalised with COVID-19 by using clinical and laboratory data.

References

1. Wang Z, Ye D, Wang M, Zhao M, Li D, Ye J, et al. Clinical features of COVID-19 patients with different outcomes in Wuhan: a retrospective observational study. BioMed research international. 2020;2020.

2. Susanto AD, Rozaliyani A, Prasetyo B, Agustin H, Baskoro H, Arifin AR, et al. Epidemiological and clinical features of covid-19 patients at national emergency hospital wisma atlet kemayoran, jakarta, Indonesia. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal). 2021.

3. Islam MT, Talukder AK, Siddiqui MN, Islam T. Tackling the COVID-19 pandemic: the Bangladesh perspective.

4. Bari R, Sultana F. Second Wave of COVID-19 in Bangladesh: An integrated and coordinated set of actions is crucial to tackle current upsurge of cases and deaths. Frontiers in Public Health. 2021;9:699918.

5. Samrin NA, Suzan MMH, Hossain MS, Mollah MSH, Haque MD. Analysis of COVID-19 Trends in Bangladesh: A Machine Learning Analysis. AI and IoT for Sustainable Development in Emerging Countries: Challenges and Opportunities: Springer; 2022. p. 611-25.

6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet.

2020;395(10229):1054-62.

7. Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D, Birkenfeld AL, et al. Practical recommendations for the management of diabetes in patients with COVID-19. The lancet Diabetes & endocrinology. 2020;8(6):546-50.

8. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. Journal of diabetes science and technology. 2020;14(4):813-21.

9. Bhatti R, Khamis AH, Khatib S, Shiraz S, Matfin G. Clinical characteristics and outcomes of patients with diabetes admitted for COVID-19 treatment in Dubai: single-centre cross-sectional study. JMIR public health and surveillance. 2020;6(4):e22471.

10. Hossain MB, Khan MN, Oldroyd JC, Rana J, Magliago DJ, Chowdhury EK, et al. Prevalence of, and risk factors for, diabetes and prediabetes in Bangladesh: Evidence from the national survey using a multilevel Poisson regression model with a robust variance. PLOS Global Public Health. 2022;2(6):e0000461.

11. Shi X, Gong E, Gao D, Zhang B, Zheng J, Gao Z, et al. Severe acute respiratory syndrome associated coronavirus is detected in intestinal tissues of fatal cases. Official journal of the American College of Gastroenterology| ACG. 2005;100(1):169-76.

12. Yang J, Feng Y, Yuan M, Yuan S, Fu H, Wu B, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabetic medicine. 2006;23(6):623-8.

13. Alqahtani F, Aleanizy F, Mohamed RAEH, Alanazi M, Mohamed N, Alrasheed M, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiology & Infection. 2019;147:e35.

14. Kulcsar KA, Coleman CM, Beck SE, Frieman MB. Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS-CoV infection. JCI insight. 2019;4(20).

15. Chan KH, Thimmareddygari D, Ramahi A, Atallah L, Baranetsky NG, Slim J. Clinical characteristics and outcome in patients with combined diabetic ketoacidosis and hyperosmolar hyperglycemic state associated with COVID-19: a retrospective, hospital-based observational case series. Diabetes research and clinical practice. 2020;166:108279.

16. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. International journal of infectious diseases. 2020;94:91-5.

17. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020;395(10223):507-13.

18. Matfin G. The metabolic syndrome: what's in a name? : SAGE Publications Sage UK: London, England; 2010. p. 39-45.

19. Wise J. Covid-19 and thrombosis: what do we know about the risks and treatment? : British Medical Journal Publishing Group; 2020.

20. Chen Y, Yang D, Cheng B, Chen J, Peng A, Yang C, et al. Clinical characteristics and outcomes of patients with diabetes and COVID-19 in association with glucose-lowering medication. Diabetes care. 2020;43(7):1399-407.

21. Bindom SM, Lazartigues E. The sweeter side of ACE2: physiological evidence for a role in diabetes. Molecular and cellular endocrinology. 2009;302(2): 193-202.