Received: 4 August 2022 | Revised: 15 November 2022 | Accepted: 10 December 2022

DOI: 10.1002/nop2.1567

EMPIRICAL RESEARCH QUANTITATIVE

NursingOpen Open Access WILEY

Predictors of mortality and ICU requirement in hospitalized COVID-19 patients with diabetes: A multicentre study

Md Asaduzzaman[1] | Mohammad Romel Bhuia[2] | Mohammad Zabed Jillul Bari[3] | Zhm Nazmul Alam[1] | Khalidur Rahman[2] | Enayet Hossain[3] | Munsi Mohammad Jahangir Alam[3]

[1]Department of Medicine, Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh

[2]Department of Statistics, Shahjalal University of Science and Technology, Sylhet, Bangladesh

[3]Department of Medicine, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh

Correspondence
Md Asaduzzaman, Sylhet MAG Osmani Medical College Hospital, Sylhet-3100, Bangladesh.
Email: asad_somc@yahoo.com

Abstract

Aim: This study aimed to identify the predictors of mortality and ICU requirements in hospitalized COVID-19 Patients with Diabetes.

Design: Cross-sectional study.

Methods: It was a retrospective study of patients hospitalized with COVID-19 infection from October 2020–February 2021 in four hospitals in Sylhet, Bangladesh. Logistic regression analysis was applied to explore the predictors of ICU requirement and in-hospital mortality.

Results: In the whole cohort ($n = 500$), 11% of patients died and 24% of patients required intensive care unit (ICU) support. Non-survivors had significantly higher prevalence of lymphopenia, thrombocytopenia and leukocytosis. Significant predictors of in-hospital mortality were older age, neutrophil count, platelet count and admission peripheral capillary oxygen saturation (SpO2). Older age, ischemic heart disease, WBC count, D-dimer and admission SpO2 were identified as significant predictors for ICU requirement.

Patient or Public Contribution: No.

KEYWORDS
COVID-19, DM, Mortality, ICU requirement

1 | INTRODUCTION

The ongoing pandemic of COVID-19 caused by the SARS-CoV-2 continues to threaten human lives, even more than one and a half years after the onset of the outbreak. The situation is becoming more challenging as new evidence is growing that some new variants of coronavirus may escape immune responses that have developed from vaccines or previous infections (Callaway, 2021). As of June 08, 2022, about 6.32 million deaths due to COVID-19 in total have been confirmed around the world (COVID live., 2022). The case fatality rate is between 0.5% and 1% (Perez-Saez et al., 2021; Verity et al., 2020). Previous studies have demonstrated comorbidities as risk factors for poor outcomes in past coronavirus-related outbreaks. (Booth et al., 2003; Hui et al., 2018;Yang, Han, et al., 2020; Yang, Yu, et al., 2020; Yang, Zhong, et al., 2020).

Earlier reports found a high prevalence of diabetes among patients hospitalized due to COVID-19 (Mithal et al., 2021; Richardson et al., 2020). Patients with diabetes mellitus are more susceptible

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.
© 2022 The Authors. *Nursing Open* published by John Wiley & Sons Ltd.

to adverse outcomes of COVID-19 disease. The prevalence of diabetes was two- to three-fold higher in patients who required intensive care unit supports (ICUs), and they had a higher death rate when compared with patients with less severe form of disease (Cariou et al., 2022; Kastora et al., 2022; Mithal et al., 2021; Zhou et al., 2020). However, people with diabetes also have a high prevalence of co-morbidities like hypertension, obesity and cardiovascular disease than non-diabetic people, and these comorbidities are linked to severe disease course and poor outcomes (Bae et al., 2021; Perez et al., 2021). Therefore, it is a need to investigate the potential associations between diabetes, other co-morbidities and COVID-19. In this study, we, therefore, aimed to directly compare people with diabetes vs. people without diabetes living in the same geographic area.

Given the high prevalence of diabetes and its strong adverse impact on outcomes related to COVID-19, finding the best evidence for improving outcomes in patients with COVID-19 and diabetes is crucial. Though several meta-analyses and systemic reviews (Bradley et al., 2022; Corona et al., 2021; Mahamat-Saleh et al., 2021) showed a close relationship between diabetes and mortality of COVID-19, studies looking for demographics & early laboratory parameters as predictors of subsequent disease courses are few (Yang, Han, et al., 2020; Yang, Yu, et al., 2020; Yang, Zhong, et al., 2020). That is why we did this study to ascertain the factors that can help in predicting subsequent composite in-hospital outcomes, like ICU requirement and mortality from COVID-19.

2 | SUBJECTS, MATERIALS AND METHODS

2.1 | Study design

A retrospective analysis has been conducted for admitted patients between October 2020 and February 2021 in four hospitals of Sylhet, Bangladesh. We collected data of all patients who got admitted during this study period. All patients were assessed at the emergency department. The diagnosis of COVID-19 was made when patients come with clinical features suggestive of COVID-19 and supported by (I) RT-PCR result positive for SARS-CoV-2, or (II) characteristic findings of COVID-19 on chest X-ray or HRCT scan. Clinical, demographic and laboratory data from all adult patients were recorded at the time of hospital admission. Blood sample was sent soon after hospital admission for laboratory studies like complete blood count, D-dimer, Serum ferritin and blood glucose. Cell count was done by fully automated analyser SYSMEX-XT2000i. All data were collected from hospital records.

This study included 500 patients (Diabetic = 322, non-diabetic = 178) with a diagnosis of COVD-19. From the whole cohort, patients with diabetes having definite in-hospital outcomes ($n = 281$) were selected for final analysis to find out the predictors of in-hospital outcomes. For the purpose of this study, DM was defined as having one or more of the following criteria: known case of DM based on medical record, already on anti-DM medications.

2.2 | Data collection

The demographic information taken here are age (in years), sex (male/female) and length of hospital stay (in days). Clinical data collected here are presenting symptoms (fever, cough, respiratory distress, fatigability, loss of smell, diarrhoea, sore throat, anorexia, chest pain, vomiting, headache); comorbidities (such as diabetes [DM], hypertension, chronic kidney disease [CKD], ischemic heart disease [IHD], chronic obstructive pulmonary disease [COPD] and cerebrovascular disease [CVD]); respiratory support required (Ventilator, NIV [non-invasive ventilation], HFNC [High flow nasal cannula], low flow oxygen and No O_2 [No supplemental oxygen]) and oxygen saturation measured by pulse oximeter (SpO2) on admission. Laboratory data included here are complete blood count (CBC), D-dimer, serum ferritin and random blood sugar (RBS). Findings of chest CT scan are also included.

2.3 | Statistical analysis

The demographics, clinical characteristics and laboratory data of patients (patients with diabetes vs. patients without diabetes and survivors vs. non-survivors) were compared. We used descriptive statistics to describe the data. Shapiro–Wilk test was used to check the normality of continuous variables. We presented continuous data using mean and standard deviation (SD) for data that followed normal distribution, and by median and interquartile range (IQR) for skewed data. The mean difference between groups (patients with diabetes vs. patients without diabetes and survivors vs. non-survivors) in a continuous variable was assessed using two independent sample mean test (*t*-test) for the normally distributed data and using non-parametric Mann–Whitney *U* test for the non-normally distributed data. Categorical variables were described using frequencies and percentages (%). Chi-square test (χ^2 test) of independence was used to determine the association (difference) among categorical variables. Logistic regression analysis has been done to identify the risk factors for in-hospital death and ICU requirements. The candidate predictors for the final model were selected based on their significance (at 10% level of significance; $p < 0.1$) in univariable analysis and by performing standard model-building procedures (backward selection and least AIC value). Initially, simple logistic regression models were fitted for each of the potential predictors. The factors that were significantly associated with in-hospital death or ICU requirement in the simple logistic regression models were included in the final multiple logistic regression model. The variables that were highly correlated with each other were excluded from the model due to multicollinearity. To make sure that there was no multicollinearity in our multivariable models, we measured the correlations among various independent variables before fitting the final models and excluded the variables that were responsible for multicollinearity (correlation, $r > 0.8$) from the multivariate analysis. We have also removed the variables having a variance inflation factor of greater than five

(VIF > 5) from the multivariable models to make sure that there was no multicollinearity in the final models. Goodness of fit of the model was tested using Hosmer–Lemeshow test. Model findings were presented using odds ratio (OR) and 95% confidence interval (CI). A p value <0.05 was considered as statistically significant. Analysis was performed using R software. This study is described following the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) (von Elm et al., 2008) statements.

3 | RESULTS

Data of 500 patients were collected. The prevalence of diabetes was 64.4% (322) in the cohort. ICU support was needed for 24% of patients and 11% of the patient died during their hospital stay. The distributions of patients by demographic and clinical characteristics are presented in Table 1.

A significant difference (<0.001) is present between the mean age of patients without diabetes (56.1 ± 15.8) and patients with diabetes (62.97 ± 11.6) group. Diabetes was found to be more prevalent in male than female (61.2% vs. 38.8%). Hypertension (n = 355; 71%) and IHD (n = 120; 24%) were the most frequent comorbidities in hospitalized COVID-19 patients; followed by CKD (n = 98; 19.60%) and COPD (n = 64; 12.80%). Patients with diabetes had significantly higher prevalence of hypertension (81.7% vs. 51.7%; $p \leq 0.001$), IHD (29.8% vs. 13.5%; $p < 0.001$) and CKD (23.6% vs. 12.4%; p = 0.004 respectively) than patients without diabetes while prevalence of COPD is significantly higher (20.8% vs. 8.4%; $p \leq 0.001$) in later group. Regarding presenting symptoms, nine out of 10 patients had fever (n = 451; 90.20%), around two-thirds of patients had cough (n = 364; 72.80%) and respiratory distress (n = 340; 68%). Other complaints at admission were fatigability (n = 264; 52.80%), diarrhoea (n = 82; 16.40%), loss of smell (n = 96; 19.20%) and sore throat (n = 62; 12.40%). Average length of hospital stay (days) was 8.5 ± 4.4. Patients with diabetes had a slightly higher length of stay than patients without diabetes (8.6 ± 4.4 vs. 8.3 ± 4.4 days). A higher death rate was observed in patients with diabetes when compared to patients without diabetes (13% vs. 7.3%; p = 0.07). A higher percentage of patients with diabetes required ICU support (26.7% vs. 19.1%; p = 0.072). Patients with diabetes required higher HFNC (12.4% vs. 9.6%), NIV (8.4% vs. 3.9%), and ventilator support (5.9 vs. 5.6).

Radiography and Laboratory findings in patients, overall and by diabetes status are presented in Table 2.

Among the whole cohort, patients with diabetes had higher median neutrophil count (6.45 vs. 6.37), platelet count (230 vs. 214), neutrophil-to-lymphocyte ratio (NLR) (4.57 vs. 4.25), D-dimer (650 vs. 518) and ferritin (352 vs. 345) in comparison to patients without diabetes while median lymphocyte count (1.42 vs. 1.46) was lower in patients with diabetes. RBS measured at admission was higher (11.8 vs. 7.7; $p \leq 0.001$) in patients with diabetes. The most common abnormalities detected on HRCT were ground-glass opacification/opacity (GGO) (60%), followed by combined GGO and consolidation (25.2%), and then isolated Consolidation (14.8). Consolidation was more frequent in patients without diabetes (39 vs. 35; p = 0.03) while GGO was more frequently observed in diabetic (61.2% vs. 57.6%; p = 0.49). Every 9 patients out of every 10 patients had evidence of bilateral lung involvement. Bilateral involvement was more common (89.8 vs. 88.1) in patients with diabetes.

The distributions of patients with diabetes by survivor status are presented in Table 3.

Among patients with diabetes, 15% suffered in-hospital death. ICU support was required in 24.20% of patients. Male patients are more in the non-survivor group (57.1% vs. 42.9%). About four-fifths (81.5%) of patients were hypertensive, one-fourth (27.76%) had IHD, and one-fifth (21.35%) had CKD. A significantly higher prevalence of COPD was observed in non-survivors (19% vs. 6.7%; p = 0.019). Though non-significant, the prevalence of CKD (33.3% vs. 19.2%), IHD (40.5% vs. 25.5%) and CVD (7.1 vs. 4.6%) was also higher in non-survivors while the prevalence of hypertension was more (82.4% vs. 76.2%) in survivors.

Fever was the presenting complaint in the majority of patients (91.1%). Other highly reported symptoms were cough (72.2%), respiratory distress (65.1%) and fatigability (58.7%). Less frequently reported complaints were loss of smell (19.9%), diarrhoea (17.4%), sore throat (10.7%), and anorexia (3.2%). As presenting symptoms, non-survivor had higher prevalence of fever (95.2% vs. 90.4%), respiratory distress (78.6% vs. 62.8%), fatigability (61.9% vs. 58.2%), diarrhoea (21.4% vs. 16.7%) and anorexia (4.8% vs. 2.9%). Sore throat as a presenting symptom was more frequent in non-survivors (21.4% vs. 8.8%; p = 0.03). Admission SpO2 was significantly lower in non-survivors (84 vs. 91.1; $p \leq 0.001$). Non-survivor required a longer hospital stay (mean; 10.57 days vs. 8.43 days; p = 0.03). A higher proportion of patients in non-survivor group required ICU admission (11.7% vs. 95.2%; $p \leq 0.001$).

Radiography and laboratory findings in patients with diabetes are presented in Table 4.

Both WBC count (median; 8.5 vs. 8.2; p = 0.003) and neutrophil count (median; 8.61 vs. 6.21; $p \leq 0.001$) were significantly higher in non-survivor group. A significantly lower lymphocyte count (median; 1.06 vs. 1.46; p = <0.001) was seen in non-survivors while a non-significant decrease in platelet count (median; 209 vs. 232; p = 0.108) was also noted in non-survivor group. Compared to patients who survived, occurrence of lymphopenia (76.2% vs. 50.6%; p = 0.004), thrombocytopenia (21.4% vs. 8.8%; p = 0.03) and leukocytosis (50% vs. 31%; p = 0.026) were more frequent in non-survivor group. Level of D-dimer (964 vs. 618), serum ferritin (534 vs. 328) and RBS (13 vs. 11.3) were higher in non-survivors. On HRCT, GGO was the commonest findings (60%). There was a higher prevalence of combined GGO and consolidation in non-survivors (35.7% vs. 25.5%).

Both univariate (Table 5) and multivariate (Table 6) analyses revealed that diabetes increased the risk of death due to COVID-19. Among the patients who died from COVID-19, 76.4% had diabetes, and 23.6% did not have diabetes. Moreover, the patients with diabetes were 2.3 (p = 0.02) times more likely to die from COVID than the patients without diabetes.

TABLE 1 Demographics and clinical characteristics of patients with COVID-19 (n = 500)

Variables	Total	Patients without diabetes (*n* = 178)	Patients with diabetes (*n* = 322)	*p* Value
Age	60.53 ± 13.61	56.11 ± 15.8	62.97 ± 11.55	<0.001
Sex				
Female	174 (34.80%)	49 (27.5%)	125 (38.8%)	0.015
Male	326 (65.20%)	129 (72.5%)	197 (61.2%)	0.012
Comorbidities				
Hypertension	355 (71.00%)	92 (51.7%)	263 (81.7%)	<0.001
IHD	120 (24.00%)	24 (13.5%)	96 (29.8%)	<0.001
CKD	98 (19.60%)	22 (12.4%)	76 (23.6%)	0.004
COPD	64 (12.80%)	37 (20.8%)	27 (8.4%)	<0.001
CVD	20 (4.00%)	6 (3.4%)	14 (4.3%)	0.768
Clinical characteristics				
Fever	451 (90.20%)	165 (92.7%)	292 (90.7%)	0.547
Cough	364 (72.80%)	133 (74.7%)	231 (71.7%)	0.541
SOB	340 (68.00%)	125 (70.2%)	215 (66.8%)	0.488
Fatigability	264 (52.80%)	87 (48.9%)	177 (55%)	0.225
Diarrhoea	82 (16.40%)	26 (14.6%)	56 (17.4%)	0.497
Loss of smell	96 (19.20%)	33 (18.5%)	63 (19.6%)	0.873
Sore throat	62 (12.40%)	26 (14.6%)	36 (11.2%)	0.331
Chest pain	10 (2.00%)	5 (2.8%)	5 (1.6%)	0.531
Anorexia	13 (2.60%)	4 (2.2%)	9 (2.8%)	0.94
Vomiting	5 (1.00%)	3 (1.7%)	2 (0.6%)	0.499
Headache	3 (0.60%)	2 (1.1%)	1 (0.3%)	0.601
Length of stay (days)	8.5 ± 4.4	8.3 ± 4.4	8.6 ± 4.4	0.431
Death	55 (11%)	13 (7.3%)	42 (13%)	0.07
ICU admission	120 (24%)	34 (19.1%)	86 (26.7%)	0.072
Admission SpO2	92(86–95)	92(88–95)	91(86–95)	0.14
Type of respiratory support required				
No oxygen	46 (9.2%)	14 (7.9%)	31 (9.6%)	0.62
Low flow	334 (66.8%)	129 (72.5%)	205 (63.7%)	0.066
HFNC	57 (11.4%)	17 (9.6%)	40 (12.4%)	0.468
NIV	34 (6.8%)	7 (3.9%)	27 (8.4%)	0.147
Ventilator	29 (5.8%)	10 (5.6%)	19 (5.9%)	1

Abbreviations: CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; CVD, Cerebrovascular disease; DM, Diabetes Mellitus; HFNC, high flow nasal cannula; IHD, Ischemic heart disease; LOS, Length of stay; NIV, noninvasive ventilation; No O_2, no oxygen required; SpO2, peripheral capillary oxygen saturation.

Table 7 shows predictors of mortality and ICU requirement of COVID-19 patients with diabetes, obtained from the logistic regression model analysis.

The simple logistic regression model has shown that age, CKD, COPD, IHD, WBC count, neutrophil count, Lymphocyte count, NLR and admission SpO2 were notably associated with in-hospital mortality of COVID-19 patients (Table 5). The odds of death were higher for patient with older age (OR = 1.04; 95% CI = 1.01–1.07), those who had CKD (OR = 2.09; 95% CI = 1.002–4.24), COPD (OR = 3.28; 95% CI = 1.24–8.07), IHD (OR = 1.98; 95% CI = 0.99–3.90), higher total count of WBC (OR = 1.00; 95% CI =1.00–1.00), higher neutrophil count (OR = 1.06; 95% CI =1.02–1.10), higher NLR (OR = 2.12; 95% CI =1.03–1.11) and lower admission SpO2 (OR = 0.92; 95% CI = 0.88–0.95).

Adjusting for other factors, the multiple logistic regression models (Table 7) demonstrated that age, neutrophil count, platelet count and admission SpO2 were the significant predictors of death of COVID-19 patients with diabetes (Table 7). While other adjusted factors are constant, with 1 year increase in age, the death risk of in-hospital COVID-patient was increased by 4% (AOR = 1.04; 95%

TABLE 2 Radiography and laboratory results of patients with COVID-19 (n = 500), median (IQR)/number (%)

Variables	Normal range	Total	Patients without diabetes (*n* = 178)	Patients with diabetes (*n* = 322)	*p* Value
TC WBC ($\times 10^9$/L)	4–10	8.5 (6.01–12.55)	8.55 (6–12.8)	8.5 (6.3–12)	0.30
Neutrophil ($\times 10^9$/L)	2–7	6.43 (4.22–9.89)	6.37 (3.92–10.33)	6.45 (4.33–9.52)	0.52
Lymphocyte ($\times 10^9$/L)	0.8–4.5	1.43 (0.97–2.01)	1.46 (1.08–2)	1.42 (0.95–2.05)	0.19
Platelet ($\times 10^9$/L)	150–350	220 (180–300)	214 (170–290)	230 (180–307)	0.46
NLR		4.41 (2.58–7.72)	4.25 (2.51–7.08)	4.57 (2.64–7.81)	0.23
D-dimer (ng/L)	0–500	622 (314–1312)	518 (271–1239)	650 (341–1342)	0.96
S. Ferritin	20–300	349 (169–787)	345 (181–913)	352 (164–717)	0.18
RBS	4.4–7.2	9.6 (7.7–13.6)	7.7 (6.3–8.9)	11.8 (8.9–15.1)	<0.001
HRCT findings					
Consolidation		74 (14.8%)	35 (19.8%)	39 (12.1%)	0.03
GGO		300 (60%)	102 (57.6%)	197 (61.2%)	0.497
GGO + Consolidation		126 (25.2%)	40 (22.6%)	86 (26.7%)	0.366
HRCT involvement					
Bilateral		446 (89.20)	156 (88.1%)	289 (89.8%)	0.685
Unilateral		54 (10.8%)	21 (11.9%)	33 (10.2%)	0.685

Abbreviations: GGO, Ground-glass opacity; NLR, neutrophil-to-lymphocyte ratio; RBS, Random blood sugar; TC WBC, total count of white blood cells.

CI = 1.01–1.08). The risk of in-hospital mortality of COVID-19 patients increases with an increase in neutrophil count (AOR = 1.04; 95% CI = 1.01–1.09), whereas the risk of in-hospital mortality of COVID-19 patients decreased with increase in platelet count (AOR = 1.00, 95% CI = 1.00–1.00) and a higher initial SpO2 (AOR = 0.92; 95% CI = 0.89–0.96). Receiver operating characteristic curve (ROC) analysis (Figure 1) revealed that the area under the curve (AUC) of the multivariable model predicting mortality is 0.8192 which is considered excellent.

In the univariate analysis (Table 7), age, CKD, COPD, IHD, WBC count, neutrophil count, lymphocyte count, NLR, D-dimer, S. ferritin and admission SpO2 were found to be significant predictors of ICU requirement.

In the multivariate model (Table 7), significant predictors of ICU requirement were age (AOR = 1.03; 95% CI = 1.005–1.07), co-morbidity IHD (AOR = 2.32; 95% CI = 1.17–4.58), WBC count (AOR = 1.00; 95% CI = 1.00–1.00), D-dimer (AOR = 1.00; 95% CI =1.00–1.00) and admission SpO2 (AOR = 0.91; 95% CI = 0.87–0.94). ROC curve analysis (Figure 2) revealed that the AUC of the multivariable model predicting ICU requirement is 0.84 which is also considered as excellent.

The multivariable logistic regression model presented in Table A1 in the Appendix shows that age, platelet count and SpO2 at admission were significant predictors of mortality in COVID patients without diabetes. All predictors of mortality in COVID-19 patients without diabetes were also included in predictors of mortality in COVID-19 patients with diabetes.

However, there was an additional predictor of death in COVID-19 patients with diabetes, which was the neutrophil count.

4 | DISCUSSION

4.1 | Statement of principal findings

Patients with diabetes were older than patients without diabetes. Comorbidities were more frequent in patients with diabetes. Clinical features did not differ significantly between these two groups. WBC count, platelet count, NLR, D-dimer, ferritin and RBS were higher in diabetic patients. The requirement of respiratory support by HFNC, NIV and ventilator was higher in diabetic patients.

Among patients with diabetes, non-survivors were older than survivor. Comorbidities like CKD, COPD, IHD and CVD were higher in non-survivor patients. Leukocytosis, lymphocytopenia and thrombocytopenia were significantly higher in the non-survivors. When compared with survivors, the non-survivor patients with diabetes had significantly higher NIV and ventilator requirements. Multiple logistic regression models revealed that higher age, leukocytosis, thrombocytopenia and lower SpO2 at admission were significant risk factors of mortality in patients with diabetes. On the other hand, higher age, presence of IHD, higher WBC count, higher D-dimer level and lower admission SpO2 were identified as significant predictors for ICU admission.

4.2 | Interpretation in the context of the wider literature

Initial studies on COVID-19 that compared risk in a defined population with or without diabetes observed a higher risk of death in those with diabetes (Barron et al., 2020; Bello-Chavolla et al., 2020).

TABLE 3 Demographics and clinical characteristics of patients with diabetes, overall and by survivor status

Variables	Total ($n = 281$)	Survivor ($n = 239$, 85%)	Non-survivor ($n = 42$, 15%)	p Value
Age	62.58 ± 11.65)	61.7 ± 11.53)	67.5 ± 11.18	0.003
Sex				0.641
Male	173 (61.57%)	149 (62.3%)	24 (57.1%)	0.678
Female	108 (38.43%)	90 (37.7%)	18 (42.9%)	0.641
Comorbidities				
Hypertension	229 (81.49%)	197 (82.4%)	32 (76.2%)	0.457
CKD	60 (21.35%)	46 (19.2%)	14 (33.3%)	0.064
COPD	24 (8.54%)	16 (6.7%)	8 (19%)	0.019
IHD	78 (27.76%)	61 (25.5%)	17 (40.5%)	0.07
CVD	14 (4.98%)	11 (4.6%)	3 (7.1%)	0.754
Clinical characteristics				
Fever	256 (91.1%)	216 (90.4%)	40 (95.2%)	0.467
Cough	203 (72.2%)	174 (72.8%)	29 (69%)	0.753
Respiratory distress	183 (65.1%)	150 (62.8%)	33 (78.6%)	0.071
Fatiguability	165 (58.7%)	139 (58.2%)	26 (61.9%)	0.776
Diarrhoea	49 (17.4%)	40 (16.7%)	9 (21.4%)	0.604
Loss of smell	56 (19.9%)	49 (20.5%)	7 (16.7%)	0.716
Sore throat	30 (10.7%)	21 (8.8%)	9 (21.4%)	0.03
Chest pain	4 (1.4%)	4 (1.7%)	0 (0%)	0.89
Anorexia	9 (3.2%)	7 (2.9%)	2 (4.8%)	0.883
Vomiting	2 (0.7%)	2 (0.8%)	0 (0%)	1
Headache	1 (0.4%)	1 (0.4%)	0 (0%)	1
SpO2 at admission	92(86–95)	91.1 (7.9)	84(70–93)	<0.001
Length of Stay (days)	8.75 ± 4.45	8.43 ± 4.07	10.57 ± 5.93	0.03
ICU requirement	68 (24.2%)	28 (11.7%)	40 (95.2%	<0.001
Type of respiratory support required				
No oxygen	46 (9.2%)	30 (12.6%)	0 (0%)	0.031
Low flow	334 (66.8%)	181 (75.7%)	2 (4.8%)	<0.001
HFNC	57 (11.4%)	25 (10.5%)	5 (11.9%)	0.993
NIV	34 (6.8%)	2 (0.8%)	20 (47.6%)	<0.001
Ventilator	16 (5.7%)	1 (0.4%)	15 (35.7%)	<0.001

Abbreviations: CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; CVD, Cerebrovascular disease; DM, Diabetes Mellitus; HFNC, high flow nasal cannula; IHD, Ischemic heart disease; NIV, noninvasive ventilation; No O_2, no oxygen required; SpO2, peripheral capillary oxygen saturation.

Consistent with this, this study also found a higher death rate (13%) in patients with diabetes than patients without diabetes (7.3%). It has also been found that patients with diabetes had longer hospital stays than patients without diabetes which is consistent with the results reported by Al-Salameh et al. (2021) but contrasts with another study done by Ciardullo et al. (2021).

Various possible mechanisms have been put forward to explain the underlying process responsible for high mortality from COVID-19 in patients with diabetes. Pluripotent stem cells-derived pancreatic beta-cells appear to be permissive for SARS-CoV-2 infection (Yang, Han, et al., 2020; Yang, Yu, et al., 2020; Yang, Zhong, et al., 2020). Analysis of pancreatic autopsies from patients infected with COVID-19 showed that beta-cells were infiltrated by SARS-CoV-2 in all patients (Steenblock et al., 2021). During infection with COVID-19, ACE2 expression decreases, and this leads to the exaggerated activity of Ang II with subsequent development of insulin resistance. And it is insulin resistance which is the main factor that triggers the activation of the inflammatory response that forestall cytokine storm (Govender et al., 2021). SARS-CoV-2 infection leads to a surge of different inflammatory mediators in the blood. Change

TABLE 4 Radiography and laboratory findings on admission in patients with diabetes, overall and by survivor status, Median (IQR)/number (%).

Variables	Normal range	Total ($n = 281$)	Survivor ($n = 239$)	Non-survivor ($n = 42$)	p Value
TC WBC ($\times 10^9$/L)	4–10	8.5 (6.3–11.6)	8.2 (6.2–11.1)	8.5 (6.3–12)	0.003
>10		16 (3.2%)	74 (31%)	21 (50%)	0.026
4–10		303 (60.6%)	159 (66.5%)	21 (50%)	0.06
<4		181 (36.2%)	7 (2.9%)	0 (0%)	0.558
Neutrophil ($\times 10^9$/L)	2–7	6.43 (4.33–9.50)	6.21 (4.22–9.25)	8.61 (5.16–13.43)	<0.001
Lymphocyte ($\times 10^9$/L)	0.8–4.5	1.42 (0.95–2.07)	1.46 (1–2.09)	1.06 (0.72–1.88)	<0.001
<0.8		83 (16.6%)	121 (50.6%)	32 (76.2%)	0.004
0.8–4.5		263 (52.6%)	115 (48.1%)	10 (23.8%)	0.006
>4.5		154 (30.8%)	3 (1.3%)	0 (0%)	1
Platelet ($\times 10^9$/L)	150–350	230 (180–310)	232 (186–310)	209 (150–254)	0.108
<150		58 (11.6%)	21 (8.8%)	9 (21.4%)	0.03
150–350		361 (72.2%)	177 (74.1%)	26 (61.9%)	0.151
>350		81 (16.2%)	41 (17.2%)	7 (16.7%)	1
NLR		4.38 (2.68–7.81)	4 (2.51–7.45)	7.08 (4.38–13.71)	<0.001
D-dimer (ng/L)	0–500	634 (344–1230)	618 (334–1220)	964 (490–1354)	0.413
S. Ferritin	20–300	346 (154–687)	328 (145–616)	534 (181–981)	0.07
RBS	4.4–7.2	11.9 (9.1–15.2)	11.3 (8.9–15.2)	13 (11.1–15)	0.069
HRCT findings					
Consolidation		74 (14.8%)	25 (10.5%)	4 (9.5%)	1
GGO		300 (60%)	153 (64%)	23 (54.8%)	0.332
GGO + Consolidation		126 (25.2%)	61 (25.5%)	15 (35.7%)	0.237
HRCT involvement					
Bilateral		241 (48.2%)	217 (90.8%)	37 (88.1%)	0.792
Unilateral		41 (8.2%)	22 (9.2%)	5 (11.9%)	0.792

Abbreviations: GGO, Ground-glass opacity; NLR, neutrophil-to-lymphocyte ratio; RBS, Random blood sugar; TC WBC, total count of white blood cells.

TABLE 5 Univariate analysis of the risk of death for COVID-19 patients with diabetes

Patient type	Number of death (%)	Chi-square	p-Value
COVID-19 patient with diabetes	42 (76.36%)	4.44	0.034
COVID-19 patient without diabetes	13 (23.64%)		

TABLE 6 Multivariate analysis of the risk of death for COVID-19 patients with diabetes

	Risk of death	
Characteristics	OR	p-Value
COVID-19 patient with diabetes		
No	—	0.015
Yes	2.34	

Note: The adjusted multivariable logistic regression model for estimating the risk of death for COVID patient with diabetes (the model is adjusted for sex and comorbidities).

in the activity of natural killer cells and IFN-γ production increase the vascular permeability for inflammatory mediators. In addition, the virus itself triggers increased production of reactive oxygen species. These pathologic processes lead to progressive lung damage resulting in acute respiratory distress syndrome (ARDS). The above-mentioned mechanisms are exaggerated in patients with diabetes (Lim et al., 2021).

Older people had increased risk of death in past respiratory viral pandemics like severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) (Choi et al., 2003; Hong et al., 2018). In compliance with this, older age is also demonstrated to be a significant risk factor of higher mortality and increased need of care in COVID-19 patients (Geriatric Medicine Research Collaborative et al., 2021). Our study also agrees with this observation as it found a higher mean age of non-survivors and it is associated with high in-hospital mortality and ICU requirement. Several possible causes may be responsible for the high mortality rate of elderly patient. The correlations between expression of ACE2 and immune signatures differ between young and elderly persons in the

TABLE 7 Predicting factors for poor outcome of the patients with COVID-19 and diabetes: Logistic regression analysis

	Need to ICU		Mortality	
Variable	**Crude OR (95% CI)**	**Adjusted[§] OR (95% CI)**	**Crude OR (95% CI)**	**Adjusted[§] OR (95% CI)**
Demographic and clinical characteristics				
Age	1.05 (1.02–1.07)* ($p = 0.00$)	1.03 (1.005–1.07)* ($p = 0.03$)	1.04 (1.01–1.07)* ($p = 0.003$)	1.04 (1.01–1.08)* ($p = 0.02$)
Sex	0.85 (0.49–1.49) ($p = 0.48$)		0.80 (0.41–1.58) ($p = 0.52$)	
Co-morbidities				
Hypertension	0.94 (0.48–1.96) ($p = 0.93$)		0.68 (0.32–1.55) ($p = 0.34$)	
CKD	1.94 (1.05–3.61)* ($p = 0.04$)		2.09 (1.002–4.24)* ($p = 0.04$)	
COPD	3.58 (1.51–8.50)* ($p = 0.004$)		3.28 (1.24–8.07)* ($p = 0.01$)	
IHD	3.22 (1.81–5.74)* ($p = 0.00$)	2.32 (1.17–4.58)* ($p = 0.02$)	1.98 (0.99–3.90) ($p = 0.05$)	
CVD	0.50 (0.11–2.32) ($p = 0.37$)		1.59 (0.34–5.38) ($p = 0.49$)	
Lab reports				
Haematological and Biochemistry parameters				
WBC	1.00 (1.00–1.00)* ($p = 0.00$)	1.00 (1.00–1.00)* ($p = 0.02$)	1.00 (1.00–1.00)* ($p = 0.004$)	
Neutrophil	1.07 (1.04–1.11)* ($p = 0.00$)		1.06 (1.02–1.10)* ($p = 0.001$)	1.04 (1.01–1.09)* ($p = 0.03$)
Lymphocyte	0.92 (0.89–0.96)* ($p = 0.00$)		0.94 (0.90–0.97)* ($p = 0.001$)	
Platelet	1.00 (1.00–1.00) ($p = 0.39$)		1.00 (1.00–1.00) ($p = 0.11$)	1.00 (1.00–1.00)* ($p = 0.03$)
NLR	1.12 (1.07–1.17)* ($p = 0.00$)		1.07 (1.03–1.11)* ($p = 0.001$)	
D-dimer	1.00 (1.00–1.00)* ($p = 0.001$)	1.00 (1.00–1.00)* ($p = 0.04$)	1.00 (1.00–1.00) ($p = 0.42$)	
Ferritin	1.00 (1.00–1.00)* ($p = 0.02$)		1.00 (1.00–1.00) ($p = 0.08$)	
RBS	1.02 (0.99–1.06) ($p = 0.24$)		1.02 (0.98–1.06) ($p = 0.33$)	
Admission SpO2	0.89 (0.86–0.93)* ($p = 0.00$)	0.91 (0.87–0.94)* ($p = 0.00$)	0.92 (0.88–0.95)* ($p = 0.00$)	0.92 (0.89–0.96)* ($p = 0.00$)

[§]Variables that were significant at 10% level of significance ($p = 0.1$) in the univariable models were included in the multivariable model.

*Effect variables (significant at 5% level of significance).

lungs, indicating that the variation in immune responses against the virus might be responsible for development of different patterns of disease severity across different age groups (Li, Deng et al., 2020; Li, Li, et al., 2020). Moreover, numerous age-related changes in the immune system of older adults, collectively known as immunosenescence, contribute to increased risk of getting infection and altered immune response to SARS-CoV-2 in elderly people (Nikolich-Zugich et al., 2020).

Observational studies that looked at epidemiologic characteristics of patients with and without diabetes reported a higher prevalence of comorbidities in patients with diabetes (Diedisheim et al., 2021; Luo et al., 2021; Moftakhar et al., 2021). Consistent with these studies, our study also observed a significantly higher prevalence of comorbidities in patients with diabetes, and non-survivors had higher burden of co-morbidities than those who survived.

The presenting clinical features did not differ significantly between patients with and without diabetes which well agrees with another study (Li, Deng et al., 2020; Li, Li, et al., 2020). Consistent with previous studies (Gaba et al., 2022; Kaminska et al., 2021), our study also observed a higher requirement of advanced respiratory support (HFNC, NIV and ventilator support) in patients with diabetes. Our study also found higher requirements of ICU in patients

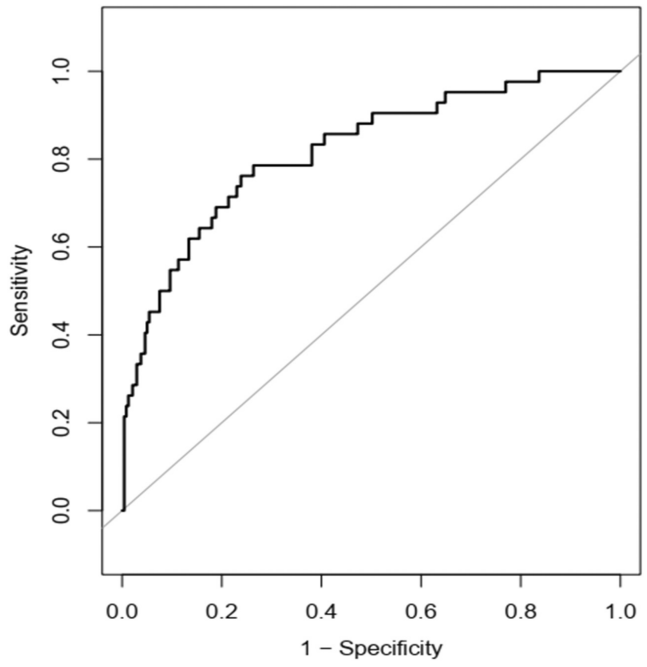

FIGURE 1 ROC curve for multivariable model predicting mortality. Area under the curve (AUC): 0.8192.

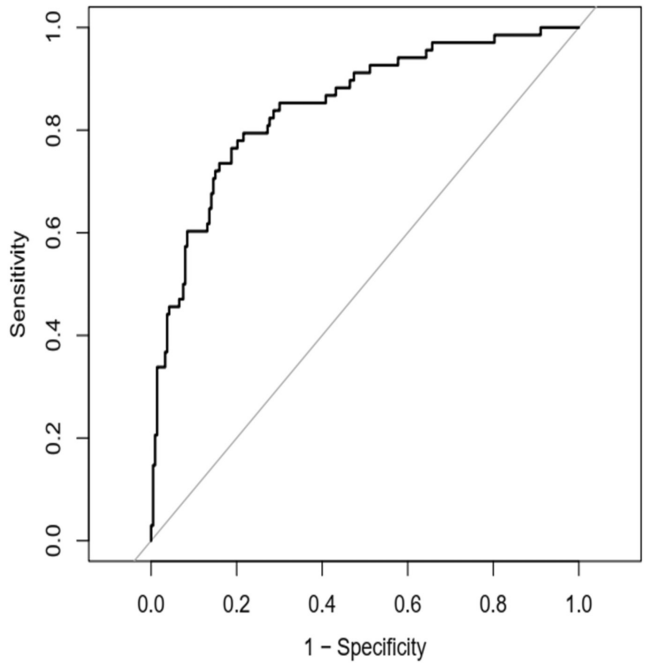

FIGURE 2 ROC curve for multivariable model predicting ICU requirement. Area under the curve (AUC): 0.8473.

with diabetes and non-survivor patients with diabetes had a significantly longer hospital stay, higher ICU requirement and higher need for advanced respiratory support.

Patients with diabetes had an increased level of neutrophil, NLR and platelet count and a lower lymphocyte count when compared with patients without diabetes which is consistent with previous studies (Corona et al., 2021; Tabrizi et al., 2021). In this study, leukocytosis, neutrophilia, lymphopenia and thrombocytopenia were more frequently seen in non-survivor patients with diabetes. Several studies (Abd El-Lateef et al., 2022; Loomba et al., 2022; Malik et al., 2021; Niu et al., 2022; Yang, Gao, et al., 2022; Yang, Huang, & Lui, 2022) found lymphopenia and thrombocytopenia as independent predictors of poor outcome which is also consistent with our study.

D-dimer, a fibrin degradation product and elevated level of it, is indicative of hypercoagulable state and secondary hyperfibrinolysis in the body. A hypercoagulable state has been described in COVID-19 patients and evidence found 71.4% of non-survivors fulfilled the diagnostic criteria of disseminated intravascular coagulation during hospitalization (Tang et al., 2020). Moreover, diabetes itself leads to endothelial damage. Emerging evidence demonstrated endothelial dysfunction in COVID-19, which makes a potential contribution to COVID-19-related coagulopathy by increasing expression of procoagulants and decreased expression of anticoagulants thrombomodulin and endothelial protein C receptor (Ma et al., 2022; Won et al., 2022). Compared to patients without diabetes, patients with diabetes had markedly increased level of markers of disturbance of coagulation system such as fibrinogen and d-dimer and higher inflammatory markers, and these findings may explain the increased vulnerability of patients with diabetes to coagulation abnormalities and inflammatory storm (Varikasuvu et al., 2021). Even patients with diabetes without other comorbidities were also at higher risk of getting severe pneumonia, excessive inflammatory responses and hypercoagulable condition (Guo et al., 2020). Several systemic reviews and meta-analyses (He et al., 2021; Zhao et al., 2021) demonstrated that d-dimer is a marker of disease progression and increased mortality. Our study also saw a higher d-dimer level in patients with diabetes, more in non-survivors, and found d-dimer as an independent predictor of subsequent ICU requirements.

Serum ferritin level is raised in infectious and inflammatory diseases (Kernan & Carcillo, 2017). Among the inflammatory biomarkers, serum ferritin has the ability to define the disease course of COVID-19 and predict the need for ICU admission and mortality (Kaushal et al., 2022; Shakaroun et al., 2022). Though our study observed a higher ferritin level in non-survivor patients, it did not prove it as a significant risk factor of ICU admission or mortality when adjusted for other factors. This observation has similarity with other studies (Aljohani et al., 2022; Carubbi et al., 2021) but contrast with other study where higher ferritin is said to be a risk factors of severe disease and mortality (Ahmed et al., 2021).

Hyperglycemia has been shown to be a risk factor of mortality in hospitalized patients with COVID-19, independent of their previous diabetes status (Lazarus et al., 2021; Vargas-Vázquez et al., 2021). This present study also found elevated level of blood glucose in non-survivor patients.

4.3 | Strengths and limitations

The main strength of this study is that it is a multicentre study, conducted in four COVID-19 dedicated tertiary level hospitals, the

largest of its kind in a region (one division out of 8 administrative divisions) of Bangladesh.

As the nature of the present study is retrospective, that is why it has several limitations. First, we did not have data on pre-hospital glycemic records. Therefore, the effect of pre-hospital blood glucose had been ignored. Second, this study included only those patients who needed hospitalization. So, our findings may not be extrapolated to all COVID-19 patients. Third, we did not consider the effects of drugs prescribed to treat COVID-19 that may affect the outcome. Fourth, we did not take into account the effect of anti-diabetic drugs, but these drugs have the potential to change the overall disease course. Fifth, data regarding duration of Diabetes, HbA1C, complications of DM, BMI were missing. So, their effect on the outcome may be overlooked here.

4.4 | Implications for policy, practice and future research

This study investigated the predictors of poor prognosis of COVID-19 patients with diabetes. Considering the rapid spread of infection and it is associated burden being placed on the healthcare system, these findings will help in prognostication and triage decisions to curtail this present crisis. Further well-designed studies with larger samples on different races in different geographic regions are needed to gather evidence on this.

5 | CONCLUSION

In summary, it has been found that in patients with diabetes, significant predictors of ICU requirement are older age, presence of co-morbidity IHD, higher WBC count, higher D-dimer level, lower admission SpO2. Age, neutrophil count and admission SpO2 are the significant predictors/risk factors of in-hospital mortality of COVID-19 patients with diabetes. The results of this study clearly emphasize the need for special care for COVID-19 patients with diabetes.

AUTHOR CONTRIBUTIONS

Conceptualization: MD Asaduzzaman, Zhm Nazmul Alam. Data Curation: MD Asaduzzaman, Zhm Nazmul ALAM, Mohammad Zabed Jillul Bari, Formal Analysis: MD Asaduzzaman. Methodology: MD Asaduzzaman, Mohammad Romel Bhuia, Khalidur Rahman. Project Administration: Zhm Nazmul Alam, Mohammad Zabed Jillul Bari, Enayet Hossain, M M Jahangir Alam. Supervision: Enayet Hossain, M M Jahangir Alam, Khalidur Rahman. Validation: Mohammad Romel Bhuia, Khalidur Rahman. Writing – review, and editing: MD Asaduzzaman, Mohammad Romel Bhuia, Enayet Hossain, M M Jahangir Alam, Zhm Nazmul Alam, Mohammad Zabed Jillul Bari. Writing –original draft: MD Asaduzzaman. The corresponding author hereby confirms that he had full access to all of the data in the study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

ACKNOWLEDGEMENTS

Special thanks to the authorities of Mount Adora Hospital, Sylhet Shahid Shamsuddin Ahmed District Hospital, Sylhet Women's Medical College Hospital and North-East Medical College Hospital, Sylhet, Bangladesh from where we collected data. Our deep respect and endless gratitude to those patients whose data we have worked with.

FUNDING INFORMATION

This research received no external funding.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The datasets analysed during the current study are not publicly available because of having no permission of the hospitals from where data were collected.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

We obtained Research Ethics Committee approval from the Ethical committee of Sylhet Women's Medical College, Sylhet, Bangladesh, and the committee waived the need for consent. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

ORCID

Md Asaduzzaman https://orcid.org/0000-0001-9558-0594
Khalidur Rahman https://orcid.org/0000-0002-2899-804X

REFERENCES

Abd El-Lateef, A. E., Ismail, M. M., Thabet, G., & Cabrido, N.-A. (2022). Complete blood cells count abnormalities in COVID-19 patients and their prognostic significance: Single center study in Makkah, Saudi Arabia: Single center study in Makkah, Saudi Arabia. *Saudi Medical Journal*, *43*(6), 572–578. https://doi.org/10.15537/smj.2022.43.6.20210893

Ahmed, S., Ansar Ahmed, Z., Siddiqui, I., Haroon Rashid, N., Mansoor, M., & Jafri, L. (2021). Evaluation of serum ferritin for prediction of severity and mortality in COVID-19- a cross sectional study. *Annals of Medicine and Surgery*, *63*, 102163. https://doi.org/10.1016/j.amsu.2021.02.009

Aljohani, F. D., Khattab, A., Elbadawy, H. M., Alhaddad, A., Alahmadey, Z., Alahmadi, Y., Eltahir, H. M., Matar, H. M. H., & Wanas, H. (2022). Prognostic factors for predicting severity and mortality in hospitalized COVID-19 patients. *Journal of Clinical Laboratory Analysis*, *36*(3), e24216. https://doi.org/10.1002/jcla.24216

Al-Salameh, A., Lanoix, J.-P., Bennis, Y., Andrejak, C., Brochot, E., Deschasse, G., Dupont, H., Goeb, V., Jaureguy, M., Lion, S., Maizel, J., Moyet, J., Vaysse, B., Desailloud, R., Ganry, O., Schmit, J. L., & Lalau, J. D. (2021). Characteristics and outcomes of COVID-19 in hospitalized patients with and without diabetes. *Diabetes/Metabolism Research and Reviews*, *37*(3), e3388. https://doi.org/10.1002/dmrr.3388

Bae, S., Kim, S. R., Kim, M.-N., Shim, W. J., & Park, S.-M. (2021). Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: A systematic review and

meta-analysis. *Heart*, *107*(5), 373–380. https://doi.org/10.1136/heartjnl-2020-317901

Barron, E., Bakhai, C., Kar, P., Weaver, A., Bradley, D., Ismail, H., Knighton, P., Holman, N., Khunti, K., Sattar, N., Wareham, N. J., Young, B., & Valabhji, J. (2020). Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: A whole-population study. *The Lancet Diabetes and Endocrinology*, *8*(10), 813–822. https://doi.org/10.1016/S2213-8587(20)30272-2

Bello-Chavolla, O. Y., Bahena-López, J. P., Antonio-Villa, N. E., Vargas-Vázquez, A., González-Díaz, A., Márquez-Salinas, A., Fermín-Martínez, C. A., Naveja, J. J., & Aguilar-Salinas, C. A. (2020). Predicting mortality due to SARS-CoV-2: A mechanistic score relating obesity and diabetes to COVID-19 outcomes in Mexico. *The Journal of Clinical Endocrinology and Metabolism*, *105*(8), 2752–2761. https://doi.org/10.1210/clinem/dgaa346

Booth, C. M., Matukas, L. M., Tomlinson, G. A., Rachlis, A. R., Rose, D. B., Dwosh, H. A., Walmsley, S. L., Mazzulli, T., Avendano, M., Derkach, P., Ephtimios, I. E., Kitai, I., Mederski, B. D., Shadowitz, S. B., Gold, W. L., Hawryluck, L. A., Rea, E., Chenkin, J. S., Cescon, D. W., … Detsky, A. S. (2003). Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA*, *289*(21), 2801–2809. https://doi.org/10.1001/jama.289.21.JOC30885

Bradley, S. A., Banach, M., Alvarado, N., Smokovski, I., & Bhaskar, S. M. M. (2022). Prevalence and impact of diabetes in hospitalized COVID-19 patients: A systematic review and meta-analysis. *Journal of Diabetes*, *14*(2), 144–157. https://doi.org/10.1111/1753-0407.13243

Callaway, E. (2021). Fast-spreading COVID variant can elude immune responses. *Nature*, *589*(7843), 500–501.

Cariou, B., Wargny, M., Boureau, A.-S., Smati, S., Tramunt, B., Desailloud, R., Lebeault, M., Amadou, C., Ancelle, D., Balkau, B., Bordier, L., Borot, S., Bourgeon, M., Bourron, O., Cosson, E., Eisinger, M., Gonfroy-Leymarie, C., Julla, J. B., Marchand, L., … CORONADO Investigators. (2022). Impact of diabetes on COVID-19 prognosis beyond comorbidity burden: The CORONADO initiative. *Diabetologia*, *65*(9), 1436–1449. https://doi.org/10.1007/s00125-022-05734-1

Carubbi, F., Salvati, L., Alunno, A., Maggi, F., Borghi, E., Mariani, R., Mai, F., Paoloni, M., Ferri, C., Desideri, G., Cicogna, S., & Grassi, D. (2021). Ferritin is associated with the severity of lung involvement but not with worse prognosis in patients with COVID-19: Data from two Italian COVID-19 units. *Scientific Reports*, *11*(1), 4863. https://doi.org/10.1038/s41598-021-83831-8

Choi, K. W., Chau, T. N., Tsang, O., Tso, E., Chiu, M. C., Tong, W. L., Lee, P. O., Ng, T. K., Ng, W. F., Lee, K. C., Lam, W., Yu, W. C., Lai, J. Y., Lai, S. T., & The Princess Margaret Hospital SARS Study Group. (2003). Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. *Annals of Internal Medicine*, *139*(9), 715–723. https://doi.org/10.7326/0003-4819-139-9-200311040-00005

Ciardullo, S., Zerbini, F., Perra, S., Muraca, E., Cannistraci, R., Lauriola, M., Grosso, P., Lattuada, G., Ippoliti, G., Mortara, A., Manzoni, G., & Perseghin, G. (2021). Impact of diabetes on COVID-19-related in-hospital mortality: A retrospective study from northern Italy. *Journal of Endocrinological Investigation*, *44*(4), 843–850. https://doi.org/10.1007/s40618-020-01382-7

Corona, G., Pizzocaro, A., Vena, W., Rastrelli, G., Semeraro, F., Isidori, A. M., Pivonello, R., Salonia, A., Sforza, A., & Maggi, M. (2021). Diabetes is most important cause for mortality in COVID-19 hospitalized patients: Systematic review and meta-analysis. *Reviews in Endocrine & Metabolic Disorders*, *22*(2), 275–296. https://doi.org/10.1007/s11154-021-09630-8

COVID live. (2022). Coronavirus statistics – worldometer [Internet]. Worldometers.info. https://www.worldometers.info/coronavirus/

Diedisheim, M., Dancoisne, E., Gautier, J.-F., Larger, E., Cosson, E., Fève, B., Chanson, P., Czernichow, S., Tatulashvili, S., Raffin-Sanson, M. L., Sallah, K., Bourgeon, M., Ajzenberg, C., Hartemann, A., Daniel, C., Moreau, T., Roussel, R., & Potier, L. (2021). Diabetes increases severe COVID-19 outcomes primarily in younger adults. *The Journal of Clinical Endocrinology and Metabolism*, *106*(9), e3364–e3368. https://doi.org/10.1210/clinem/dgab393

Gaba, U., Altamish, M., Azharuddin, M., Adil, M., Ghosh, P., Gyawali, B., Yadav, Y., & Sharma, M. (2022). Risk factors and outcomes associated with diabetes mellitus in COVID-19 patients: A meta-analytic synthesis of observational studies. *Journal of Diabetes and Metabolic Disorders*, *21*, 1–11. https://doi.org/10.1007/s40200-022-01072-6

Geriatric Medicine Research Collaborative, Covid Collaborative, & Welch, C. (2021). Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: Results of an international multi-centre study. *Age and Ageing*, *50*(3), 617–630. https://doi.org/10.1093/ageing/afab026

Govender, N., Khaliq, O. P., Moodley, J., & Naicker, T. (2021). Insulin resistance in COVID-19 and diabetes. *Primary Care Diabetes*, *15*(4), 629–634. https://doi.org/10.1016/j.pcd.2021.04.004

Guo, W., Li, M., Dong, Y., Zhou, H., Zhang, Z., Tian, C., Qin, R., Wang, H., Shen, Y., du, K., Zhao, L., Fan, H., Luo, S., & Hu, D. (2020). Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes/Metabolism Research and Reviews*, *36*, e3319. https://doi.org/10.1002/dmrr.3319

He, X., Yao, F., Chen, J., Wang, Y., Fang, X., Lin, X., Long, H., Wang, Q., & Wu, Q. (2021). The poor prognosis and influencing factors of high D-dimer levels for COVID-19 patients. *Scientific Reports*, *11*(1), 1830. https://doi.org/10.1038/s41598-021-81300-w

Hong, K.-H., Choi, J.-P., Hong, S.-H., Lee, J., Kwon, J.-S., Kim, S.-M., Park, S. Y., Rhee, J. Y., Kim, B. N., Choi, H. J., Shin, E. C., Pai, H., Park, S. H., & Kim, S. H. (2018). Predictors of mortality in Middle East respiratory syndrome (MERS). *Thorax*, *73*(3), 286–289. https://doi.org/10.1136/thoraxjnl-2016-209313

Hui, D. S., Azhar, E. I., Kim, Y.-J., Memish, Z. A., Oh, M.-D., & Zumla, A. (2018). Middle East respiratory syndrome coronavirus: Risk factors and determinants of primary, household, and nosocomial transmission. *The Lancet Infectious Diseases*, *18*(8), e217–e227. https://doi.org/10.1016/s1473-3099(18)30127-0

Kaminska, H., Szarpak, L., Kosior, D., Wieczorek, W., Szarpak, A., Al-Jeabory, M., Gawel, W., Gasecka, A., Jaguszewski, M. J., & Jarosz-Chobot, P. (2021). Impact of diabetes mellitus on in-hospital mortality in adult patients with COVID-19: A systematic review and meta-analysis. *Acta Diabetologica*, *58*(8), 1101–1110. https://doi.org/10.1007/s00592-021-01701-1

Kastora, S., Patel, M., Carter, B., Delibegovic, M., & Myint, P. K. (2022). Impact of diabetes on COVID-19 mortality and hospital outcomes from a global perspective: An umbrella systematic review and meta-analysis. *Endocrinology, Diabetes & Metabolism*, *5*(3), e00338. https://doi.org/10.1002/edm2.338

Kaushal, K., Kaur, H., Sarma, P., Bhattacharyya, A., Sharma, D. J., Prajapat, M., Pathak, M., Kothari, A., Kumar, S., Rana, S., Kaur, M., Prakash, A., Mirza, A. A., Panda, P. K., Vivekanandan, S., Omar, B. J., Medhi, B., & Naithani, M. (2022). Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. *Journal of Critical Care*, *67*, 172–181. https://doi.org/10.1016/j.jcrc.2021.09.023

Kernan, K. F., & Carcillo, J. A. (2017). Hyperferritinemia and inflammation. *International Immunology*, *29*(9), 401–409. https://doi.org/10.1093/intimm/dxx031

Lazarus, G., Audrey, J., Wangsaputra, V. K., Tamara, A., & Tahapary, D. L. (2021). High admission blood glucose independently predicts poor prognosis in COVID-19 patients: A systematic review and dose-response meta-analysis. *Diabetes Research and Clinical Practice*, *171*, 108561. https://doi.org/10.1016/j.diabres.2020.108561

Li, G., Deng, Q., Feng, J., Li, F., Xiong, N., & He, Q. (2020). Clinical characteristics of diabetic patients with COVID-19. *Journal of Diabetes Research*, *2020*, 1652403. https://doi.org/10.1155/2020/1652403

Li, M.-Y., Li, L., Zhang, Y., & Wang, X.-S. (2020). Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infectious Diseases of Poverty*, *9*(1), 45. https://doi.org/10.1186/s40249-020-00662-x

Lim, S., Bae, J. H., Kwon, H.-S., & Nauck, M. A. (2021). COVID-19 and diabetes mellitus: From pathophysiology to clinical management. *Nature Reviews. Endocrinology*, *17*(1), 11–30. https://doi.org/10.1038/s41574-020-00435-4

Loomba, R. S., Villarreal, E. G., Farias, J. S., Aggarwal, G., Aggarwal, S., & Flores, S. (2022). Serum biomarkers for prediction of mortality in patients with COVID-19. *Annals of Clinical Biochemistry*, *59*(1), 15–22. https://doi.org/10.1177/00045632211014244

Luo, S.-K., Hu, W.-H., Lu, Z.-J., Li, C., Fan, Y.-M., Chen, Q.-J., Chen, Z. S., Ye, J. F., Chen, S. Y., Tong, J. L., Wang, L. L., Mei, J., & Lu, H. Y. (2021). Diabetes patients with comorbidities had unfavorable outcomes following COVID-19: A retrospective study. *World Journal of Diabetes*, *12*(10), 1789–1808. https://doi.org/10.4239/wjd.v12.i10.1789

Ma, Z., Yang, K. Y., Huang, Y., & Lui, K. O. (2022). Endothelial contribution to COVID-19: an update on mechanisms and therapeutic implications. *Journal of Molecular and Cellular Cardiology*, *164*, 69–82. https://doi.org/10.1016/j.yjmcc.2021.11.010

Mahamat-Saleh, Y., Fiolet, T., Rebeaud, M. E., Mulot, M., Guihur, A., El Fatouhi, D., Laouali, N., Peiffer-Smadja, N., Aune, D., & Severi, G. (2021). Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: A systematic review and meta-analysis of observational studies. *BMJ Open*, *11*(10), e052777. https://doi.org/10.1136/bmjopen-2021-052777

Malik, P., Patel, U., Mehta, D., Patel, N., Kelkar, R., Akrmah, M., Gabrilove, J. L., & Sacks, H. (2021). Biomarkers and outcomes of COVID-19 hospitalisations: Systematic review and meta-analysis. *BMJ Evidence-Based Medicine*, *26*(3), 107–108. https://doi.org/10.1136/bmjebm-2020-111536

Mithal, A., Jevalikar, G., Sharma, R., Singh, A., Farooqui, K. J., Mahendru, S., Krishnamurthy, A., Dewan, A., & Budhiraja, S. (2021). High prevalence of diabetes and other comorbidities in hospitalized patients with COVID-19 in Delhi, India, and their association with outcomes. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*, *15*(1), 169–175. https://doi.org/10.1016/j.dsx.2020.12.029

Moftakhar, L., Moftakhar, P., Piraee, E., Ghaem, H., Valipour, A., & Azarbakhsh, H. (2021). Epidemiological characteristics and outcomes of COVID-19 in diabetic versus non-diabetic patients. *International Journal of Diabetes in Developing Countries*, *41*(3), 383–388. https://doi.org/10.1007/s13410-021-00930-y

Nikolich-Zugich, J., Knox, K. S., Rios, C. T., Natt, B., Bhattacharya, D., & Fain, M. J. (2020). SARS-CoV-2 and COVID-19 in older adults: What we may expect regarding pathogenesis, immune responses, and outcomes. *GeroScience*, *42*(2), 505–514. https://doi.org/10.1007/s11357-020-00186-0

Niu, J., Sareli, C., Mayer, D., Visbal, A., & Sareli, A. (2022). Lymphopenia as a predictor for adverse clinical outcomes in hospitalized patients with COVID-19: A single center retrospective study of 4485 cases. *Journal of Clinical Medicine*, *11*(3), 700. https://doi.org/10.3390/jcm11030700

Perez, A., Naljayan, M., Shuja, I., Florea, A., & Reisin, E. (2021). Hypertension, obesity, and COVID-19: A collision of pandemics. *Current Hypertension Reports*, *23*(6), 36. https://doi.org/10.1007/s11906-021-01153-6

Perez-Saez, J., Lauer, S. A., Kaiser, L., Regard, S., Delaporte, E., Guessous, I., Stringhini, S., Azman, A. S., Alioucha, D., Arm-Vernez, I., Bahta, S., Barbolini, J., Baysson, H., Butzberger, R., Cattani, S., Chappuis, F., Chiovini, A., Collombet, P., Courvoisier, D., … Zeballos Valle, A. (2021). Serology-informed estimates of SARS-CoV-2 infection fatality risk in Geneva, Switzerland. *The Lancet Infectious Diseases*, *21*(4), e69–e70. https://doi.org/10.1016/S1473-3099(20)30584-3

Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., The Northwell COVID-19 Research Consortium, Barnaby, D. P., Becker, L. B., Chelico, J. D., Cohen, S. L., Cookingham, J., Coppa, K., Diefenbach, M. A., Dominello, A. J., Duer-Hefele, J., Falzon, L., Gitlin, J., Hajizadeh, N., … Zanos, T. P. (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new York City area. *JAMA*, *323*(20), 2052–2059. https://doi.org/10.1001/jama.2020.6775

Shakaroun, D. A., Lazar, M. H., Horowitz, J. C., & Jennings, J. H. (2022). Serum ferritin as a predictor of outcomes in hospitalized patients with Covid-19 pneumonia. *Journal of Intensive Care Medicine*, *38*, 21–26. https://doi.org/10.1177/08850666221113252

Steenblock, C., Richter, S., Berger, I., Barovic, M., Schmid, J., Schubert, U., Jarzebska, N., von Mässenhausen, A., Linkermann, A., Schürmann, A., Pablik, J., Dienemann, T., Evert, K., Rodionov, R. N., Semenova, N. Y., Zinserling, V. A., Gainetdinov, R. R., Baretton, G., Lindemann, D., … Bornstein, S. R. (2021). Viral infiltration of pancreatic islets in patients with COVID-19. *Nature Communications*, *12*(1), 3534. https://doi.org/10.1038/s41467-021-23886-3

Tabrizi, M., Rasmi, F., Hosseinzadeh, Y., Rezaei, E., Balvardi, S., Kouchari, M., & Ebrahimi, G. (2021). Diabetes is associated with higher mortality and severity in hospitalized patients with COVID-19. *EXCLI Journal*, *20*, 444–453.

Tang, N., Li, D., Wang, X., & Sun, Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis*, *18*(4), 844–847. https://doi.org/10.1111/jth.14768

Vargas-Vázquez, A., Bello-Chavolla, O. Y., Ortiz-Brizuela, E., Campos-Muñoz, A., Mehta, R., Villanueva-Reza, M., Bahena-López, J. P., Antonio-Villa, N. E., González-Lara, M. F., Ponce de León, A., Sifuentes-Osornio, J., & Aguilar-Salinas, C. A. (2021). Impact of undiagnosed type 2 diabetes and pre-diabetes on severity and mortality for SARS-CoV-2 infection. *BMJ Open Diabetes Research & Care*, *9*(1), e002026. https://doi.org/10.1136/bmjdrc-2020-002026

Varikasuvu, S. R., Varshney, S., & Dutt, N. (2021). Markers of coagulation dysfunction and inflammation in diabetic and non-diabetic COVID-19. *Journal of Thrombosis and Thrombolysis*, *51*(4), 941–946. https://doi.org/10.1007/s11239-020-02270-w

Verity, R., Okell, L. C., Dorigatti, I., Winskill, P., Whittaker, C., Imai, N., Cuomo-Dannenburg, G., Thompson, H., Walker, P. G. T., Fu, H., Dighe, A., Griffin, J. T., Baguelin, M., Bhatia, S., Boonyasiri, A., Cori, A., Cucunubá, Z., FitzJohn, R., Gaythorpe, K., … Ferguson, N. M. (2020). Estimates of the severity of coronavirus disease 2019: A model-based analysis. *The Lancet Infectious Diseases*, *20*(6), 669–677. https://doi.org/10.1016/S1473-3099(20)30243-7

von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P., & STROBE Initiative. (2008). The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Journal of Clinical Epidemiology*, *61*(4), 344–349. https://doi.org/10.1016/j.jclinepi.2007.11.008

Won, T., Wood, M. K., Hughes, D. M., Talor, M. V., Ma, Z., Schneider, J., Skinner, J. T., Asady, B., Goerlich, E., Halushka, M. K., Hays, A. G., Kim, D. H., Parikh, C. R., Rosenberg, A. Z., Coppens, I., Johns, R. A., Gilotra, N. A., Hooper, J. E., Pekosz, A., & Čiháková, D. (2022). Endothelial thrombomodulin downregulation caused by hypoxia contributes to severe infiltration and coagulopathy in COVID-19 patient lungs. *eBioMedicine*, *75*, 103812. https://doi.org/10.1016/j.ebiom.2022.103812

Yang, K. Y., Huang, Y., & Lui, K. O. (2022). Endothelial contribution to COVID-19: An update on mechanisms and therapeutic implications. *Journal of Molecular and Cellular Cardiology*, *164*, 69–82. https://doi.org/10.1016/j.yjmcc.2021.11.010

Yang, L., Han, Y., Nilsson-Payant, B. E., Gupta, V., Wang, P., Duan, X., Tang, X., Zhu, J., Zhao, Z., Jaffré, F., Zhang, T., Kim, T. W., Harschnitz, O.,

Redmond, D., Houghton, S., Liu, C., Naji, A., Ciceri, G., Guttikonda, S., … Chen, S. (2020). A human pluripotent stem cell-based platform to study SARS-CoV-2 tropism and model virus infection in human cells and organoids. *Cell Stem Cell*, *27*(1), 125–136.e7. https://doi.org/10.1016/j.stem.2020.06.015

Yang, Q., Gao, J., Zeng, X., Chen, J., & Wen, D. (2022). Relationship between platelet count and in-hospital mortality in adult patients with COVID-19: A retrospective cohort study. *Frontiers in Medicine*, *9*, 802412. https://doi.org/10.3389/fmed.2022.802412

Yang, X., Yu, Y., Xu, J., Shu, H., Xia, J., Liu, H., Wu, Y., Zhang, L., Yu, Z., Fang, M., Yu, T., Wang, Y., Pan, S., Zou, X., Yuan, S., & Shang, Y. (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*, *8*(5), 475–481. https://doi.org/10.1016/S2213-2600(20)30079-5

Yang, Y., Zhong, W., Tian, Y., Xie, C., Fu, X., & Zhou, H. (2020). The effect of diabetes on mortality of COVID-19: A protocol for systematic review and meta-analysis. *Medicine*, *99*(27), e20913. https://doi.org/10.1097/md.0000000000020913

Zhao, R., Su, Z., Komissarov, A. A., Liu, S.-L., Yi, G., Idell, S., Matthay, M. A., & Ji, H. L. (2021). Associations of D-dimer on admission and clinical features of COVID-19 patients: A systematic review, meta-analysis, and meta-regression. *Frontiers in Immunology*, *12*, 691249. https://doi.org/10.3389/fimmu.2021.691249

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet*, *395*(10229), 1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3

How to cite this article: Asaduzzaman, M., Romel Bhuia, M., Zabed Jillul Bari, M., Nazmul Alam, Z., Rahman, K., Hossain, E., & Alam, M. M. J. (2022). Predictors of mortality and ICU requirement in hospitalized COVID-19 patients with diabetes: A multicentre study. *Nursing Open*, *00*, 1–13. https://doi.org/10.1002/nop2.1567

APPENDIX 1

TABLE A1 The predictors for mortality for COVID-19 patient without diabetes

Characteristics	OR	*p*-Value
Age	1.08	0.001
Platelet count	1.00	0.04
Admission SpO2	0.90	0.01