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Predictors of COVID-19 outcome in type 2 diabetes mellitus: a hospital-based study

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Abstract

Background Diabetes has become a significant risk factor for COVID-19-related severe illness and death.

Methods This was a retrospective cohort study of 104 patients, with or without type 2 (diabetes mellitus) DM, diagnosed with COVID-19 between June and September 2021 in Benha University Hospital, Egypt. Outcome measures including discharge after recovery, transfer to ICU and intubation, or death were recorded. Univariate and multivariate logistic regression analysis was done for the prediction of death in diabetic patients.

Results Length of hospital stay was significantly higher in diabetic (median 15 days) compared to non-diabetic patients (median 10 days). ICU admission and intubation among diabetic patients were substantially higher than non-diabetics. Univariate regression analysis established that old age ($p = 0.02$: OR = 1.03: CI 1.00–1.07), multiple comorbidities ($p = 0.005$: OR = 8.66: CI 1.9–38.5), diabetic complications ($p = 0.000$: OR = 6.401:CI 2.5–16.3), HbA1c ($p = 0.01$: OR = 1.22: CI 1.04–1.43), length of hospital stay ($p = 0.005$: OR = 1.07: CI 1.02–1.12), and ICU admission ($p = 0.00$: OR = 44.1: CI 9.4–205.3) were predictors of death for diabetic patients as well as neutrophilic count, D-dimer, and CRP levels. Multivariate regression analysis concluded that ICU admission was the most significant predictor of death in diabetic patients.

Conclusion Type 2 DM patients, infected with the COVID-19 virus exhibited more admission to ICU and intubation with longer hospital stays compared to those without diabetes with a similar death rate. Old age, HbA1C, comorbidities, diabetic complications, length of hospital stay and ICU admission, and inflammatory parameters were significant predictors of death in diabetic patients.

Keywords COVID-19, Diabetes mellitus, Outcome

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was, to begin with, depicted in Wuhan, China, in December 2019, and after that, it spread around the world. It was evaluated that the death rate for COVID-19 is roughly 0.5–1.0% [1–3]. COVID-19 pandemic-hit zones have been confronting basic deficiencies with respect to supplies such as ventilators and intensive care units (ICU) [4]. SARS-CoV-2 is a positive-stranded RNA infection that's encompassed by a protein-decorated lipid bilayer containing a single-stranded RNA genome; SARS-CoV-2 has 82% homology with human SARS-CoV, which causes severe acute respiratory disorder (SARS) [5]. In human cells, SARS-CoV-2 enters the angiotensin-converting protein 2 (ACE2) receptor [6] which is profoundly found in lung alveolar cells, cardiac myocytes, vascular endothelium, and different other cell sorts [7]. Like

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SARS-CoV and the related Middle Eastern respiratory syndrome (MERS)-CoV, SARS-CoV-2 infection causes mild symptoms in the first 2 weeks of infection however has the potential to develop severe illness, including a systemic inflammatory response, acute respiratory distress syndrome (ARDS), multi-organ affection and shock [8]. Individuals of old age, male sex, cardiovascular disease (CVD), obesity, type 1 diabetes mellitus (DM), or type 2 diabetes mellitus (DM) are at a high risk of developing severe COVID-19 or passing away [9–11]. In addition, Studies have shown that patients with COVID-19 admitted to ICUs frequently have underlying CVD and DM [12, 13]. The fundamental and clinical understanding of the potential interactions between COVID-19 and DM has been reviewed [14]. Diabetes has become a significant risk factor for COVID-19-related severe illness and death [15]. The first aspect to point out is that patients with COVID-19 also exhibit elevation of other inflammatory markers, such as D-dimer, ferritin, and IL-6 [16] which might raise the risk of microvascular and macrovascular complications originating from low-grade vascular inflammation in patients with DM [17]. Furthermore, one should not forget that SARS-CoV-2 infection increases the risk of thromboembolism and is more likely to induce cardiorespiratory failure in diabetic individuals [18]. And then, good glycemic control in the acute hospital setting in China was an important factor for better outcomes in patients with pre-existing type 2 DM [15]. In the present study, the outcome of COVID-19 in diabetic compared to non-diabetic populations will be clarified for patients admitted to Benha University Hospital.

Patients and methods

This was a retrospective observational study on patients admitted to Benha University Hospital by COVID-19 infection from June to September 2021. The study was approved by the Ethics Committee of Benha Faculty of Medicine, Benha University (RC;3-5-2021). A total number of 104 patients with age ≥ 18 years old were divided into 2 groups; group with type 2 DM and group without diabetes mellitus. Diagnosis of COVID-19 infection was determined by a positive reverse transcription-PCR (RT-PCR) from a nasopharyngeal swab. Type 2 diabetes diagnosis according to the American Diabetes Association (ADA) 2021 [19]. Diabetic groups were further classified according to glycemic control into controlled (HbA1c ≤ 7) and uncontrolled groups (HbA1c > 7). Pregnant and lactating females, patients < 18 years, and type 1 diabetes mellitus were excluded from the study.

Data collection

All patients were subjected to full history taking with stress on age, sex, comorbidities, medication history, presence of DM, and diabetes-related complications. Treatment given to the patients was recorded including medications given for COVID-19 treatments. Clinical examination was performed in detail including vital signs, SpO_2 on arrival to the emergency department, and body mass index (BMI).

Laboratory data

Hematological and biochemical data on the day of COVID-19 diagnosis were collected containing; complete blood count (CBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum ferritin, D-dimer, lactate dehydrogenase (LDH), glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), kidney function tests (KFT), and liver function tests (LFT). Radiological imaging in the form of chest X-ray and CT chest findings was registered. All laboratory parameters were performed in the Clinical Pathology Department in Benha University Hospital according to the local routine methods.

CT findings

Pulmonary affection of COVID-19 infection was evaluated by the COVID-19 Reporting and Data System (CO-RADS) [20].

Outcome measures

Data starting from admission at the emergency department to either ICU, word, or word then ICU transfer with length of hospital stay were registered. The outcome of the disease includes discharge after recovery, transfer to ICU, or death. Medications for COVID-19 as well as intubation whenever needed were recorded.

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 26 software (Spss Inc., Chicago, ILL Company). Categorical data were presented as numbers and percentages while quantitative data were expressed as mean ± standard deviation/median and interquartile range. Inter-group comparison of categorical data was performed by using the chi-square test ($\chi 2$ value) and Fisher exact test, Student's t test was used to compare the mean of two groups of numerical (parametric) data, for continuous non-parametric data, Mann-Whitney U test was used for inter-group analysis. Some investigated parameters were entered into a logistic regression model to determine which of these factors is considered a significant predictor. P value < 0.05 was considered statistically significant.

Results

Analysis of clinical and laboratory characteristics

This study analyzed the demographic, laboratory, and clinical features of 104 COVID-19 patients confirmed by PCR who were hospitalized in Benha University Hospital from June to September 2021. Forty-seven patients (43.9%) were males and 57 (56.1%) were females. Age was significantly higher in diabetic patients (median 61 years) compared to non-diabetics (median 55 years) ($p = 0.03$) with ages ranging from 18 to 92 years. As shown in Table 1, sex was not statistically significant ($p = 0.29$) between diabetic and non-diabetic patients. There was no significant difference between the diabetic and non-diabetic groups regarding residence of the patients ($p = 0.09$) and smoking status (0.44). Median BMI in diabetic patients was 28.3 kg/m^2 compared to 27 kg/m^2 in non-diabetic patients with no significant difference ($p > 0.05$). No CT abnormality was found in 8.9% of diabetic patients versus 16.9% of non-diabetic patients. CT picture of COVID-19 (CO-RADS categories) was not substantially different ($p = 0.23$) between diabetic and non-diabetic groups. Comorbidities associated with the patients were named renal (polycystic k and CKD), vascular (hypertension, IHD, stroke), respiratory (COPD, B.A), CNS, GIT, endocrinal (hypothyroidism), and others. Comorbidities were almost similar between diabetic and non-diabetic COVID-19 patients ($p = 0.94$). Concerning the treatment of COVID-19; all the study population received supportive treatment in the form of vitamin C, vitamin D, and azithromycin, hydroxychloroquine; 64.5% and 50.8% of diabetic and non-diabetic patients respectively received anticoagulants in the form of LMWH; 24.5% diabetic versus 30.5% non-diabetic patients received steroids treatment with dexamethasone or Methylprednisolone; 6.7% diabetic vs. 1.7% non-diabetics received antiviral treatment with Favipiravir; and 4.4% diabetic vs. 1.7% non-diabetic patients used Actimra. Types of treatment for COVID-19 did not significantly differ between diabetic and non-diabetic patients ($p = 0.125$). All diabetic patients were using either diet control (3 patients), oral hypoglycemic agents (30 patients), or insulin (12 patients) while after the COVID-19 infection, hyperglycemia caused 14 non-diabetic patients to use insulin therapy and only one non-diabetic started to use oral hypoglycemic agents. Also, 66.7% of diabetic patients were on oral hypoglycemic drugs prior to COVID-19 infection *vs.* only 6.7% after COVID-19 infection, while the percentage of diabetic patients on insulin had increased from 26.7 to 88.9%. In terms of biochemical measures, neutrophils, FPG, HbA1c, s. creatinine was significantly higher in diabetic compared to non-diabetic patients (Table 2). Total leucocytic count, neutrophilic counts, and ESR were significantly higher in uncontrolled diabetic patients (HbA1c > 7%) (Table 3).

Analysis of outcome of COVID-19

Length of hospital stay was significantly higher in diabetic (median 15 days) compared to non-diabetic patients (median 10 days) ($p = 0.025$). ICU admission (either from the start or afterward admission) among diabetic patients (No. 25) was substantially higher than among non-diabetics (No. 19) ($p = 0.01$). Intubation was done for 48.9 % of diabetic patients but for 27.1 % of non-diabetic patients ($p = 0.02$). Mortality was non-significant between diabetic and non-diabetic groups ($p = 0.134$) (Table 1). The bad outcome of COVID-19 infections was noted in the form of higher ICU admissions in the uncontrolled diabetic patients (22 patients) compared to the controlled group (7 patients) ($p = 0.001$) while non-significant difference concerning the length of hospital stay, death, and intubation between the same groups (Table 4). By using univariate regression analysis, predictors of death for COVID-19 infection in diabetic patients were; old age ($p = 0.02$: OR = 1.03: CI 1.00–1.07), comorbidities (p=0.005: OR = 8.66: CI 1.9–38.5), diabetic complications ($p = 0.000$: OR = 6.401: CI 2.5–16.3), HbA1c ($p = 0.01$: OR = 1.22: CI 1.04–1.43), length of hospital stay ($p = 0.005$: OR = 1.07: CI 1.02–1.12), and ICU admission ($p = 0.00$: OR = 44.1: CI 9.4–205.3). Moreover, neutrophilic count, D-dimer, and CRP levels were significant predictors of death in diabetics. On performing multivariate regression analysis, we concluded that ICU admission was the most significant predictor of death in diabetic patients ($p = 0.04$: OR = 223.2: CI 2.09–2386.7) (Table 5).

Discussion

This was a retrospective cohort study to describe the differences in clinical, laboratory features, and outcomes of COVID-19 patients with and without type 2 DM. Diabetic patients are more susceptible to infections, including the flu and pneumonia. Good glycemic control can lessen this risk; however, it cannot entirely eliminate it. It is advised that all diabetics have annual influenza and pneumococcal vaccines. Moreover, diabetes patients who contract respiratory viruses have a serious illness [21]. Previous studies revealed that people with DM had COVID-19 with greater severity [18]. Patients involved in the current study were admitted at Benha University Hospital in Egypt from June to September 2021 after following the Ministry of Health's protocol for supportive care and treatment of patients with COVID-19 infection (November 2020, version 1.4). 56.1% of the patients were females and 43.9% of them were males with ages ranging from 18 to 92 years. Diabetic patients using insulin were 26.7% after COVID-19 infection, 88.9% of diabetic patients were using insulin therapy

Table 1 Clinical characteristics and outcome data of COVID-19-infected patients

Variables	DM *N* = 45(%)	Not DM *N* = 59(%)	Test of significance	*p* value
Male	23 (51.1)	24 (40.7)	$\chi 2 = 1.12$	0.29
Female	22 (48.9)	35 (59.3)		
Residence				
Urban	40 (91.5)	45 (76.3)	$\chi 2 = 2.72$	0.09
Rural	5 (8.5)	14 (23.7)		
Smoking	5 (11.1)	4 (6.8)	FET = 0.61	
Yes	40 (88.9)	55 (93.2)		0.44
No				
Diabetes complications				
No	22 (48.9)			
Nephropathy	14 (31.1)			
Diabetic foot	1 (2.2)			
Stroke	2 (4.4)			
IHD	6 (13.3)			
Medication of diabetic patients before COVID-19 infection				
Diet control	3 (6.7)			
Oral hypoglycemic	30 (66.7)			
Insulin	12 (26.7)			
Medication of DM after COVID infection				
Diet control	2 (4.4)	44 (74.6)	FET = 50.9	< .001**
Oral hypoglycemic	3 (6.7)	1 (1.7)		
Insulin	40 (88.9)	14 (23.7)		
Comorbidities			$\chi 2 = 0.11$	0.94
No	20 (44.4)	28 (47.5)		
One comorbidity	19 (42.2)	24 (40.7)		
Multiple comorbidities	6 (13.3)	7 (11.9)		
Treatment of COVID				
Supportive	(100)	(100)	$\chi 2 = 8.2$	0.125
Anticoagulant	(64.5)	(50.8)		
Steroids	(24.5)	(30.5)		
Antiviral	3 (6.7)	1(1.7)		
Actimra	2 (4.4)	1(1.7)		
CT picture			$\chi 2 = 1.42$	
CO RAD 1	4 (8.9)	10 (16.9)		0.23
CO RAD 2-5	41 (91.1)	49 (83.1)		
ICU admission				
Yes	25(55.6)	19 (32.2)	$\chi 2 = 5.7$	0.01*
No	20(44.4)	40 (67.8)		
Intubation				
Yes	22 (48.9)	16 (27.1)	$\chi 2 = 5.2$	0.02*
No	23 (51.1)	43 (72.9)		
Discharge	30 (66.7)	47 (79.7)	$\chi 2 = 2.24$	0.134
Death	15 (33.3)	12 (20.3)		

*Significant as *P* value $\leq$ 0.05

**High significant as *P* value $\leq$ 0.001

Table 2 Laboratory data of COVID-19 infection patients in diabetic and non-diabetic

Variables	Diabetic *N* = 45	Non-diabetic *N* = 59	Mann-Whitney *U* test	*p* value
AST (IU/L):				
Median	34	37		> 0.05
Min-max	14–84	15–120	1237	
ALT (IU/L):				
Median	30	30		> 0.05
Min-max	15–62	12–175	1317	
D. Dimer:	s			
Median	0.8	0.7		
Min-max	0.1–6.5	0.1–6.7	1163	> 0.05
S. ferritin:				
Median	350	320		
Min-max	15–1169	10.7–1116	1102	> 0.05
HB(g/dl):				
Median	11	11.1		
Min-max	6.4–15.4	6.4–15.3	1304	> 0.05
WBCs:				
Median	9.9	8.4		> 0.05
Min-max	2.4–21.3	2.5–27	1079	
Neutrophils:				
Median	7.5	6.5		0.04*
Min-max	1.6–18.4	1.1–25.2	1026	
Lymphocytes:				
Median	1.1	1.2	1143	> 0.05
Min-max	0.2–3.75	0.3–6		
Platelets:				
Median	209	210		> 0.05
Min-max	81–452	28–662	1308	
ESR:				
Median	70	65		> .05
Min-max	12–130	7–140	1076	
CRP:				
Median	38	25		> .05
Min-max	6–250	4.3–233	1172	
FPG (mg/dl):				
Median	210	120	452	
Min-max	115–500	80–370		< 0.001**
HbA1c(%):				
Median	9.4	5.4		
Min-max	5.2–14	1–14.6	214	< 0.001**
LDH:				
Median	360	340		> 0.05
Min-max	29–870	29–936	1127.5	
BUN:				
Median	56	40		> 0.05
Min-max	20–150	18–150	1081	
Creatinine:				
Median	1.4	1.0		
Min-max	0.5–10.5	0.2–10.6	668.5	< 0.001**

*Significant as *P* value ≤ 0.05

**High significant as *P* value ≤ 0.001

for treatment of DM while 23.7% of non-diabetic patients used insulin for hyperglycemia after COVID-19 infection. At admission, it was noted the finding of elevation of the fasting plasma glucose (median FPG was 120 mg/dl) in patients with HbA1c < 6.5% (non-diabetic group). Stress hyperglycemia, which is typically defined as a brief increase in blood sugar in the presence of an acute illness or following surgery in a patient with an A1C below 6.5%, is linked to an extended hospital stay, an extended amount of time spent managing the patient's ventilator, and an increased mortality rate in critically ill patients [22]. Due to a lack of follow-up after hospital release, it is impossible to determine if these patients should be classified as newly diagnosed type 2 DM, having glucocorticoid effect during treatment of COVID-19, or suffering stress-induced acute hyperglycemia in the study.

In our results, it was illustrated that no significant difference in comorbidities between diabetic and non-diabetic patients. In contrast, it was found that Diabetic patients have more comorbid diseases than non-diabetics, including hypertension, coronary artery disease, chronic renal disease, asthma, and cerebrovascular disease [23]. Univariate logistic regression in the present study identified that multiple comorbidities were a predictor for death in diabetic patients. In another study, it was found that congestive heart failure was the only comorbidity that is strongly related to increased mortality [24]. According to multicenter research from Turkey, among patients with CKD, 21.9% were admitted to the ICU, and 14.2% died [25]. All our patients in the present study received hydroxychloroquine according to the protocol of treatment of the Egyptian Ministry of Health. However, according to certain studies, using hydroxychloroquine as a therapy for COVID-19 is not effective [26]. In the current study, steroid treatment was given to 24.5% of diabetic compared to 30.5% of non-diabetic patients in the form of dexamethasone or Methylprednisolone. Contrarily, the administration of corticosteroids as low-dose or pulse therapy has been a recognized method of treating patients with acute respiratory distress syndrome (ARDS) and other acute lung disorders to have an immediate immunosuppressive effect [27]. Our results revealed that serum ferritin, CRP, D-dimer, ESR, and lymphocytes were non significantly different between diabetic and non-diabetic patients, while only neutrophilic count was significantly higher in the diabetic group compared to the non-diabetic group. Total leucocytic count, neutrophilic counts, and ESR were significantly higher in uncontrolled diabetic patients. Neutrophil, D-dimer, and CRP were significant predictors of death in diabetic patients. Neutrophils, CRP, and lymphocytes were not significant predictors of death among diabetics, according to one

Table 3 Laboratory features of controlled and uncontrolled diabetic patients

Variables	Controlled diabetes (HBA1c < 7) *N* = 12	Uncontrolled diabetes (HBA1c ≥ 7) *N* = 33	Test of significance Mann*Whitney test	*p* value
AST (IU/L): Median Min-max	40 18–84	33 14–70	118	0.04*
ALT (IU/L): Median Min- max	38 16–60	30 15–62	161.5	0.34
D. Dimer: Median Min-max	.900 3.4.5	.800 0.1–6.5	195	0.94
S. ferritin: Median Min-max	365.5 190–850	350 15–1169	190	0.83
HB(g/dl): Median Min-max	10.5 6.4–15	11.1 7–15.4	172	0.50
WBCs: Median Min-max	7.55 2.4–12	11 5.1–21.3	94.5	0.008**
Neutrophils: Median Min-max	5.25 1.6–8.7	8.8 3.7–18.4	75	0.002**
Lymphocytes: Median Min-max	1.00 0.2–3.7	1.1 0.3–3.5	192.5	0.88
Platelets: Median Min-max	207 96–286	210 81–452	173	0.52
ESR: Median Min-max	59.5 12–88	75 22–130	102	0.01*
CRP: Median Min-max	29 6–96	38 11–250	157.5	0.29
LDH: Median Min-max	345 100–520	400 29–870	178	0.60
BUN: Median Min-max	135 40–310	57 20–244	126	0.06
Creatinine: Median Min-max	1.85 0.9–9	1.4 0.5–10.5	169.5	0.46

*Significant as *P* value ≤ 0.05

**High significant as *P* value ≤ 0.001

study that examined 42 regressors (variables) in unbiased multivariate logistic regression analysis against the primary outcome of death [28].

Absolute neutrophil count (ANC) and CRP were greater in type 2 DM patients than in non-diabetic controls, and lymphocytic and eosinophilic counts were lower [29]. In addition, one study disclosed higher levels of C-reactive protein in diabetic COVID019 patients [30].

In our study, the death rate was non significantly higher in diabetic patients than in non-diabetics. The death rate in our study represented 25.9% overall of admitted COVID-19 infection with 33.3% in diabetic patients vs. 20.3% in non-diabetic patients. However, one study found a 10% death rate [24] and another study revealed high mortality in diabetic people and older age groups [31]. A study of 174 Chinese COVID-19-positive patients

Table 4 Outcome of controlled and uncontrolled diabetic patients

Variables	Controlled Diabetic *N* = 12	Uncontrolled diabetic *N* = 33	Test of significance	*p* value
ICU admission (either from the start or after admission) (*n* = 29)	7(24.1)	22(75.9)	7.75	< 0.001**
Intubation	4 (33.3)	10 (30.3)	.037	1.00
Outcome of COVID-19 infection				
Discharge	9(75)	21(63.6)	0.51	0.72
Death	3(25)	12(36.4)		

**High significant as *P* value ≤ 0.001

Table 5 Univariate and multivariate logistic regression analysis of various variables for prediction of death among diabetic patients

	Univariate analysis				Multivariate analysis			
	***p* value**	**OR**	**95%CI**		***p* value**	**OR**	**95%CI**	
Age	0.022*	1.039	1.005	1.073				
Sex	0.589	0.783	0.322	1.904				
HbA1c	0.011*	1.227	1.048	1.436				
Comorbidities	0.005*	8.667	1.950	38.521				
Complications	0.000*	6.401	2.509	16.330				
Hospital stay	0.005*	1.073	1.021	1.128				
ICU admission	0.000*	44.118	9.480	205.309	0.04*	223.2	2.09	2386.7
Smoking	0.599	1.479	.343	6.376				
Residence	0.998	0.75	0.66	1.86				
BMI	0.381	1.036	.958	1.120				
Lymphocyte	0.117	.657	.389	1.111				
neutrophile	0.002*	1.181	1.061	1.315				
D-dimer	0.001*	1.659	1.225	2.248				
CRP	< 0.001*	1.026	1.013	1.038				
Ferritin	0.200	1.001	.999	1.003				

*Significant as *P* value ≤ 0.05

reported that patients with diabetes who had no other comorbidities had higher mortality rates (16.7% vs. 0%, $P = 0.03$) [32]. Another study demonstrated death of hospitalized positive COVID-19 was higher in diabetic patients [16]. Initial records in the UK indicated that diabetic patients constituted one-third of COVID-19 patients dying in hospitals [33]. However, the presence of DM was not independently related to in-hospital fatalities, according to data from a large-scale, multi-center, retrospective investigation in Wuhan that included 1561 COVID-19 patients [34]. Data from 463 COVID-19 patients in the USA further demonstrates that there is no connection between diabetes mellitus (DM) and death, ICU admission risk, or need for mechanical ventilation [35]. In contrast, death was significantly higher in diabetic compared to non-diabetic patients in another study [33]. Our data constituted a small-sized sample in comparison to other studies so we could not assess the real mortality in the Egyptian population. we evaluated the death among the admitted cases, not the whole population. Univariate logistic regression in the present study identified that HbA 1c was a predictor for death in diabetic patients. Poorer glycemic control may increase the risk of worse health outcomes, according to preclinical research on the mechanistic relationships between glucose control and Middle East respiratory syndrome coronavirus (MERS-CoV) infection and the impact of long-term glycemic control on the clinical outcomes of COVID-19-infected subjects with type 2 diabetes [36]. In mice that have a longer time to respond to MERS-CoV infection, type 2 diabetes mellitus is linked to a slower inflammatory response. By decreasing immune system components including leukocyte chemotaxis and phagocytosis, hyperglycemia itself has harmful effects. According to estimates, major infections like COVID-19 would cause substantial levels of morbidity and death due to these host response deficits in people with diabetes [31]. Angiotensin-converting enzyme 2 (ACE2) immunostaining was also found in pancreatic islet cells, which are identical to the myocardium and lung alveolar epithelium. This was discovered using immunohistochemistry labeling of cadaveric pancreatic tissue. Direct islet cell toxicity during infection appears plausible as a cause of acute hyperglycemia, and ACE2 is a recognized receptor protein for coronavirus attachment [29, 37]. In the current study, ICU admission and endotracheal intubations in diabetics were significantly higher than in non-diabetic patients. Also, the admissions to the ICU were significantly higher in uncontrolled diabetic patients than in controlled diabetic patients. Patients with type 2 diabetes had a threefold higher risk of hospitalization and a fourfold higher risk of ICU admission during the 2009 influenza A (H1N1) pandemic. However, a nationwide analysis in China that included roughly one-third as many patients as those included in our studies revealed that patients with diabetes had higher rates of death (10.0% vs. 2.5%) and ICU admission (14.6% vs. 5.5%) compared to those without diabetes [31]. In our results, older age is a predictor for death in diabetics (confidence interval, CI 1.00–1.07; $p = 0.02$) Similar to a previous

study [24]. The reason for such differences in severity and outcomes in diabetic patients with COVID-19 is likely due to the multifactorial syndromic nature of diabetes. In our cohort, for instance, we found that diabetic patients had a higher percentage of death rate (25.9 % overall with 33.3% in diabetics vs. 20.3% in non-diabetic patients) but our data was among admitted patients with COVID-19 infection only.

Conclusion

Our findings demonstrated that type 2DM patients, infected with the COVID-19 virus, were exhibited more admission to ICU and intubation with longer hospital stays compared to those without diabetes. However, mortality rates were similar in both groups. Glycemic control additionally, could worsen the inflammatory response and the need for ICU admission. Old age, HbA1C, comorbidities, diabetic complications, length of hospital stay and ICU admission, neutrophil count, D-dimer, and CRP levels were significant predictors of death in diabetic patients. As recommended by national recommendations, doctors should manage stress hyperglycemia and uncontrolled diabetes in critically ill patients with basal-bolus insulin therapy in the majority of non-ICU patients and continuous insulin infusion in the critically sick.

Strength of the study

Our results evaluated the effect of glycemic control on the inflammatory response and outcome of the COVID-19 infection.

Limitations of the study

Firstly, retrospective observational research was done on patients who had recorded incidents. Data on pertinent risk variables may therefore not be taken into consideration given their potential to have a significant impact on COVID-19 progression. For that reason, the impact of diabetes on the clinical outcomes would not have been as accurate as in a prospective study. Secondly, the sample size is small. Thirdly, this study did not consider detailed diabetes history such as duration, treatments, and complications of diabetes as well as type 1 DM. Lastly, age is an important risk factor in COVID-19 outcomes and the diabetic patient's group was significantly older than the control (not diabetic) group, which caused bias in the results so it was better to choose an age-matched control group.

Abbreviations

SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
ACE2	Angiotensin-converting protein 2
MERS	Middle Eastern respiratory syndrome
ARDS	Acute respiratory distress syndrome
DM	Diabetes mellitus.
CVD	Cardiovascular disease
CBC	Complete blood count
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
LDH	Lactate dehydrogenase
HbA1c	Glycated hemoglobin
FPG	Fasting plasma glucose
KFT	Kidney function tests
LFT	Liver function tests
CO-RADS	COVID-19 Reporting and Data System

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Authors' contributions

Amira M. E. wrote the manuscript. Ahmed E. M., Rasha O. A., and Ahmed W. M. collected data from the patients. Eman M. A. performed the statistical analysis. Maha H.M. was responsible for biochemical data recruitment. Mohamad S.E. revised the manuscript. All authors have confirmed the final version of the paper.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The protocol of the study was approved by the Ethics Committee of Benha Faculty of Medicine, Benha University, Egypt (RC;3-5-2021).

Competing interests

The authors declare that they have no conflicts of interest.

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References

1. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N et al (2020) Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 20(6):669–677. https://doi.org/10.1016/S1473-3099(20)30243-7
2. Perez-Saez J, Lauer SA, Kaiser L, Regard S, Delaporte E, Guessous I et al (2021) Serology-informed estimates of SARS-CoV-2 infection fatality risk in Geneva, Switzerland. Lancet Infect Dis 21(4):e69–e70. https://doi.org/10.1016/S1473-3099(20)30584-3
3. Salje H, Tran Kiem C, Lefrancq N, Courtejoie N, Bosetti P, Paireau J et al (2020) Estimating the burden of SARS-CoV-2 in France. Science (New York, NY) 369(6500):208–211. https://doi.org/10.1126/science.abc3517
4. Faust JS, Del Rio C (2020) Assessment of deaths from COVID-19 and from seasonal influenza. JAMA Intern Med 180(8):1045–1046. https://doi.org/10.1001/jamainternmed.2020.2306
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y et al (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet (London, England) 395(10223):507–513. https://doi.org/10.1016/S0140-6736(20)30211-7
6. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D (2020) Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell 181(2):281–292.e6. https://doi.org/10.1016/j.cell.2020.02.058

7. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS (2020) Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med 46(4):586–590. https://doi.org/10.1007/s00134-020-05985-9
8. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the chinese center for disease control and prevention. JAMA 323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648
9. Holman N et al (2020) Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. Lancet Diabetes Endocrinol 8:823–833
10. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A et al (2020) Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 323(16):1574–1581. https://doi.org/10.1001/jama.2020.5394
11. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A (2020) Clinical Characteristics of Covid-19 in New York City. N Engl J Med 382(24):2372–2374. https://doi.org/10.1056/NEJMc2010419
12. Piva S, Filippini M, Turla F, Cattaneo S, Margola A, De Fulviis S et al (2020) Clinical presentation and initial management critically ill patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Brescia, Italy. J Crit Care 58:29–33. https://doi.org/10.1016/j.jcrc.2020.04.004
13. Myers LC, Parodi SM, Escobar GJ, Liu VX (2020) Characteristics of hospitalized adults with COVID-19 in an integrated health care system in California. JAMA 323(21):2195–2198. https://doi.org/10.1001/jama.2020.7202
14. Drucker DJ (2020) Coronavirus Infections and Type 2 Diabetes-Shared Pathways with Therapeutic Implications. Endocr Rev 41(3):bnaa011. https://doi.org/10.1210/endrev/bnaa011
15. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J et al (2020) Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab 31(6):1068–1077.e3. https://doi.org/10.1016/j.cmet.2020.04.021
16. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet (London, England) 395(10229):1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3
17. Cheema AK, Kaur P, Fadel A, Younes N, Zirie M, Rizk NM (2020) Integrated Datasets of Proteomic and Metabolomic Biomarkers to Predict Its Impacts on Comorbidities of Type 2 Diabetes Mellitus. Diabetes Metab Syndr Obes 13:2409–2431. https://doi.org/10.2147/DMSO.S244432
18. Lim S, Bae JH, Kwon HS, Nauck MA (2021) COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nat Rev Endocrinol 17(1):11–30. https://doi.org/10.1038/s41574-020-00435-4
19. American Diabetes Association (2021) Diabetes Care 44(Supplement 1):S211–S220. https://doi.org/10.2337/dc21-S015
20. Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford H, Stöger L, Beenen L et al (2020) CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation. Radiology 296(2):E97–E104. https://doi.org/10.1148/radiol.2020201473
21. Gupta R, Ghosh A, Singh AK, Misra A (2020) Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes Metab Syndr 14(3):211–212. https://doi.org/10.1016/j.dsx.2020.03.002
22. Olariu E, Pooley N, Danel A, Miret M, Preiser JC (2018) A systematic scoping review on the consequences of stress-related hyperglycaemia. PLoS One 13(4):e0194952. https://doi.org/10.1371/journal.pone.0194952
23. Sonmez A, Demirci I, Haymana C, Tasci I, Dagdelen S, Salman S et al (2021) Clinical characteristics and outcomes of COVID-19 in patients with type 2 diabetes in Turkey: a nationwide study (TurCoviDia). J Diabetes 13(7):585–595. https://doi.org/10.1111/1753-0407.13171
24. Sheshah E, Sabico S, Albakr RM, Sultan AA, Alghamdi KS, Madani A et al (2021) Prevalence of diabetes, management and outcomes among Covid-19 adult patients admitted in a specialized tertiary hospital in Riyadh, Saudi Arabia. Diabetes Res Clin Pract 172:108538. https://doi.org/10.1016/j.diabres.2020.108538
25. Satman I, Demirci I, Haymana C, Tasci I, Salman S, Ata N et al (2021) Unexpectedly lower mortality rates in COVID-19 patients with and without type 2 diabetes in Istanbul. Diabetes Res Clin Pract 174:108753. https://doi.org/10.1016/j.diabres.2021.108753
26. Magagnoli J, Narendran S, Pereira F, Cummings TH, Hardin JW, Sutton SS et al (2020) Outcomes of hydroxychloroquine usage in United States veterans hospitalized with COVID-19. Med (New York, NY) 1(1):114–127.e3. https://doi.org/10.1016/j.medj.2020.06.001
27. Macauley P, Martin A, Epelbaum O (2020) Corticosteroids in the treatment of severe covid-19 lung disease: the pulmonology perspective from the first United States epicenter. Int J Infect Dis S1201–9712(20):30670–30676
28. Izzi-Engbeaya C, Distaso W, Amin A, Yang W, Idowu O, Kenkre JS et al (2021) Adverse outcomes in COVID-19 and diabetes: a retrospective cohort study from three London teaching hospitals. BMJ Open Diabetes Res Care 9(1):e001858. https://doi.org/10.1136/bmjdrc-2020-001858
29. Soliman AT, Prabhakaran Nair A, Al Masalamani MS, De Sanctis V, Abu Khattab MA, Alsaud AE (2020) Prevalence, clinical manifestations, and biochemical data of type 2 diabetes mellitus versus nondiabetic symptomatic patients with COVID-19: A comparative study. Acta Biomed 91(3):e2020010. https://doi.org/10.23750/abm.v91i3.10214
30. Alshukry A, Abbas MB, Ali Y, Alahmad B, Al-Shammari AA, Alhamar G et al (2021) Clinical characteristics and outcomes of COVID-19 patients with diabetes mellitus in Kuwait. Heliyon 7(4):e06706
31. You JH, Lee SA, Chun SY, Song SO, Lee BW, Kim DJ et al (2020) Clinical outcomes of COVID-19 patients with type 2 diabetes: a population-based study in Korea. Endocrinol Metab (Seoul, Korea) 35(4):901–908. https://doi.org/10.3803/EnM.2020.787
32. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C et al (2020) Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev 36:e3319
33. Alguwaihes AM, Al-Sofiani ME, Megdad M et al (2020) Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: a single-centre retrospective study. Cardiovasc Diabetol 19:205. https://doi.org/10.1186/s12933-020-01184-4
34. Shi Q, Zhang X, Jiang F, Zhang X, Hu N et al (2020) Clinical characteristics and risk factors for mortality of COVID-19 patients with diabetes in Wuhan, China: a two-center, Retrospective study. Diabetes Care 43(7):1382–1391. https://doi.org/10.2337/dc20-0598
35. Suleyman G, Fadel RA, Malette KM et al (2020) Clinical characteristics and mor-bidity associated with Coronavirus disease 2019 in a series of patients in metropolitan detroit. JAMA Netw Open 3(6):e2012270. https://doi.org/10.1001/jamanetworkopen.2020.12270
36. Kulcsar KA, Coleman CM, Beck SE, Frieman MB (2019) Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS CoV infection. JCI Insight 4(20):e131774. https://doi.org/10.1172/jci.insight.131774)
37. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R et al (2020) Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. J Diabetes Sci Technol 14(4):813–821. https://doi.org/10.1177/1932296820924469

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