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Ashraf M. A. Eid
Shebin El-Kom Teaching Hospital

Ehab K. El Melegy
Shebin El-Kom Teaching Hospital

El-Saied A. Shahin
Shebin El-Kom Teaching Hospital, shahins6666@yahoo.com

Khaled S. A. Elkelany
Shebin El-Kom Teaching Hospital

Mariam A. Fouad
Shebin El-Kom Teaching Hospital

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Original Article

Coronavirus disease 2019 and diabetes mellitus

El-Saied A. Shahin[a], Ashraf M.A. Eid[b], Ehab K. El Melegy[c], Khaled S.A. Elkelany[d], Mariam A. Fouad[e]

Departments of [a]Internal Medicine, [b]Gastroenterology, Hepatology and Infectious Disease, [c]Cardiology, [d]Pediatric, [e]Clinical Pathology Department, Shebin El-Kom Teaching Hospital, Menoufia, Egypt

Abstract

Introduction

In late 2019, a new virus severe acute respiratory syndrome coronavirus-2, which causes a new serious disease called coronavirus disease 2019 (COVID-19), spread quickly all over the world. Many complications of diabetes mellitus (DM) such as microvascular and macrovascular complications increase the risk for COVID-19-related severity and mortality.

Objective

To assess the effect of DM on outcome and severity of COVID-19.

Patients and methods

This work was a retrospective observation that included confirmed COVID-19-infected patients (PCR positive for COVID-19) who were admitted to Shebin El-Kom Teaching Hospital, Menoufia, Egypt, from March 2021 to March 2022. Laboratory investigations such as age, sex, and sings of severity of COVID-19 were studied. In this study, patients were divided into three main groups as follows: group 1 diabetic patients had known DM, group 2 (hyperglycemic group) patients were without past history of DM but were known to have hyperglycemia with COVID-19, and group 3 (control) had normal blood glucose.

Results

A total of 300 patients were divided into diabetic and hyperglycemic groups and were compared with the control group. It was found that diabetic and hyperglycemic groups were significantly associated with severe and critical disease, long hospital stay, increased number of admissions in critical care unit, increased number of patients under mechanical ventilation, and increased mortality rate from COVID-19 compared with the control group.

Conclusions

Patients with DM are more liable for severe acute respiratory syndrome coronavirus-2 infection, ICU admission, and increase in the rate of death. In addition, new hyperglycemia, even without history of DM, increased the severity of COVID-19 infection. Special care should be given for diabetic patients. Therefore, glucose monitoring and tight control of blood glucose are essential for all.

Keywords: Coronavirus disease 2019 infection, diabetes mellitus, hyperglycemia, respiratory failure

Introduction

In late 2019, a new coronavirus, identified as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), appeared in China. This coronavirus virus quickly spread all over the world and triggered coronavirus disease 2019 (COVID-19). The WHO stated the outbreak of COVID-19 as a pandemic disease on March 2020. Many clinical manifestations of COVID-19 exist, such as increase in body temperature, headache, cough, anosmia, dyspepsia, muscle pain, respiratory problems and failure, and death in severe cases [1].

Severity of COVID-19 or mortality rate depends on many risk factors, including old age, male sex, obesity, and chronic diseases such as chronic heart disease, and also, DM associated with many complications such as cardiovascular disease, heart failure, and diabetic nephropathy increases the mortality of patients with COVID-19 [2].

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Correspondence to: El-Saied A. Shahin, MD, Department of Internal Medicine, Shebin El-Kom Teaching Hospital, Menoufia, Egypt.
Postal Code: 32841; Tel: +20 100 948 3001;
E-mail: shahins6666@yahoo.com

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Increased glucose level in diabetic patients directly increases the replication of SARS-CoV-2 in monocyte, and glycolysis sustains the virus replication, through the increase in the activation of hypoxia- inducible factor 1α and increase in mitochondrial reactive oxygen species [3].

Patients with impaired blood glucose or DM show deterioration of blood glucose level owing to COVID-19. For instance, in patients dependent on insulin intake, the virus infection may increase the dose of insulin (often equal or >100 IU/day). Increase in the levels of inflammatory cytokines is associated with increased dose of insulin [4]. Although type 1 diabetes is more liable to ketoacidosis (DKA) complication, in patients with COVID-19, DKA can also occur in patients with type 2 DM. In a previous study, 77% of patients with COVID-19 with complicated DKA had type 2 DM [5].

Postmortem findings in lungs with fatal COVID-19 show increased alveolar damage and increased infiltration with inflammatory cells with increase in hyaline membranes [6]. Other findings include liver with lymphocyte infiltration, inflammation of myocardial muscle, infiltration in the brain with macrophage as well as axonal injuries, and glomeruli of kidney show microthrombi and focal pancreatitis [6]. Increased insulin resistance can be explained by several mechanisms: COVID-19 increases insulin resistance by induction of inflammation, and there is an increase in the number of inflammatory cells in major organs of insulin response such as the liver and skeletal muscle, which are the main organs for insulin-mediated glucose uptake [7]. Another study concluded that DM is associated with 19–30% of COVID-19 cases [8]. Severe COVID-19 and diabetic patients are at a higher need for critical care and mechanical ventilation [9].

Patients and Methods

This retrospective study was carried out on 300 COVID-19-infected patients from the Internal Medicine Department and special ICU for COVID-19, Shebin El-Kom Teaching Hospital, Menoufia, Egypt, during the period from March 2021 to March 2022 number of approval certificate 11 S 11 00038 from Consent statement.

All COVID-19-infected patients were subjected to the following: complete medical history and physical examination. Laboratory investigations included blood glucose monitoring, such as postprandial blood glucose, fasting blood glucose, and glycated hemoglobin; complete blood count; urea; creatinine; electrolytes; lactate dehydrogenase; erythrocyte sedimentation rate (ESR); C-reactive protein (CRP); D-dimer; and ferritin. Chest radiograph and computed tomography chest were done. Patients' progress during hospitalization was assessed and categorized as follows: (a) moderate disease, if imaging positive and oxygen saturation more than or equal to 92%; (b) severe disease, if oxygen saturation less than 92%, respiratory rate more than 30 breath/min, or pulmonary infiltrate more than 50%; and (c) critical disease, if shock due to sepsis, failure of respiration, and/or multiorgan dysfunction. Mild cases were excluded as they were treated outside the hospital. The prognosis of disease was assessed by the period of hospitalization, admission in ICU, the need for mechanical ventilation, and number of dead patients.

Finally, three groups of patients were arranged as follows: (a) diabetic (group 1), having an glycated hemoglobin level more than 6.5, random blood glucose more than 200 mg, and fasting blood glucose more than 126 mg; (b) hyperglycemic (group 2), having an glycated hemoglobin less than 6.5 and random blood glucose more than 140 mg/dl and without past history of diabetes; and (c) control group, having normal glucose tolerance.

Statistical analysis

The data were analyzed using IBM SPSS.22 from Egypt. All variables such as frequencies and percentage were assessed. Data were expressed as mean ± SD, *t* test, or χ^2 test to check the association between variables. Statistical significance was set at *P* value less than 0.05 (Figs. 1–6).

Results

Table 1 shows that the number of diabetic COVID-19-infected patients was 140 (group 1), the number of hyperglycemic COVID-19-infected patients was 20 (group 2), and the number of nondiabetic COVID-19-infected patients was 140 (group 3), as a control group. In the diabetic group, the number of type 1 diabetes cases was 5, whereas the number of type 2 diabetes cases was 135. The number of moderate COVID-19-infected patients was 80, the number of severe cases was 89, and the number of critical patients was 131.

Table 2 shows laboratory data between diabetic (group 1) and control (groups 3). It shows that there was a significant increase in white blood cell, neutrophils, creatinine, blood urea nitrogen, CRP, ESR, and D-dimer in the diabetic group versus the control group. There was a significant decrease in lymphocyte counts in group 1 versus group 3 ($P < 0.05$).

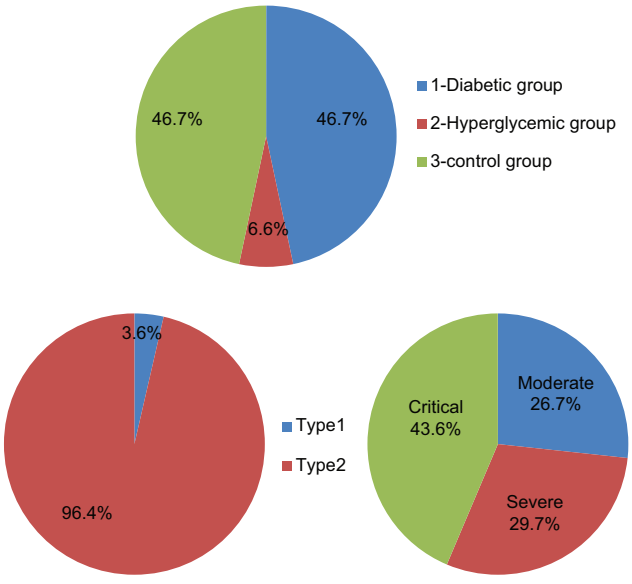

Figure 1: (a) Diabetic status. (b) Type of diabetes. (c) Severity of COVID-19. COVID-19, coronavirus disease 2019.

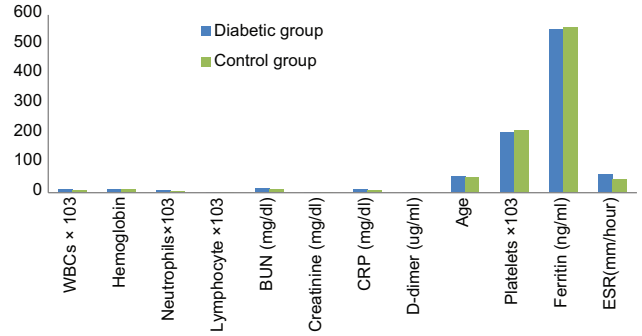

Figure 2: Comparison of laboratory data between diabetic and control groups.

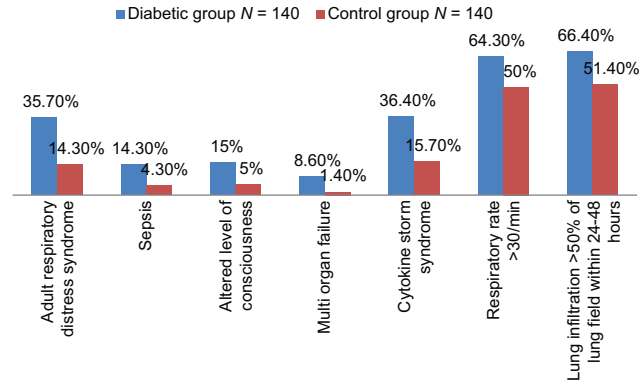

Figure 4: Comparison of clinical manifestation and investigation of COVID-19 infection between diabetic and control groups. COVID-19, coronavirus disease 2019.

Table 1: Baseline characteristics

Variables	Groups	*n* (%)
Diabetic status	Diabetic group	140 (46.7)
	Hyperglycemic group	20 (6.6)
	Control group	140 (46.7)
Type of diabetes	Type 1	5 (3.6)
	Type 2	135 (96.4)
Severity of COVID-19	Moderate	80 (26.7)
	Severe	89 (29.7)
	Critical	131 (43.6)

COVID-19, coronavirus disease 2019.

Table 3 shows a statistically significant increase in the severity of COVID-19 in group 1 versus group 3 ($P < 0.05$).

Table 4 shows that there was a statistically significant increase in the number of patients with lung infiltration more than 50% of lung field, respiratory rate more than 30/min within 24–48 h, acute respiratory distress syndrome, sepsis, multiorgan failure, altered consciousness level, and cytokine storm in group 1 (diabetic) versus group 3 (control).

Table 5 compares the outcomes between group 1 and group 3. It showed that there was a statistically significant increase in the length of stay in hospital, need for ventilation, intensive care admission, and death in group 1 versus group 3 ($P < 0.05$).

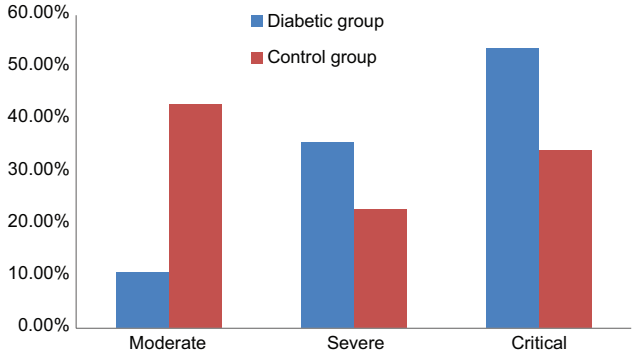

Figure 3: Comparison of severity of COVID-19 infection between diabetic and control groups. COVID-19, coronavirus disease 2019.

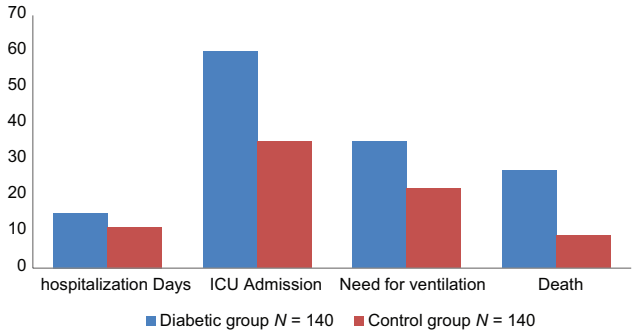

Figure 5: Comparison of outcomes between diabetic and control groups.

Table 6 compares the outcome and severity of COVID-19 between group 2 (hyperglycemic) and group 3 (control group). It showed that there was a statistically significant increase in severity, hospital stay, mechanical ventilation, ICU admission, and death in the group 2 (hyperglycemic) versus group 3 ($P < 0.05$).

Discussion

DM has many complications, such as diabetic nephropathy, retinopathy, and neuropathy, and is a high-risk factor for viral infection, owing to defects in innate and adaptive immunity, which can increase morbidity and mortality [10].

Our study presented with critical and severe COVID-19. Although outpatient COVID-19 presents in most patients as mild or moderate disease, a minority of outpatients present with severe or critical illness [11]. However, our study was inpatient based rather than outpatient based because most patients with critical or severe disease are transferred to the hospital. These finding are supported by Wang and colleagues.

In the present study, the severity-related biomarkers and inflammatory markers (white blood cells, neutrophils, CRP, D-dimer lactate dehydrogenase, and ESR) were increase in the DM group. In addition, renal function tests (blood urea nitrogen and creatinine) were increased in the diabetic group, meaning increased incidence of acute kidney injury in agreement with Zhang and colleagues.

In the present study, most patients with DM presented mainly with severe (35.7%) and critical (53.6%) disease. Moreover, they had most complications, such as adult respiratory distress syndrome, septic shock, altered mental status, multiorgan dysfunction, and inflammatory storm syndrome. These findings were supported by Argan and colleagues.

COVID-19 activates higher stress conditions and increases hormones of hyperglycemia (catecholamines and glucocorticoids), so increases blood sugar levels. Decrease in lymphocyte cell proliferative response and decrease in function of macrophage/monocyte cells and neutrophil are associated with uncontrolled diabetes [12]. An inflammatory storm formed after COVID-19 in DM can be explained by the increase in time in starting adaptive immunity, leading to failure of respiration and increase in the deterioration of other organs [13]. Moreover, there is an increase in virus virulence in diabetes owing to a high level of plasminogen [14]. Additionally, impaired gas exchange and pulmonary microvasculature caused by diabetes can cause a change of structural lung [11]. Blood glucose instability, which is either increase in blood glucose or decrease in blood glucose, can increase COVID-19 severity [15]. Fortunately, good control of blood sugar levels in COVID showed decreased mortality rates versus poorly control levels of blood sugar [9]. In our study, the diabetic group had more dependence on mechanical ventilation, had prolonged hospital stays, had increase in the number of ICU admissions, and had increase in the number of deaths than those without DM. Bode *et al*. [16] concluded that there was a long duration of stay in diabetic patients or impaired blood glucose versus patients without DM. Other studies showed a death rate from 17 to 20% in COVID-19 infection with DM [17], which is similar to our finding of 19.3% death rate.

We found that the hyperglycemic group is more liable to critical outcomes, including increased risk of admission in ICU, longer hospitalization, dependent on mechanical ventilation, and even

Table 2: Baseline of laboratory data between control (group 3) and diabetic groups (group 1)

Variables	Diabetic group	Control group	*P*
Sex (male/female)	80/60	78/62	>0.05
Age	55±5.5	53±6.5	>0.05
WBCs×10^3	11.1±5.1	8.2±5.5	<0.05
Hemoglobin	13.1±8.2	12.9±8.1	>0.05
Platelets×10^3	205±60	210±55	>0.05
Neutrophils×10^3	7.9±5.5	5.6±4.4	<0.05
Lymphocyte×10^3	1.1±0.8	1.5±0.9	<0.05
BUN (mg/dl)	16.1±9.1	12.9±10.3	<0.05
Creatinine (mg/dl)	1.3±0.5	1.1±0.6	<0.05
ESR (mm/h)	64±40	44±35	<0.05
CRP (mg/dl)	11.5±5.7	9.2±5.5	<0.05
D-dimer (µg/ml)	1.45±0.5	0.8±0.48	<0.05
Ferritin (ng/ml)	550±220	560±225	>0.05

BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell.

Table 3: Degree of severity of coronavirus disease 2019 in group 1 (diabetic group) versus group 3 (control group)

Severity	Diabetic group (*n*=140) [*n* (%)]	Control group (*n*=140) [*n* (%)]	*P*
Moderate	15 (10.7)	60 (42.9%	
Severe	50 (35.7)	32 (22.9)	*P*<0.05
Critical	75 (53.6)	48 (34.2)	

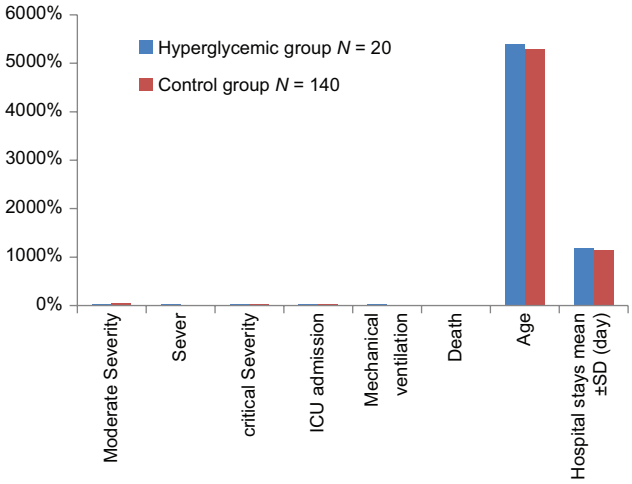

Figure 6: Comparison of outcome and severity of COVID-19 between (group 2) hyperglycemic and (group 3) control groups. COVID-19, coronavirus disease 2019.

Table 4: Clinical manifestation and investigation of coronavirus disease 2019 between (group 1) diabetic versus (group 3) control group

Variables	Diabetic group (*n*=140) [*n* (%)]	Control group (*n*=140) [*n* (%)]	*P*
Respiratory rate >30/min			
Pulmonary infiltration	90 (64.3)	70 (50)	<0.05
>50% of lung field within 1-2 days	93 (66.4)	72 (51.4)	<0.05
Adult respiratory distress syndrome	50 (35.7)	20 (14.3)	<0.05
Sepsis	20 (14.3)	6 (4.3)	<0.05
Altered level of consciousness	21 (15)	7 (5)	<0.05
Multiorgan failure	12 (8.6)	2 (1.4)	<0.05
Cytokine storm syndrome: D-dimer >1 µg/ml and/or ferritin >600µg	51 (36.4)	22 (15.7)	<0.05

Table 5: Comparison of outcomes between diabetic and control group

Variables	Diabetic (group 1) (*n*=140) [*n* (%)]	Control (group 3) (*n*=140) [*n* (%)]	*P*
Duration of hospitalization (mean±SD) (day)	15.3±11.5	11.4±9.4	<0.05
ICU admission	60 (42.9)	35 (25)	<0.05
Need for ventilation	35 (25)	22 (15.7)	<0.05
Death	27 (19.3)	9 (5)	<0.05

Table 6: Outcome and severity of coronavirus disease 2019 between group 2 and group 3 control group

Variables	Hyperglycemic (group 2) (*n*=20) [*n* (%)]	Control (group 3) (*n*=140) [*n* (%)]	*P*
Sex (male/female)	12/8	78/62	>0.05
Age	75-31	73-29	>0.05
Severity			
Moderate	5 (25)	60 (42.9)	
Severe	7 (35)	32 (22.9)	<0.05
Critical	8 (40)	48 (34.2)	
Outcome			
Hospital stays (mean±SD) (day)	11.8±8.8	11.4±9.4	>0.05
ICU admission	8 (40)	35 (25)	<0.05
Mechanical ventilation	5 (25)	22 (15.7)	<0.05
Death	3 (15)	9 (5)	<0.05

death. This was agreed by Cai and colleagues, who stated that patients with hyperglycemic are more liable to acute respiratory failure and acute respiratory distress syndrome.

Apicella and colleagues concluded that SARS-CoV-2 infection may cause damage to β-cell of pancreas, which leads to a novel DM or prolonged hyperglycemia, so could precipitate to diabetic coma as DKA or hyperglycemic hyperosmolar coma.

Conclusions

Patients with DM are more liable to SARS-CoV-2 infection, ICU admission, and increase in the rate of death. In addition, new hyperglycemia, even without history of DM, increased the severity of COVID-19 infection. Special care should be given for diabetic patients. Therefore, glucose monitoring and tight control of blood glucose are essential for all.

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Nil.

Conflicts of interest

None declared.

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