ORIGINAL ARTICLE

The Association between COVID-19 and Hyperglycemia

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ABSTRACT

Objectives: **COVID-19 is associated with hyperglycemia in people with and without known diabetes and new onset hyperglycemia without prior history of diabetes is a common finding. We aimed to evaluate the association between COVID-19 and hyperglycemia.**

Patients & Methods: **This was a cross-sectional prospective study including 90 in-patients infected with COVID-19. Demographic, clinical and laboratory characteristics and comorbidities (DM, HTN, ischemic heart disease, CKD, stroke& asthma) were studied. Patients were divided in to three groups: euglycemic patients (51,56.6%), diabetics with hyperglycemia (25, 27.8%) and hyperglycemia with no history of DM (14,15.6%). Patients were followed up for 28 days; during which the outcome was hospital mortality.**

Results: **Advanced age, comorbidities, ≥ 50% lung involvement, increased respiratory rate and low SPO2 level were significantly associated with the development of new onset hyperglycemia. The mortality rate in patients with new onset hyperglycemia was 71.43% compared to 40% and 13.73 in patients with history of DM and euglycemic patients, respectively with significant difference ($p < 0.001$).**

Conclusions: **Advanced age, comorbidities and disease severity are significant risk factors for the development of new onset hyperglycemia in patients with COVID-19. New onset hyperglycemia with or without history of DM increases the mortality in COVID-19 patients.**

KEY WORDS

COVID-19, hyperglycemia, diabetes mellitus, outcome

INTRODUCTION

Severe hyperglycemia is common in critically ill patients infected with COVID-19 and is often seen as a marker of disease severity. Several studies have reported that COVID-19 is associated with hyperglycemia in people with and without known diabetes[1]. One study from Wuhan of hospitalized, COVID-19 patients reported that 21.6% had a history of DM, and 20.8% were newly diagnosed with DM[2]. Among 7162 COVID-19 patients with accompanying information on underlying health conditions, diabetes was present in 24% of non-ICU and 32% of ICU patients[3].

The Center for Disease Control's (CDCs) COVID-19—Associated Hospitalization Surveillance Network identified the presence of hyperglycemia in 28.3% of 178 hospitalized patients[4]. The New York Department of Health's COVID-19 patient fatality dashboard reported that diabetes was present in 3490 of 9371 patients who died (37%)[5].

Potential Mechanisms for Hyperglycemia

A number of interrelated etiologies are responsible behind the development of hyperglycemia in people with COVID-19 including pancreatic injury (PI), preadmission diabetes, anti-covid-19 medications and stress hyperglycemia[6].

In COVID-19, PI may occur either by direct invasion of SARS-CoV-2 or indirectly through the induction of cytokine storm (CS)[7]. SARS-CoV-2 affects both pancreatic lipase and peripheral adipose tissue leading to PI and lipotoxicity that contribute to CS induction[8].

One reason for new-onset DM is that these patients may have had undetected diabetes prior to admission, potentially as a consequence of recent weight gain due to changes in lifestyle and worsening of hyperglycemia mainly due to self-isolation, social distancing, reduced physical activity, and poor diets as a result of mental health issues. These lifestyle changes could lead to insulin resistance, which would further trigger inflammatory pathways, leading to new-onset diabetes[9].

Currently used drugs for COVID-19 treatment may affect blood glucose variability in both DM and non-DM patients. For example, hydroxychloroquine has potent anti-inflammatory and immunomodulating effects, it improves glycemic indices, β-cell function, and insulin secretion; thus, it may lead to hypoglycemia[10]. Corticosteroids, such as dexamethasone, have shown to be effective in COVID-19 patients, namely, reducing the exaggerated immune response-induced ARDS. Its administration is associated with hyperglycemia even in non-DM patients; especially if a high-dose methylprednisolone is used[11]. Studies have shown that patients with newly diagnosed diabetes have higher levels of inflammatory markers such as CRP, ESR, and WBC[12].

Mortality in Hyperglycemia induced by COVID-19

Mortality rate of COVID-19 patients with hyperglycemia was found to be high. A study by Carrasco *et al*.[13] showed higher mortality rate in patient with blood sugar level on admission > 180 mg/dl (41.1%) than in patient with blood sugar level on admission 140 ─ 180 mg/dl (33.0%) and < 140 mg/dl (15.71%).

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Hyperglycemia could disrupt the defensive capacity of airway epithelial, and it will induce oxidative stress production; resulting in thrombosis[14]. Hyperglycemia impair the pulmonary function by decreasing vital capacity and (FEV1) due to microangiopathy development. In hypoxemic and hyperglycemic condition, high lactate and LDH level is associated with high mortality in COVID-19 patients[15].

Aim of the Study

The present study aimed to evaluate the association between COVID-19 and hyperglycemia.

PATIENTS AND METHODS

Design and Settings

This was a cross-sectional prospective study including 90 patients infected with SARS-CoV-2 who were admitted at Al-Shefaa Center/ Baghdad during the period from 1st April to 1st September 2021. Patients were diagnosed after nasopharyngeal swab examination of SARS-CoV-2 RNA by RT- PCR. Clinical diagnosis in patients with a negative RT-PCR was made in collaboration with infection disease specialists if the patient had typical symptoms and typical findings on a chest CT scan with no other explanation of the symptoms (i. e, bacterial infection).

Inclusion Criteria: All adult patients confirmed with SARS-CoV-2 infection

Exclusion criteria

- Patients who refused to participate in the study.
- Age < 18 years

Ethical consideration

A verbal consent from each participant was obtained prior to data collection after explaining the aim of study. The confidentiality of data throughout the study was guaranteed and the patients were assured that data will be used for research purpose only.

Data Collection: The following data were collected for all patients at admission:

Demographics: Age, gender, smoking habit and the comorbidities (DM, Hypertension, Stroke, ESRD, IHD, Heart failure, Asthma) and others including chronic liver disease& malignancy.

Clinical Characteristics: Pulse rate (PR), respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), lung involvement by computed tomography (CT) scan, O2 saturation, ventilation mode, type of treatment, and disease severity which was determined as follows[16]:

A) Mild: fever < 38°C, with or without cough, no dyspnea, no gasping, no chronic disease, No imaging findings of pneumonia.
B) Moderate: Fever, respiratory symptoms, imaging findings of pneumonia.
C) Severe: Respiratory distress, RR ≥ 30 times/min, SpO2 < 93% at rest, PaO2/FiO2 ≤ 300 mmHg, showing a rapid progression (≥ 50%) on CT imaging within 24- 48 hours should be managed as severe.
D) Critical: Respiratory failure, need mechanical assistance, shock, extrapulmonary organ failure, intensive care unit is needed.

Definition of variables

- **Stroke**: Is defined as a neurological deficit attributed to an acute focal injury of the central neurological system which is documented by brain CT scan or MRI[17].
- **Hypertension**: Office-based BP as systolic pressure ≥ 140mmHg or diastolic pressure ≥ 90 mmHg or presence of history of HTN on treatment[18].
- **Ischemic heart disease**: Is defined by history of angina or MI documented by ECG and ECHO[19].
- **Heart failure**: Is defined by the presence of prior or current characteristic symptoms such as fatigue and dyspnea and evidence of cardiac dysfunction as a cause of these symptoms documented by ECHO[20].
- **ESKD**: End stage kidney disease refers to chronic kidney failure treated with either dialysis or transplantation[21].
- **Asthma**: Is defined by having variable and recurring symptoms of airway obstruction, bronchial hyper-responsiveness and underlying inflammation documented by PFT or use of inhaler[22].

Laboratory Findings[23]

Laboratory Findings	Reference Range
Glycated Hemoglobin (HbA1c)	4-6%
Total Leukocyte Count	4-11 x 109/L
Absolute Lymphocyte Count	1.5-4 x 109/L
Platelet Count	150-300 x 109/L
Serum Creatinine	0.27-1.11 mg/dl
D-dimer	< 500 ng/ml
Ferritin	20-300 µ/L for Male 15-200 µ/L for Female
C-Reactive Protein	< 5mg/dl

Study Groups: Patients were divided into three subgroups based on their blood sugar level (mean of 3 samples):

1- Euglycemic patients (51,56.6%): non-diabetics or those patients with T2DM who did not meet the criteria of hyperglycemia during their hospital stay.

2- Hyperglycemia with T2DM group (25, 27.8%): Blood sugar ≥ 180 mg/dl and the patient had been previously diagnosed with T2DM[23].

3-Hyperglycemia with no history of DM (14, 15.6%): Blood sugar ≥ 180 mg/dL and no history of T2DM[23].

Patients were followed up for 28 days and the primary outcome was the hospital mortality.

Statistical Analysis

All data were analyzed with SPSS for windows, v.25.0; IBM Corp, Armonk, New York, USA. Continuous data were subjected to normality test (Shapiro Wilk test). Data with normal distribution were presented as mean and standard deviation, and analyzed with parametric analysis of variance (ANOVA), while the least significant difference (LSD) was used as post hoc analysis. Data with non-normal distribution were presented as median and range and analyzed with Kruskal Wallis, and pairwise comparison. Binomial data were presented as frequency percentages. Comparison between quantitative data was performed by the, while the comparison between binomial data was done by the Chi square test. A p-value of ≤ 0.05 was considered as statistically significant.

RESULTS

Demographic Characteristics of the Patients according to Glycemic Status

The mean age of hyperglycemic patients without a history of diabetes was significantly higher than that of hyperglycemic patients with a history of diabetes and euglycemic patients. Comorbid diseases differed significantly between the three tested subgroups, especially DM and HTN ($p < 0.001$ and $p = 0.008$, respectively). Furthermore, Lung involvement (by CT scan) differed significantly between the three tested groups ($p = 0.002$); as shown in Table 1.

Association of Vital Signs and Oxygen Saturation with Glycemic Status

Table 2 shows that the RR was significantly higher in hyperglycemic patients without a history of diabetes than in euglycemic patients but not in hyperglycemic patients with a history of diabetes. In contrast, the saturated PO_2% was significantly lower in hyperglycemic patients without DM compared to euglycemic patients.

Association of Hematologic and Biochemical Parameters with Glycemic Status

The HbA1c level was significantly different between the three tested groups ($p < 0.001$). Serum creatinine levels were lower in euglycemic patients when compared to hyperglycemic patients with DM ($p = 0.018$) as shown in Table 3.

Table 1: Distribution of demographic data based on glycemic status

Parameters	Euglycemia (51, 56.6%)	Hyperglycemia with history of DM (25, 27.8%)	Hyperglycemia without history of DM (14, 15.6%)	p-Value
Age, years				
Mean ± SD	59.65 ± 18.89a	65.16 ± 13.37a	77.29 ± 10.63b	**0.003**
Range	19-85	27-83	54-94	
Gender				
Male	33(64.71%)	15(60%)	10(71.43%)	0.804
Female	18(35.29)	10(40%)	4(28.57%)	
Smoking				
No	42(82.35%)	21(84%)	11(78.57%)	0.831
Yes	9(17.45%)	4(16%)	3(21.43%)	
Comorbidities*	40(78.43%)	25(100%)	6(42.86%)	**< 0.001**
DM	7(13.73%)	23(92%)	0(0%)	**< 0.001**
Hypertension	23(45.1%)	19(76%)	4(28.57%)	**0.008**
Stroke	12(23.53%)	8(20%)	2(14.29%)	0.454
ESRD	5(9.8%)	3(12%)	0(0%)	0.424
IHD	8(15.69%)	8(20%)	4(28.57%)	0.227
Heart failure	0(0%)	3(12%)	0(0%)	0.018
Asthma	2(3.92%)	3(12%)	0(0%)	0.216
Others	10(19.61%)	2((8%)	1(7.14%)	0.280
Lung involvement/CT	46(90.2%)	24(96%)	8(57.14%)	**0.002**
< 50%	5(9.8%)	1(4%)	6(42.86%)	
≥ 50%				
Disease severity				
Mild	6(11.76%)	1(4%)	0(0%)	0.054
Moderate	11(21.5%)	3(12(%)	0(0%)	
Severe	28(54.9%)	12(48%)	9(64.29%)	
Critical	6(11.76%)	9(36%)	5(35.71%)	

Different small letters indicate significant difference

* Patient may have more than one comorbid disease. SD: Standard deviation; DM: Diabetes mellitus; ESRD: End-stage renal disease; IHD: Ischemic heart disease.

Table 2: Distribution of vital signs and saturated PO2 of the study population based on glycemic status

Parameters	Euglycemia (51, 56.6%)	Hyperglycemia with history of DM (25, 27.8%)	Hyperglycemia without history of DM (14, 15.6%)	p-Value
Pulse rate/min				
Mean ± SD	97.10 ± 17.52	99.36 ± 18.901	103.79 ± 13.71	0.439
Range	67-134	62-130	80-129	
Respiratory rate/min				
Mean ± SD	28.0 ± 6.33[a]	30.2 ± 5.36a[b]	32.43 ± 4.75[b]	**0.033**
Range	20-46	22-42	24-45	
Systolic BP, mmHg				
Mean ± SD	131.25 ± 17.4	126.32 ± 18.15	128.57 ± 18.44	0.515
Range	100-199	85-160	90-170	
Diastolic BP, mmHg				
Mean ± SD	75.25 ± 10.55	71.84 ± 14.04	71.36 ± 9.03	0.338
Range	50-100	50-100	60-85	
Saturated PO_2				
Mean ± SD	86.51 ± 10.35[a]	84.08 ± 8.52[ab]	78.64 ± 8.63[b]	**0.028**
Range	55-99	57-97	60-90	

Different small letters indicate significant difference

SD: Standard deviation; DM: Diabetes mellitus; BP: Blood pressure.

Table 3: Distribution of hematologic and biochemical parameters based on glycemic status

Parameters	Euglycemia (51, 56.6%)	Hyperglycemia with history of DM (25, 27.8%)	Hyperglycemia withou0t history of DM (14, 15.6%)	p-Value
HbA1c, %				
Mean ± SD	6.03 ± 0.68a	8.84 ± 1.51b	7.01 ± 1.42c	**< 0.001**
Range	4.3-9.5	6.2-12	5.5-11	
WBC, x 10^9/L				
Median	9.5	9.1	10.15	0.612
Range	2.3-32	3.8-33	8-17	
Lymphocyte, x 10^9/L				
Median	0.8	0.6	0.5	0.243
Range	0.1-3.4	0.1-4.8	0.1-5.4	
Platelet, x 10^9/L				
Median	234.0	186.0	226.0	0.078
Range	91-776	105-336	160-350	
S. Creatinine, mg/dL				
Median	0.8a	1.2b	1.05ab	**0.018**
Range	0.37-12	0.37-11	0.5-13.2	
D-dimer, ng/mL				
Median	1.5	2.03	1.58	0.344
Range	0.05-16	0.47-16	0.7-16	
Ferritin, µg/L				
Median	506.0	521.0	714.0	0.184
Range	13-2000	19-1000	102-1000	
CRP, mg/dL				
Median	82.0	93.0	120.0	0.488
Range	2-233	4-220	5-220	

Different small letters indicate significant difference

SD: Standard deviation; DM: Diabetes mellitus; HbA1c: Glycosylated hemoglobin; S.: Serum;

CRP: C-reactive protein; WBC: White blood cells.

Association of Clinical Management, Drugs and Outcome with Glycemic Status

Bipap and NRM were more frequent among hyperglycemic patients without history of DM compared with euglycemic and hyperglycemic patients with history of DM. As shown in Table 4, the mortality rate in patients without history of DM was 71.43% compared to 40% and 13.73% in patients with history of DM and euglycemic patients, respectively with significantly difference ($p < 0.001$).

Association of Demographic and clinical factors with the Outcome

About one-fourth of the died patients had ≥ 50% lung involvement compared with 7.94% of survived patients with such involvement ($p = 0.021$). Finally, critical disease was reported in 40.47% and 14.29% of died and survived patients, respectively with a significant difference as shown in Table 5.

Association of Vital Signs with the Outcome

Both PR and RR were higher in deceased patients than survived patients with significant differences. In contrast, the mean SPO2 in deceased and survived patients was 78.48 ± 9.43% and 87.24 ± 8.97%, respectively, with a significant difference as shown in Table 6.

Association of Hematologic, Biochemical Parameters and Clinical Management with the Outcome

The median level of ferritin in deceased patients was higher than that of survived patients with a significant difference. Bipap was used for one-third of deceased patients compared with 12.7% of survived patients. In contrast, S mask was more common in survived than deceased patients with a significant difference; as shown in Table 7.

DISCUSSION

According to the result of the present study; 14 non-diabetic patients out of 90 (15.5%) developed new hyperglycemia. This rate is lower than previous studies in this regard. In Le *et al*. 2022[24] study; a total of 517 COVID 19 patients included; hyperglycemia was documented in 65.6% of patients: diabetic patients (44.8%) and new-onset hyperglycemia (20.8%).

Bode *et al*. 2020[25] studied more than 1000 COVID-19 patients and found that 38.5% were having either diabetes by HbA1C criteria or uncontrolled hyperglycemia. In a retrospective study including 453 patients were admitted to Union Hospital in Wuhan, the incidence of hyperglycemia was 28.4%[26].

Ad'hiah *et al*. 2021[27] conducted a cross-sectional study on 213 patients with COVID-19 who were not diabetics at hospital admission. One week after hospitalization, it was found that 25.4, 22.5 and 52.1% of COVID-19 patients were classified as normoglycemia, prediabetes and diabetes, respectively.

Few possible factors might partially explain the lower incidence of hyperglycemia in the present study. It was conducted after nearly 2 years of COVID-19 recording in the country. The medical staff have acquired the sufficient experience to deal with this pandemic, especially in management of hyperglycemia and coagulation abnormalities. Furthermore, collected data may be obtained during partial restrictions of movement which allows easy medical access.

In the present study, older ages, low SPO2, increased RR and increased the percentage of lung involvement were significantly associated with the development of hyperglycemia in patients without history of T2DM. Le *et al*.2022[24] found that RR, corticosteroid therapy, and a higher level of procalcitonin were risk factors for hyperglycemia in diabetic patients, whereas cardiovascular diseases, respiratory failure, were risk factors for hyperglycemia in non-diabetic patients. The levels of CRP (72.7 mg/L vs. 57.9 mg/L), D-dimer (1540 ng/mL vs. 1139 ng/

Table 4: Distribution of management, medications, and outcome based on the glycemic status

Parameters	Euglycemia (51, 56.6%)	Hyperglycemia with history of DM (25, 27.8%)	Hyperglycemia without history of DM (14, 15.6%)	p-Value
Clinical management				
IV	3(5.8%)	3(12%)	1(7.14%)	
Bipap	7(13.73%)	6(24%)	4(28.57)	0.221
S mask	19(37.25%)	6(24%)	2(14.29%)	
RA	10(19.61%)	3(12%)	0(0%)	
NRM	12(23.53%)	7(28%)	7(50%)	
Treatment*				
Glixan	31(60.78%)	13(52%)	12(85.7%)	0.108
Decadrone	39(76.47%)	21(84%)	13(92.86%)	0.348
Ceftriaxone	20(39.22%)	12(48%)	3(21.43%)	0.263
Remedisvir	19(37.25%)	4(16%)	4(28.57%)	0.163
Heparin	5(9.8%)	7(28%)	1(7.14%)	0.074
Vancomycin	4(7.84%)	2(8%)	1(7.14%)	0.995
Levofloxacin	15(29.41%)	5(20%)	4(28.57%)	0.673
Meropenem	9(17.65%)	6(24%)	5(35.71%)	0.343
Insulin	6(11.76%)	8(32%)	4(28.57%)	0.080
Prednisolone	4(7.84%)	1(4%)	0(0%)	0.485
Tazocine	2(3.92%)	2(8%)	1(7.14%)	0.737
Cefrazimide	5(9.8%)	0(0%)	1(7.14%)	0.273
Others	3(5.88%)	3(12%)	1(7.14%)	0.643
Outcome				
Discharged	44(86.27%) [a]	15(60%) [b]	4(28.57%) [c]	**< 0.001**
Died	7(13.73%)	10(40%)	10(71.43%)	

Different small letters indicate significant difference

*: Patient may use more than one type of drug

IV: Invasive ventilation; Bipap: Biphasic positive airway pressure; RA: Room air; S. Mask: Simple mask; NRM: Nonrebreather mask.

Table 5: Distribution of demographic& clinical data based on outcome

Parameters	Died (27,30%)	Discharged (63,70%)	p-Value
Age, years			
Mean ± SD	70.81 ± 12.38	60.97 ± 18.52	**0.013***
Range	42-94	19-85	
Gender			
Male	20(74.07%)	38(60.32%)	0.212
Female	7(25.93%)	25(39.68%)	
Smoking			
No	21(77.78%)	38(60.32%)	0.470
Yes	6(22.22%)	25(39.68%)	
Comorbidities**	22(81.48%)	50(79.37%)	0.818
Diabetes mellitus	9(33.33%)	21(33.33%)	1.0
Hypertension	13(48.25%)	32(50.79%)	0.818
Stroke	7(25.93%)	15(23.81%)	0.830
ESRD	2(27.4%)	6(9.52%)	0.746
IHD	6(22.22%)	14(22.22%)	1.0
Heart failure	1(3.7%)	2(3.17%)	1.0
Asthma	3(11.11%)	2(3.17%)	0.157
Others	4(14.81%)	9(12.29%)	0.948
Lung involvement/CT			
< 50%	20(74.07%)	58(92.06%)	**0.021***
≥ 50%	7(25.93%)	5(7.94%)	
Disease severity			
Mild	0(0%)	7(11.11%)	
Moderate	1(3.7%)	13(20.63%)	**0.006***
Severe	15(55.56%)	34(53.97%)	
Critical	11(40.74%)	9(14.29%)	

*: Significant difference; ** Patient may have more than one comorbid disease.

SD: Standard deviation; ESRD: End-stage renal disease; IHD: Ischemic heart disease.

Table 6: Distribution of vital signs based on outcome

Parameters	Died (27, 30%)	Discharged (63, 70%)	p-Value
Pulse rate/min			
Mean ± SD	105.81 ± 19.45	95.75 ± 15.61	**0.011***
Range	70-134	62-134	
Respiratory rate/min			
Mean ± SD	33.37 ± 5.27	27.55 ± 5.5	**< 0.001***
Range	24-45	20.46	
Systolic BP, mmHg			
Mean ± SD	131.25 ± 17.4	126.32 ± 18.15	0.515
Range	100-199	85-160	
Diastolic BP, mmHg			
Mean ± SD	75.25 ± 10.55	71.84 ± 14.04	0.338
Range	50-100	50-100	
Saturated PO2, %			
Mean ± SD	78.48 ± 9.43	87.24 ± 8.97	**< 0.001***
Range	57-95	55-99	

*: significant difference

SD: Standard deviation; BP: Blood pressure.

Table 7: Distribution of Hematologic, biochemical parameters and type of management based on outcome

Parameters	Died (27, 30%)	Discharged (63, 70%)	p-Value
HbA1c, %			
Mean ± SD	7.36 ± 01.69	6.82 ± 1.69	0.170
Range	5.3-11	4.3-12	
WBC, x 10^9/L			
Median	11	9.0	0.063
Range	3.8-33.0	2.3-32.0	
Lymphocyte, x 10^9/L			
Median	0.6	0.8	0.090
Range	0.1-5.4	0.1-3.4	
Platelet, x 109/L			
Median	222	231	0.362
Range	134-776	91-405	
S. Creatinine, mg/dL			
Median	1.13	0.9	0.090
Range	0.4-12.0	0.4-11.0	
D-dimer, ng/mL			
Median	2.15	1.4	0.156
Range	0.6-16.0	0.1-16.0	
Ferritin, µg/L			
Median	648.0	500	**0.012***
Range	19.0-1000	19-2000	
CRP, mg/dL			
Median	117.0	81.0	0.292
Range	4.0-220	2.0-233	
Clinical management			
IV	3(11.11%)	4(6.35%)	
Bipap	9(33.33%)	8(12.7%)	**0.011***
S mask	5(18.82%)	22(34.92%)	
RA	0(0%)	13(20.63%)	
NRM	10(37.03%)	16(25.4%)	

*: Significant difference. SD: Standard deviation; HbA1c: Glycosylated hemoglobin; S.: Serum; CRP: C-reactive protein; WBC: White blood cells; IV: Invasive ventilation, Bipap: Biphasic positive airway pressure, RA: Room air, S. Mask: Simple mask, NRM: Nonrebreather mask.

mL), and the proportion of patients requiring invasive mechanical ventilation (30.8% vs. 23.3%) on admission were higher in the new-onset than in the T2DM hyperglycemia group.

Similarly, Cai *et al*. 2020[28] reported that hyperglycemia is associated with a higher risk of ARDS and acute respiratory failure. Xiao *et al*. 2022[29] found that the initial and mid-term blood glucose levels were related to markers of infection, such as CRP and the ESR, which indicates that hyperglycemia might be associated with the release of more inflammatory cytokines. Accordingly, it has been hypothesized that SARSCoV-2 may reduce insulin secretion through its effects on pancreatic β-cell function. The SARS-CoV-2 receptor (ACE2) has been shown to be expressed by pancreatic cells, as well as other metabolic organs and tissues (for instance, adipose tissue, intestine and kidneys).

In the present study, the new-onset hyperglycemia was associated with poor outcome in COVID-19 patients. Compared to the non-hyperglycemia group, the risk of death was highest in the new-onset hyperglycemia than T2DM hyperglycemia or euglycemic patients.

Le *et al*. 2022[24] demonstrated that the risk of the 28-day mortality rate was highest in the new-onset hyperglycemia (p = 0.011), which was higher than hyperglycemia in T2DM patients.

Al Argan *et al*. 2021[30] evaluated the impact of hyperglycemia in non-diabetic individuals on the severity and outcome of COVID-19 infection on a total of 414 patients. Compared to the control group, pre-existing DM was found to be significantly associated with severe, critical disease, ICU admission, and death from COVID-19 infection. Hyperglycemia without known DM was also found to be associated with critical COVID-19 pneumonia (P = 0.001), higher ICU admission, mechanical ventilation, and death from COVID-19 infection (P < 0.0001).

Zhang *et al*. 2020[14] reported an association of hyperglycemia without DM with a higher risk of critical care admission, mechanical ventilation, and death. Moreover, mortality rate of COVID-19 was reported to be worse in patients with higher fasting blood glucose even when it is in the normal range (P = 0.003).

Multiple mechanisms were postulated to explain the worst outcome in diabetic or hyperglycemic patients with COVID-19 infection. First, high markers of inflammation are strongly associated with critical infection and mortality. Second, COVID-19 disease has been associated with risk of thrombosis and abnormal coagulation pattern.

CONCLUSIONS

1. Advanced age, comorbidities and disease severity are significant risk factors for the development of new onset hyperglycemia in patients with COVID-19.
2. In general, there is no significant impact of treatment type on the development of new onset hyperglycemia in patients with COVID-19.
3. New onset hyperglycemic status or hyperglycemia with prior history of DM increases the mortality rate in COVID-19 patients.

ETHICAL APPROVAL

All patients were informed before participation in the study that their information and clinical data will be used for research purposes. This study has been approved by the ethical committee of Arab Board for Health Specialization in the Medical City.

COMPETING INTEREST

None

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