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ORIGINAL ARTICLE

Glycemic State in Hospitalized Coronavirus Disease 2019 Patients

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Abstract

Background: **Diabetes mellitus (DM) has become an important risk factor for major morbidity and death, hospitalizations, disease severity, acute renal failure, acute respiratory distress syndrome, ICU admissions, and patient death with coronavirus disease 2019 (COVID-19).**

Aim: **To study glycemic changes and outcomes in DM and non-DM patients hospitalized with COVID-19.**

Patients and methods: **In this retrospective study, 500 hospitalized adult patients over 18 years of age with COVID-19 were referred to Al-Azhar, Assiut and Chest-Assiut University Hospitals with nasopharyngeal vaccination against severe acute respiratory syndrome coronavirus 2. Our study spanned ~7 months of confirmed COVID-19 from January 2021 to July 2021.**

Results: **Patients with COVID-19 were divided into two groups based on their glycemic status: DM-COVID group: 217 patients were included. There was no statistically significant difference between the two groups in terms of age ($P > 0.05$). The significant difference between the COVID-with-DM group and the COVID-without-DM group in terms of hypertension, hemoglobin levels, chest area, random blood glucose measurements, need for ICU, and need for mechanical ventilation was significantly greater in DM-COVID-19 group. The COVID group without DM measured mortality ($P < 0.001$) since the COVID group with DM had significantly higher mortality.**

Conclusion: **The prevalence of the COVID-19 pandemic has significantly increased morbidity and mortality in diabetics. Diabetes and hyperglycemia are independent markers of death in people infected with severe acute respiratory syndrome coronavirus 1.**

Keywords: Coronavirus disease 2019, Diabetes mellitus, Glucose, Glycemic

1. Introduction

Diabetes mellitus (DM) has emerged as a major risk factor for serious illness and mortality from coronavirus disease 2019 (COVID-19),[1] and for hospitalization, disease severity, acute kidney damage, chronic or acute respiratory failure, death in intensive care units (ICU), and death from the year 2019.[2] The American Diabetes Association and American Association of Clinical Endocrinologists recommend a blood glucose target range of 7.83−10.0 mmol/l. They met the primary endpoint in the ICU.[3] Several abnormalities of the immune system have been postulated to explain the association between hyperglycemia and immunodeficiency, including impaired chemotaxis, monocytic and polymorphonuclear cells in white blood cells, and Phagocytosis and cytokine function and dysregulation. Furthermore, immunohistochemical staining of cadaveric pancreatic tissue revealed immunostaining of angiotensin-converting enzyme 2 in pancreatic islet cells, which resemble the lung alveolar epithelium and myocardium and contribute to hyperglycemia acute. On the other hand, activated inflammation, islet damage caused by viral infection, and corticosteroid therapy can in

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turn lead to poor glycemic control in people with diabetes and act as a memory loop, making memory loss worse. Therefore, blood glucose monitoring is of great importance in people with COVID-19, especially those who are seriously ill. The findings could help reduce the death toll in the fight against COVID-19.[4]

Therefore; the study aim to determine glycemic changes and outcomes in DM and non- DM hospitalized patients with COVID-1.

2. Patients and methods

In this retrospective cohort study, 500 hospitalized adult patients over 18 years of age with confirmed COVID-19 received nasopharyngeal vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) targeted at Al-Azhar-Assiut and Chest-Assiut University Hospitals. The duration of our study was ~7 months from the confirmation of COVID-19 in the period January 2021 to July 2021. Hospitalized patients older than 18 years and in whom COVID-19 had been confirmed by nasopharyngeal immunization against SARS-CoV-2 were included became, patients under 18 years of age, pregnant women, patients with incomplete data, patients with hepatic cell failure or renal replacement therapy, patients undergoing chemotherapy or radiotherapy, patients with active malignancy within 1 month of admission and patients on immunosuppressive therapy.

All patients were included, including: patients hospitalized for more than 24 h, patients with high hemoglobin A1c concentration within 3 months of admission, patients with blood glucose 180 mg/dl and severe hyperglycemia with a mean glucose value of over 24 h. Hospitalization and minimum glycemia 70 mg/dl.[5]

The study was approved by the Ethics Committee of Al-Azhar University Hospital in Asyut. Informed consent of the patient is not required if the study is retrospective. The data collected were tabulated and statistically analyzed using SPSS. A P value less than 0.05 was assumed as the significance level, which is significant, otherwise greater than 0.05 nonsignificant.

Table 1. Distribution of the studied patients as per clinical history ($n = 500$).

	Studied patients ($N = 500$) [n (%)]
DM	
No	283 (56.6)
Yes	217 (43.4)

3. Results

Patients with COVID-19 were divided into two groups based on their glycemic status: DM-COVID group: 217 patients were included. There was no statistically significant difference between the two groups in terms of age ($P > 0.05$). The significant difference between the COVID-with-DM group and the COVID-without-DM group in terms of hypertension, hemoglobin levels, chest area, random blood glucose measurements, need for ICU, and need for mechanical ventilation was significantly greater in DM-COVID-19 group. The COVID group without DM measured mortality ($P < 0.001$) since the COVID group with DM had significantly higher mortality (Tables 1–12).

4. Discussion

In 2020, the world was hit by the COVID-19 pandemic. This created an unprecedented crisis that prompted the scientific community to quickly understand the virus and the immune system's response.[6] Shortly after SARS-CoV-2 was isolated as a causative agent, DM emerged as a major risk factor for mortality in infected patients, as several epidemiological studies have shown.[7]

Table 2. Comparison between the studied groups Socio-demographic characters.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	P value
Sex				
Male	162 (57.2)	105 (48.4)	$\chi^2 = 3.87$	**0.049**
Female	121 (42.8)	112 (51.6)		
Age (y)				
Mean ± SD	63.05 ± 12.82	64.29 ± 10.17	Z = MWU 0.552	0.581
Median	65.0	65.0		
Range	20.0–94.0	27.0–91.0		
Age groups				
18–30 years	6 (2.1)	0	$\chi^2 = 8.43$	0.059
31–50 years	38 (13.4)	22 (10.1)		
51–60 years	57 (20.1)	56 (25.8)		
> 60 years	182 (64.3)	139 (64.1)		

Table 3. Comparison between the studied groups clinical presentation.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
Dyspnea				
No	11 (3.9)	8 (3.7)	$\chi^2 = 0.013$	0.908
Yes	272 (96.1)	209 (96.3)		
Cough				
No	40 (14.1)	19 (8.8)	$\chi^2 = 3.72$	0.156
Dry	102 (36.0)	78 (35.9)		
Productive	141 (49.8)	120 (55.3)		
Fever				
No	32 (11.3)	32 (14.7)	$\chi^2 = 1.302$	0.254
Yes	251 (88.7)	185 (85.3)		
Chest Pain				
No	260 (91.9)	186 (85.7)	$\chi^2 = 4.84$	**0.028**
Yes	23 (8.1)	31 (14.3)		
L.L. edema				
No	275 (97.2)	209 (96.3)	$\chi^2 = 0.293$	0.588
Yes	8 (2.8)	8 (3.7)		

Table 4. Comparison between the two studied groups regarding vital signs.

	COVID without DM group ($N = 283$)				COVID with DM group ($N = 217$)				Mann–Whitney U test	
	Mean ± SD	Median	Minimum	Maximum	Mean ± SD	Median	Minimum	Maximum	Test value	*P* value
Systolic BP (mm/Hg)	121.84 ± 13.45	120.0	80.0	170.0	124.86 ± 15.37	130.0	80.0	180.0	2.08	0.037 (S)
Diastolic BP (mm/Hg)	77.49 ± 9.99	80.0	50.0	100.0	78.05 ± 10.80	80.0	10.0	100.0	0.860	0.390 (NS)
Heart rate (beats/min)	92.63 ± 14.71	90.0	50.0	207.0	91.28 ± 14.48	90.0	44.0	133.0	0.745	0.456 (NS)

Table 5. Comparison between the two studied groups regarding laboratory data.

	COVID without DM group ($N = 283$)				COVID with DM group ($N = 217$)				Mann–Whitney U test	
	Mean ± SD	Median	Minimum	Maximum	Mean ± SD	Median	Minimum	Maximum	Test value	*P* value
Hemoglobin (g/dl)	12.36 ± 1.86	12.50	5.60	19.30	12.07 ± 2.03	12.10	3.90	23.40	2.30	**0.021 (S)**
Platelets count (10^9/l)	275.37 ± 106.91	257.00	41.0	803.0	270.29 ± 100.80	264.0	37.00	566.0	0.177	0.859 (NS)
WBCs (10^9/l)	9.69 ± 5.33	8.40	0.10	28.20	10.57 ± 9.50	9.05	2.50	129.50	1.297	0.194 (NS)
Lymphocytes	1.38 ± 0.99	1.10	0.10	7.30	1.36 ± 0.79	1.20	0.10	6.50	0.744	0.457 (NS)
Monocytes	0.47 ± 0.45	0.30	0.0	3.20	0.57 ± 1.31	0.40	0.10	19.0	2.113	**0.035 (S)**
Neutrophils	8.22 ± 5.54	6.90	00.40	55.00	8.87 ± 7.38	7.55	0.10	81.0	1.161	0.246 (NS)
Serum urea (mg/dl)	52.42 ± 30.16	43.00	18.0	222.0	60.31 ± 33.63	50.00	18.00	207.00	3.597	<0.001 (HS)
Serum creatinine (mg/dl)	1.28 ± 0.59	1.15	0.40	4.90	1.40 ± 0.75	1.20	0.30	6.70	2.277	0.023 (S)
AST	30.71 ± 26.57	24.0	5.0	325.0	29.10 ± 14.54	26.00	6.00	124.0	0.750	0.453 (NS)
ALT	28.23 ± 15.32	23.0	7.0	112.0	27.71 ± 13.27	25.00	7.00	76.0	0.217	0.828 (NS)
Ferritin	503.87 ± 535.78	410.0	19.00	4918.0	555.54 ± 569.06	413.00	32.00	4471.0	1.07	0.284 (NS)
D. dimer	3.28 ± 29.63	0.60	0.03	361.0	2.43 ± 23.23	0.54	0.01	340.0	0.025	0.980 (NS)
CRP	57.29 ± 36.07	51.00	1.30	394.0	78.62 ± 287.03	52.00	9.0	4256.0	0.517	0.606 (NS)

The main objective of this study was to examine glycemic changes and outcomes in hospitalized DM and non-DM with COVID-19. This retrospective cohort study, retrospective cohort study was conducted on 500 hospitalized adult patients over 18 years of age with confirmed COVID-19 nasopharyngeal swabs for SARS-CoV-2 who were referred to Al-Azhar University Hospitals-Asyut and Chest. The duration of the study varied between 6 and 12 months.

Table 6. Comparison between the two studied groups regarding ABG and serum electrolytes.

	COVID without DM group ($N = 283$)				COVID with DM group ($N = 217$)				Mann–Whitney U test	
	Mean ± SD	Median	Minimum	Maximum	Mean ± SD	Median	Minimum	Maximum	Test value	*P* value
pH	7.46 ±00 .09	7.48	6.90	7.61	7.44 ±00 .22	7.47	4.49	7.63	1.178	0.239 (NS)
PCO2	34.87 ± 10.32	33.00	15.00	95.0	35.14 ± 12.90	32.00	3.90	135.0	0.396	0.692 (NS)
HCO3	24.86 ± 5.66	24.40	4.10	47.0	24.96 ± 9.07	23.90	5.70	93.0	0.917	0.359 (NS)
SO2	86.53 ± 15.44	92.0	14.0	100.0	86.66 ± 13.08	90.0	9.30	100.0	1.484	0.138 (NS)
Na	138.11 ± 8.53	136.0	113.0	193.0	136.53 ± 8.75	135.0	104.0	181.0	2.422	**0.015 (S)**
k	3.45 ± 2.08	3.20	1.70	30.0	3.55 ± 1.66	3.30	1.50	24.0	1.848	0.065 (NS)

Table 7. Comparison between the studied groups glycemic status.

Description	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
Glycemic status				
Normal-controlled	163 (57.6)	26 (12.0)	$\chi^2 = 108.7$	**<0.001**
Hyperglycemia-uncontrolled	120 (42.4)	191 (88.0)		
Random blood sugar (mg/dl)				
Mean ± SD	194.3 ± 89.13	328.1 ± 119.83	Z = MWU 12.6	**<0.001**
Median	170.0	318.0		
Range	77.0–570.0	70.0–644.0		

Table 8. Comparison between the studied groups regarding acetone and albuminuria.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
Acetone				
Negative	279 (98.6)	188 (86.6)	$\chi^2 = 28.5$	**<0.001 (HS)**
Positive	4 (1.4)	29 (13.4)		
Albuminuria				
No	273 (96.5)	212 (97.7)	$\chi^2 = 0.638$	0.424 (NS)
Yes	10 (3.5)	5 (2.3)		

Table 9. Comparison between the studied groups computed tomography chest.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
CT chest				
Normal	113 (39.9)	67 (30.9)	$\chi^2 = 4.37$	**0.037 (S)**
Ground glass appearance	170 (60.1)	150 (69.1)		

Table 10. Comparison between the studied groups regarding ICU admission.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
Need for ICU admission				
No	273 (96.5)	151 (69.6)	$\chi^2 = 66.8$	**<0.001(HS)**
Yes	10 (3.5)	66 (30.4)		

Table 11. Comparison between the studied groups regarding need of mechanical ventilation.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	*P* value
Need for mechanical ventilation				
No	210 (96.8)	227 (80.2)	$\chi^2 = 30.6$	**<0.001 (HS)**
Yes	7 (3.2)	56 (19.8)		

Table 12. Comparison between the studied groups regarding mortality rate.

Variable	COVID without DM group ($N = 283$) [n (%)]	COVID with DM group ($N = 217$) [n (%)]	Test value	P value
Mortality				
No (improved)	210 (96.8)	227 (80.2)	$\chi^2 = 30.6$	**<0.001 (HS)**
Yes (Died)	7 (3.2%)	56 (19.8%)		

The present study showed that DM was present in 217 (43.4%) patients. There was no statistically significant difference between the two groups with regard to age ($P > 0.05$). Significant difference between the COVID group with DM and the COVID group without DM in terms of hypertension ($P < 0.001$) as it was significantly higher in the COVID group with DM. There was no statistically significant difference between the two groups for heart disease ($P > 0.05$).

Our results were supported by a study by Moghaddam Tabrizi *et al.*,[8] the mean age of DM was 64 years-old and non-DM 49 years-old. Significantly higher prevalence of comorbidities in diabetics compared with non-DM.

The current study showed that there was no significant difference between the COVID group with DM and the COVID group without DM in terms of clinical presentation ($P > 0.05$), with the exception of chest pain, which was reported in the COVID group with DM were reported and showed an increase ($P = 0.028$). Regarding systolic blood pressure, there was no significant difference between the COVID group with DM and the COVID group without DM ($P = 0.037$). There were no significant differences between the two groups in diastolic blood pressure and heart rate (P value > 0.05).

While, in the study of Moghaddam Tabrizi *et al.*,[8] Cough, loss of smell, and slight increase in systolic blood pressure was highly significant in diabetic group, although; followed by fatigue, dyspepsia and fever. In addition respiratory rate among diabetic and non DM patients.

The current study found that in terms of laboratory measurements; the COVID group with DM showed a significant decrease in hemoglobin levels compared with the COVID group without DM ($P = 0.021$), while the COVID group with DM showed a significant increase in monocyte levels compared with the COVID group. Without MS ($P = 0.035$). There was no significant difference between the two groups in terms of platelet count (P value > 0.05). In addition, there was no significant difference between the two groups for leukocytes, lymphocytes, monocytes, and neutrophils (P value > 0.05). The COVID group with DM showed a significant increase in serum urea compared with the COVID group without DM ($P < 0.001$). In addition, the COVID group with DM showed a significant increase in creatinine levels compared with the COVID group without DM ($P = 0.023$). The COVID group with DM showed a significant decrease in Na levels compared with the COVID group without DM ($P = 0.015$). However, there was no significant difference between the two groups in terms of pH and PCO_2 (P value > 0.05). There was no significant difference between the two groups in terms of oxygen saturation, HCO_3 content, and k (P value > 0.05). There was no significant difference between the two groups for AST and ALT (P value > 0.05). There were no significant differences between the two groups for ferritin, D-dimer, and CRP levels (P value > 0.05). There is a significant difference between the two groups in glycemic status ($P < 0.001$). It was found that 120 (42.4%) cases in the non-DM COVID group had hyperglycemia. The COVID group with DM showed a significant increase in voluntary blood glucose compared with the COVID group without DM ($P < 0.001$). The COVID group with DM showed a significantly higher percentage of positive urinary acetone compared with the COVID group without DM ($P < 0.001$). There was no significant difference between the COVID group with DM and the COVID group without DM in albuminuria ($P > 0.05$).

However, in the study by Moghaddam Tabrizi *et al.*,[8] highly significant differences of glucose levels among diabetic patients other than non-DM, in addition; creatinine and d-dimer nonsignificantly differences among diabetic and non-DM group. erythrocyte sedmentation rate (ESR), lactate dehydrogenase (LDH), C-reactive protein and complete blood count was highly significant among diabetic group.

In the study of Yadaiah *et al.*,[9] HbA1C level was highly significant observed in un-controlled group other than controlled group.

In the study that we have in hand, concerning CT, a significant difference between the COVID group with DM and the COVID group without DM compared with chest CT ($P = 0.037$), as the ground glass appearance was significantly more prevalent in the COVID DM group. A significant difference between the COVID group with DM and the COVID group without DM in terms of need for ICU admission ($P < 0.001$). A difference difference

significant between the COVID group with DM group and the COVID group without DM regarding the need for mechanical ventilation ($P < 0.001$), because the COVID group with DM had a significantly greater mechanical difference between the COVID group with DM and COVID group with DM had a significantly higher mortality.

Consistent with our review of the results of Moghaddam Tabrizi *et al.*,[8] Patients with bilateral lung lesion on CT chest was commonly observed among DM group other than non-DM patients.

Additionally, Bhatti *et al.*,[10] Death rate was lower in HbA1C, fasting glucose and random blood sugar. However, intensive care treatment was highly needed among HbA1C patients, in addition patients with high random blood sugar and fasting glucose was highly needed to mechanical ventilation.

4.1. Conclusion

The prevalence of the COVID-19 pandemic has significantly increased morbidity and mortality in DM. DM and hyperglycemia are independent markers of death in people infected with SARS-CoV-1.

Conflicts of interest

There are no conflicts of interest.

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