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Clinical Outcome of Covid-19 Patients with Pre-Existing Diabetes Mellitus at King Abdulaziz University Hospital

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ABSTRACT

Aims: To investigate the clinical outcome of patients with confirmed COVID-19 who had diabetes mellitus as a comorbidity at King Abdulaziz University Hospital, Jeddah.

Methods: Retrospective study conducted at an academic tertiary hospital, included 147 adults with a confirmed diagnosis of diabetes mellitus, and a confirmed diagnosis of COVID-19. The data included: age, gender, body mass index (BMI), HbA1c level, medications, co-morbidities, length of hospital stay, the clinical outcome of the patients, and complications related to COVID-19 during the hospital stay. Data were analyzed using Stata version 16.

Results: 54% had HbA1c levels >9%. With regard to other health problems, 73% reported having health problems. 31% and 18% required ICU admission and intubation respectively. Median length of hospital stay was 12 days. Regarding clinical outcomes, the majority recovered without complications (78%), while 9% recovered with complications and 13% died.

Conclusions: The difference in outcomes based on HbA1c levels was not statistically significant, therefore there was no difference in other clinical parameters based on the different levels of HbA1c. Further, large studies should be conducted to determine the relationships between diabetes, antidiabetic medications, and COVID-related morbidity and mortality.

Keywords: Covid19, Diabetes, King Abdulaziz University Hospital, Sars-cov2, Saudi Arabia.

INTRODUCTION

In December 2019, the novel coronavirus that causes severe respiratory distress syndrome 2 (SARS-CoV-2) appeared in Wuhan, China, and subsequently led to the historic, and currently ongoing, pandemic that has caused a global crisis [1,2].

SARS-CoV-2 binds to angiotensin-converting enzyme 2 receptor via a protein called glycoprotein S; ten to twenty times more aggressive than previous SARS coronaviruses. As this receptor is present in multiple vital organs, COVID-19 is associated with end-organ failure of numerous organs and related mortality [3].

As of August 13, 2021, there were a total of 205 million confirmed cases of COVID-19 and 4 million resulting deaths globally according to the WHO dashboard [4]. Saudi Arabia, a country with a population of 33.2 million citizens [5] in the Middle East, has recorded 537,374 confirmed cases and 8388 deaths (mortality rate, 1.56%) [4].

Several published studies have shown that COVID-19 patients with comorbidities, such as diabetes mellitus, hypertension, cardiovascular diseases, and chronic lung disease, had worse clinical outcomes and prognosis than those without these comorbidities [6,7].

In the United States, a study showed that hospitalized COVID-19 patients with uncontrolled diabetes had a longer length of stay and higher mortality rate than those without diabetes [8].

Other studies have also identified diabetes mellitus as a risk factor in COVID-19 patients to develop adverse overall clinical outcomes in the form of greater need for hospitalization, especially in those with higher HbA1c levels, increased length of stay during hospitalization, occurrence of acute respiratory distress syndrome, and death [8-11].

Similarly, in Saudi Arabia, a study conducted at King Salman Bin Abdul-Aziz Hospital in Al Riyadh found that diabetes mellitus is a common comorbidity among hospitalized patients with COVID-19[12]. Another study conducted at Prince Sultan Military Medical City, Riyadh, also found diabetes mellitus to be the most commonly associated disease in admitted patients with COVID-19[13].

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AIM OF THE STUDY

To assess the effect of diabetes control as defined by HbA1c on the outcome of hospitalized patients with COVID-19, and the clinical outcome in those patients at King Abdulaziz University Hospital, Jeddah. As COVID-19 is still a relatively new and complex disease, we believe that the findings will make an important contribution to the countrywide data, as well as the global data, on the outcome of COVID-19 in patients with diabetes mellitus as a co-morbidity.

PATIENTS AND METHODS

Patients and data collection

This was a retrospective study conducted at a single tertiary hospital, King Abdulaziz University Hospital, from July 1, 2020, until the end of November 2020. This study included patients aging 18 years old and above, with a confirmed diagnosis of diabetes mellitus type 1 and 2, with Hba1c levels 6.5% and above according to lab tests done within the 3 months before admission, and a confirmed diagnosis of COVID-19 by nasopharyngeal swab RT-PCR for SARS-CoV-2.

According to our exclusion criteria, patients below the age of 18 years, any pregnant patient, patients who developed diabetes secondary to steroid use (iatrogenic diabetes mellitus), and terminally ill patients (with a Do Not Resuscitate order, or patients on palliative treatment for terminal illness such as malignancies), were excluded.

Ethical considerations:

This study was approved by the ethics board of Biomedical Research Ethics Committee and Department of Medicine at King Abdul-Aziz University in Jeddah Saudi Arabia.

An informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The following data were collected and entered into a Google form: age, gender, body mass index (BMI), HbA1c level by percentage, medications, co-morbidities, total length of hospital stay, ICU admission or intubation, the clinical outcome of the patients, and complications related to COVID-19 during the hospital stay.

The data were transferred into an Excel sheet and analyzed using Stata version 16 (StataCorp LLP, College Station, Texas, USA).

Statistical analysis

Frequencies and percentages were used to describe categorical data, while means, standard deviations (SD), and range were used to describe normally distributed continuous data and median and interquartile range (IQR) were used to describe abnormally distributed continuous data.

The association between the health-related variables and HbA1c were tested using chi-square test and Fisher exact test for categorical variables. One-way ANOVA was used to compare normally distributed continuous data and Kruskal-Wallis test was used to compare abnormally distributed continuous data.

Multinomial logistic regression analysis adjusting for age, sex and BMI was performed to explore the effect of HbA1c levels on different clinical outcomes. The significance level was set at 0.05. Data were analyzed using Stata version 16 (StataCorp LP, College Station, Texas, USA).

RESULTS

A total of 147 diabetic patients were included int study. The health-related characteristics of the study population are displayed in table 1.

Table 1: characteristics of the study population		
Variables	**N**	**%**
N	147	100
Age (years) Mean (SD) Range	60.51 (13. 48) (19 – 101)	
Gender		
Male	97	66.0
female	50	34.0
BMI (kg/m^2)		
Healthy (<24.9)	42	28.6
Overweight (25-29.9)	62	42.2
Obese (>30)	43	29.2
HbA1c (%)		
<7	29	19.7
7-7.9	20	13.6
8-8.9	18	12.2
>9	80	54.4
Medications		
Oral hypoglycemic drugs	69	46.9
Insulin	25	17.0
Both insulin and oral drugs	11	7.5
No medications	27	18.4
Unknown	15	10.2
Comorbidities		
None	39	26.5
Hypertension	100	68.0
Chronic lung disease	10	6.8
Heart failure	15	10.2
Ischemic heart disease	26	17.7
Cerebrovascular accident	14	9.5
Chronic kidney disease	13	8.8
Others	14	9.5
ICU admission		
Yes	45	30.6
No	102	69.4
Intubation		
Yes	26	17.7
No	121	82.3
Length of stay in the hospital (days)		
Median (IQR)	12 (22-8)	
Clinical outcome		
Recovered without complications	114	77.6
Recovered with complications	14	9.5
Died	19	12.9
Complications of covid-19		
None	114	77.6
Arrhythmias	6	4.1
Hemodialysis	9	6.1
Pulmonary embolism	3	2.0
Pulmonary fibrosis	9	6.1
Secondary infections	6	4.1
Septic shock	10	6.8
Ischemic heart disease	4	2.7
Stroke	4	2.7
Note: N: number, SD: standard deviation, BMI: body mass index, HbA1c: hemoglobin A1c, ICU: intensive care unit, IQR: interquartile range		

Table 2 shows the association between HbA1c and health-related characteristics. Patients with high HbA1c (>9) were insignificantly younger. There was some evidence suggested that patients with high HbA1c (>9) had the highest proportion (73.8%) of male. However, there was no evidence of any significant difference in BMI, ICU admission, length of stay in the hospital, intubation, or clinical outcomes across the different levels of HbA1c.

Table2: Means (SD) and counts (%) of the characteristics of the study population by Hemoglobin A1c levels.

	Hemoglobin A1c				**P value***
	< 7	**7 - 7.9**	**8 - 8.9**	**> 9**	
Counts (%)	29 (19.7)	20 (13.6)	18 (12.2)	80 (54.4)	
Age, years Mean (SD)	63.1 (14.3)	65.1 (11.8)	62.8 (11.6)	57.9 (13.6)	0.077
Gender (%)					
Male	13 (44.8)	14 (70.0)	11 (61.1)	59(73.8)	0.041
Female	16 (55.2)	6 (30)	7 (38.9)	21(26.3)	
BMI (%)					
Healthy	8 (27.6)	2 (10.0)	4 (22.2)	28 (35.0)	
Overweight	12 (41.4)	10 (50.0)	9 (50.0)	31 (38.8)	0.433
Obese	9 (31.0)	8 (40.0)	5 (27.8)	21 (26.3)	
ICU admission (%)					
Yes	7 (24.1)	9 (45.0)	7 (38.9)	22 (27.5)	0.325
No	22 (75.9)	11 (55.0)	11 (61.1)	58 (72.5)	
Intubation (%)					
Yes	4 (13.8)	4 (20.0)	4 (22.2)	14 (17.5)	0.861
No	25 (86.1)	16 (80.0)	14 (77.9)	66 (82.3)	
Length of stay in the hospital (days) Median, (IQR)	11 (22-8)	15.5 (28-9.5)	12.5 (20-9)	11.5 (22-7)	0.567
Comorbidities					
None	8 (27.6)	3 (15.0)	3 (16.7)	25 (31.3)	0.407
Hypertension	18 (62.1)	17 (85.0)	14 (77.8)	51 (63.8)	0.214
Chronic lung disease	3 (10.3)	4 (20.0)	1 (5.6)	2 (2.5)	0.024
Heart failure	5 (17.2)	1 (5.0)	2 (11.1)	7 (8.8)	0.548
Ischemic heart disease	3 (10.3)	4 (20.0)	6 (33.3)	13 (16.3)	0.234
Cerebrovascular accident	3 (10.3)	1 (5.0)	2 (11.1)	8 (10.0)	0.922
Chronic kidney disease	4 (13.8)	0 (0.0)	3 (16.7)	6 (7.5)	0.201
Others	5 (17.2)	3 (15.0)	1 (5.6)	5 (6.25)	0.230
Clinical outcomes (%)					
Recovered without complications	24 (82.8)	15 (75.0)	12 (66.7)	58 (72.5)	
Recovered with complications	2 (6.9)	3 (15.0)	4 (22.2)	9 (11.25)	0.749
Died	3 (10.34)	2 (10.0)	2 (11.1)	13 (16.3)	

Notes:
N: number, SD: standard deviation, BMI: body mass index, HbA1c: hemoglobin A1c, ICU: intensive care unit, IQR: interquartile range

DISCUSSION

HbA1c is used to measure glycemic control in diabetic patients for the preceding 90 days. A raised HbA1c level indicates suboptimal blood sugar control, which correlates with worse clinical outcome, in comparison with good glycemic control, by accelerating the development of microvascular and macrovascular complications that may increase mortality[14]. Hyperglycemia predicted worse outcomes in hospitalized patients with COVID, whether the patient was diabetic or not. Additionally, poor glycemic control impairs the immune system in diabetic patients, resulting in adverse clinical outcomes, and tight glycemia control during hospitalization decreases mortality in COVID-19 patients[15-17]. Therefore, in our study, we were expecting that the higher the HbA1c level the worse is clinical outcome, but it was not the case.

In our study, the median length of hospital stay was 12 days, which is similar to that reported in previous studies, in which the median length of stay was 10 to 13 days[18,19]. However, there was no evidence of any difference in BMI, ICU admission, intubation, length of stay at the hospital, or clinical outcomes between patients with different levels of HbA1c.

In August 2020 study including 1126 patients showed that levels of HbA1c were not correlated with mortality from COVID-19 in unadjusted or adjusted analyses, but an outpatient regimen with any insulin treatment was strongly predictive [20]. Another study from July 2021 demonstrated that there were no significant adverse clinical outcomes across different HbA1c levels in diabetic patients who were hospitalized with COVID-19 and stated that HbA1c levels should not be used for risk stratification in these patients[21].

Dexamethasone is currently being used for COVID-19 as it results in a decrease in mortality in patients requiring respiratory support[22,23]. However, dexamethasone causes decreased insulin sensitivity and β-cell dysfunction, resulting in hyperglycemia[24]. According to some studies, treatment with insulin preadmission and during admission for hyperglycemia was predictive of increased mortality[20,25] via an unknown mechanism. Currently, in treatment of hyperglycemia in hospitalized (especially critically ill) patients, glycemic control is achieved using insulin intravenously as the agent of choice, however no optimal treatment is yet established to decrease hospital admission for diabetic patients with COVID-19, nor to decrease mortality[26].

One of the main limitations of the present study is it was conducted in a single tertiary hospital in Saudi Arabia. Multiple studies are required to reinforce our results. There was also a lack of sufficient data about medication use, as 18.4% of the patients were not taking diabetic medications and for 10.2% their medications were unknown, making analysis for the remaining patients statistically insignificant. Therefore, we could not determine whether the clinical outcomes were related to medication regimen. Another limitation is that we wanted to identify if certain complications of COVID-19 were associated with different HbA1c levels, but most of the patients recovered without any complications (74.1%). Therefore, the sample size was too small to obtain significant findings.

CONCLUSION

The difference in outcomes based on HbA1c levels was not statistically significant, therefore there was no difference in other clinical parameters based on the different levels of HbA1c. Further, large studies should be conducted to determine the relationships between diabetes, antidiabetic medications, and COVID-related morbidity and mortality.

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