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Effects of hyperglycemia among non-diabetics on Covid-19 outcomes

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Abstract

Objectives: Diabetic individuals have a poorer prognosis when infected with COVID-19, a coronavirus disease. However, the impact of hyperglycemia on COVID-19 patients without a history of diabetes is not well understood. This study aimed to determine the prevalence of hyperglycemia and its effect on the prognosis of non-diabetic COVID-19 patients. Materials and Methods: A hospital-based cross-sectional study was conducted at the Jabra Isolation Centre in Sudan with 252 non-diabetic COVID-19 patients. The data collected included demographics, oxygen saturation, respiratory rate, ICU admission, length of hospital stay, and outcomes. The CURB-65(Confusion, Uremia, Respiratory rate, BP, age ≥ 65 years) pneumonia severity score was also evaluated for each participant. Blood glucose levels above 180 mg/dl were considered indicative of hyperglycemia. Results and Conclusion: A significant portion of non-diabetic COVID-19 patients exhibited hyperglycemia upon admission, which was strongly associated with a high CURB-65 score, severe COVID-19 infection, ICU admission, and a poor prognosis regarding length of hospital stay (LOHS) and mortality.

Keywords: COVID-19, hyperglycemia, outcomes, severity, Sudan

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, triggered by SARS-CoV-2, has had a substantial impact on global health. Diabetics have a lower outlook than others. However, the link between hyperglycemia and COVID-19 results in non-diabetic patients is less clear. The purpose of this study is to assess the prevalence of hyperglycemia and how it affects the prognosis of non-diabetic COVID-19 patients. The hypothesis is that hyperglycemia at admission is related with worse outcomes in non-diabetic COVID-19 patients. and caused over 24,000 deaths in Italy to date, nearly 10% of those infected. Furthermore, 5-10% of COVID-19 patients require mechanical ventilation and hospitalization in an intensive care unit (ICU). Hyperglycemia is common among acute hospital admissions and critically ill patients, even those without a prior history of diabetes. It is defined as a blood glucose level greater than 7.77 mmol/L and can occur in individuals with or without diabetes hospitalized for COVID-19.[1]Diabetes is a significant risk factor for a poor COVID-19 prognosis. Several studies have also shown that poor glucose control or hyperglycemia can worsen the severity of the condition. Therefore, investigating the impact of hyperglycemia on COVID-19 treatment admissions in Sudan is crucial. In 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency of international concern.[2]

Hyperglycemia in COVID-19 patients can be harmful. The virus can infect endocrine pancreas cells by binding to angiotensin-converting enzyme 2 (ACE2) receptors and inhibit insulin release by beta cells. Additionally, COVID-19-related inflammation can cause insulin resistance. The resulting hyperglycemia increases ACE2 expression and glycosylation, facilitating the virus's entry into cells.[3]In non-diabetic hospitalized severe and critically ill medical or surgical patients, hyperglycemia is a more significant predictor of poor prognosis and mortality than diabetes mellitus itself.[4]

The mechanisms by which hyperglycemia damages cells include altered osmolality, blood flow, intracellular acidosis, and increased superoxide production, leading to immune, coagulation, and endothelial function derangement, as well as neuropathy and myopathy. Insulin therapy to maintain normoglycemia can partially mitigate these changes.[5] Significance of the study The prognosis for diabetic individuals with COVID-19 is poor. Unfortunately, the impact of hyperglycemia on non-diabetic COVID-19 patients is not well understood. This study aimed to determine the prevalence of hyperglycemia and its effect on the prognosis of non-diabetic COVID-19 patients.

As a result, the goals of this study are to determine the prevalence of hyperglycemia among non-diabetic COVID-19 patients and to assess the relationship between hyperglycemia and their prognosis, which includes infection severity, ICU admission rates, length of hospital stay, and mortality rates.

Materials and Methods

Research Design and Setting

A hospital-based cross-sectional investigation was done at Sudan's Jabra Isolation Centre. Data were collected in Khartoum, Sudan, between February and June 2021, during the second wave of the COVID-19 epidemic. This design comprises a systematic strategy to gathering data from a subset of individuals or entities within a broader population, with the goal of providing a detailed and accurate portrayal of the features, behaviors, beliefs, or attitudes prevalent in the target group.

Sampling Method

The participants were selected using a convenience sampling method. This approach was adopted because to the study's practical constraints and the need for quick data gathering during the pandemic. Patients admitted to the Jabra Isolation Centre during the study period who met the inclusion criteria were enrolled sequentially until the target sample size was reached.

Sample Size

The study involved 252 COVID-19 participants who had not been diagnosed with diabetes. The sample size was determined using the study goals, taking into account the projected prevalence of hyperglycemia in non-diabetic COVID-19 patients and guaranteeing appropriate power to detect significant relationships.

Inclusion Criteria

1-Adults (over the age of 18).

2-Individuals who had not been diagnosed with diabetes prior to their current admission.

3- Residents of Sudan have certified that they have COVID-19.

Tools for Data Collection

A data collecting sheet was used to capture patient information such as demographics, oxygen saturation, respiratory rate, ICU admissions, length of hospital stay, and patient outcomes. This study examined two outcomes: discharge and death. Each patient had their CURB-65 pneumonia severity score analyzed. Hyperglycemia was defined as blood glucose levels exceeding 180 mg/dL. Each patient was evaluated. Hyperglycemia was diagnosed when blood glucose levels exceeded 180 mg/dL.

Statistical Analysis

Based on what the research questions addressed in relation to the questions contained in the research, the following statistics were conducted:

1- The data were analyzed using version 26.0 of the Statistical Package for the Social Sciences (SPSS) software.

2-The study population's demographic and clinical features were summarized using descriptive statistics. Categorical data were estimated as frequencies and percentages, whilst continuous variables were calculated as means and standard deviations.

3- Chi-square tests were employed to determine the relationship between categorical variables such blood glucose levels, respiratory characteristics, ICU admission, outcomes, and CURB-65 scores.

4- A p-value of <0.05 was judged statistically significant.

5-The odds ratios (OR) and 95% confidence intervals (CI) were used to assess the strength of associations.

6- In addition, logistic regression analysis was used to compensate for potential confounds and uncover independent predictors of severe COVID-19 outcomes.

Validity

A panel of specialists assessed the tools to ensure content validity, and improvements were made as needed.

Ethical Considerations

Participants were told that their participation was voluntary and that their privacy would be respected. Data were gathered using a data collection sheet. The General Administration of Strategic and Innovation, Development, and Scientific Research of the Ministry of Health in Khartoum, Sudan, issued ethical approval under serial number KMOH-REC-06410-2022. Before any data was collected, each participant provided written informed consent. To protect confidentiality, data was collected anonymously, and no individual research participants were identified. Prior to data collection, all patients signed an informed written consent form.

Results

The findings show that hyperglycemia at admission is significantly associated with a variety of COVID-19 outcomes. For example, hyperglycemia was substantially linked to higher CURB-65 scores, more ICU admissions, and higher mortality rates. These data show that hyperglycemia could be a useful marker for identifying non-diabetic COVID-19 patients who are at higher risk of severe consequences. However, it is important to note that these relationships do not imply causation, and more research is needed to investigate the underlying mechanisms.

Data were analyzed, tabulated, and presented using appropriate statistical methods. The questionnaire aimed to fulfill the study's objectives and answer its research questions, as shown in Table 1.

Table 1: Demographic characteristics

Variable	Category	Frequency	Percent
Gender	Male	100	39.7
	Female	152	60.3
Age	< 40	16	6.3
	40-65	107	42.5
	> 65	129	51.2

Table 1reveals that 60.3% of the participants are female, and 39.7% are male.Among the participants, 51.2% are older than 65 years, 42.5% are between 40 and 65 years, and 6.3% are younger than 40 years.

Table 2: Respiratory features

Variable	Category	Frequency	Percent
Oxygen saturation	88 %	135	53.6
	88 - 93 %	93	36.9
	> 93 %	24	9.5
ICU admission	Yes	163	64.7
	No	89	35.3
Length of hospital stay	< 8 days	122	48.4
	8-14 days	85	33.7
	14 days	45	17.9
Blood sugar at admission	<140	75	29.8

(mg/dl)	From 140-180	74	29.4
	>180	103	40.9
CURB-65	Low mortality	110	43.7
	Intermediate mortality	93	36.9
	High mortality	49	19.4
Outcomes	Discharge	92	36.5
	Death	160	63.5

Table 2shows that 53.6% of participants have an oxygen saturation of 88%, 36.9% have an oxygen saturation between 88% and 93%, and 9.5% have an oxygen saturation higher than 93%.Additionally, 64.7% of participants were admitted to the ICU, while 35.3% were not.Regarding hospital stay, 48.4% of participants stayed for less than 8 days, 33.7% stayed for 8 to 14 days, and 17.9% stayed for more than 14 days.Blood sugar levels at admission were higher than 180 mg/dl for 40.9% of participants, less than 140 mg/dl for 29.8%, and between 140 to 180 mg/dlfor 29.4%. Regarding mortality risk, 43.7% of participants were in the low mortality group, 36.9% in the intermediate group, and 19.4% in the high mortality group.Among the participants, 63.5% died, and 36.5% were discharged.

Table 3: Differences in respiratory features according to blood sugar at admission

Variable		Blood sugar at admission			Total	p-value	Chi-Square(df)
		<140	140-180	>180			
Oxygen saturation	<88	27	39	69	135	.001	18.835(2)
	88-93	39	25	29	93		
	>93	9	10	5	24		
ICU admission	Yes	43	43	77	163	.021	7.750(2)
	No	32	31	26	89		
Outcomes	Discharge	33	33	26	92	.008	9.543(1)
	Death	42	41	77	160		
Length of hospital stay	<8 days	40	42	40	122	.122	7.280(2)
	8-14 days	22	23	40	85		
	>14 day	13	9	23	45		
CURB-65	Low mortality	38	39	33	110	.000	24.878(2)
	Intermediate mortality	29	29	35	93		
	High mortality	8	6	35	49		

Table 3 shows significant differences in oxygen saturation and ICU admission rates based on blood sugar levels at admission, with p-values of 0.001 and 0.021, respectively, implying that those with lower oxygen saturation and higher ICU admission rates had higher blood sugar levels when admitted. There was no significant difference in length of hospital stay based on blood sugar levels at admission (p=0.122). Significant disparities in CURB-65 scores and outcomes were found depending on blood sugar levels upon admission, with those who died having greater levels.

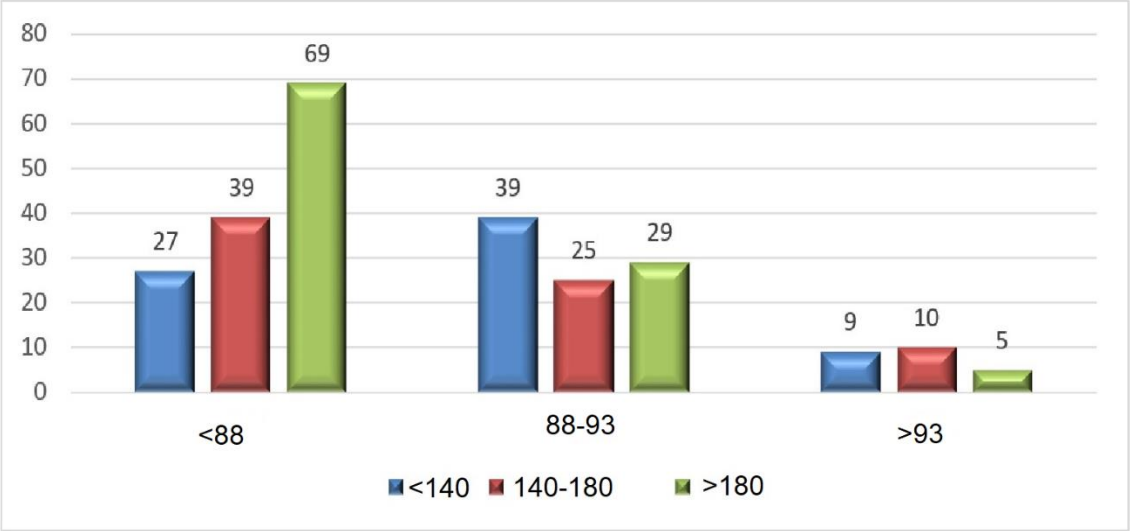

Figure 1: Oxygen saturation

The chart in figure 1 illustrates that there is a difference in oxygen saturation according to blood sugar at oxygen saturation (<88), and have the highest percentage of blood sugar at admission (>180).

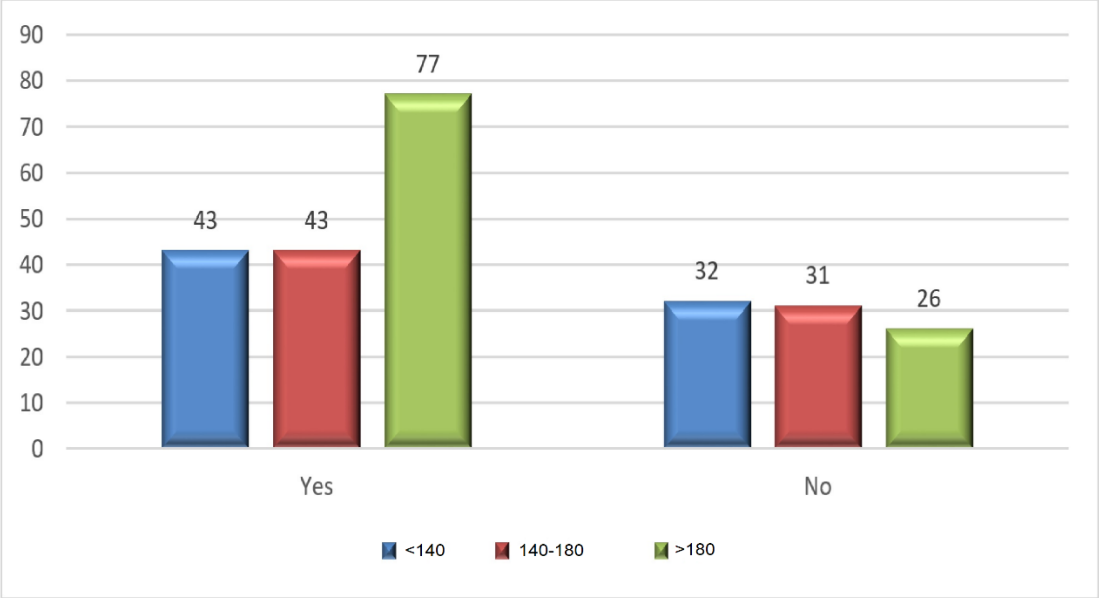

Figure 2: ICU admission

There is a significant difference in ICU admission according to blood sugar at admission where (sig=0.021) less than (0.05) where participants who admitted to ICU have the highest percentage of blood sugar at admission (>180).

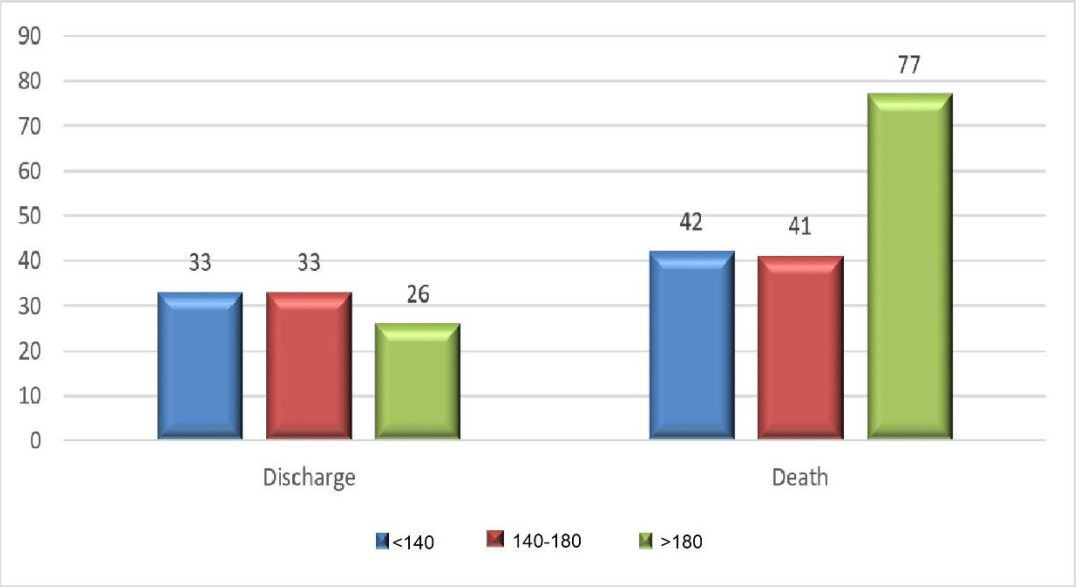

Figure 3: Outcomes

There is a significant difference in outcomes according to blood sugar at admission where (sig=0.008) less than (0.05) where participants who dead have the highest percentage of blood sugar at admission (>180).

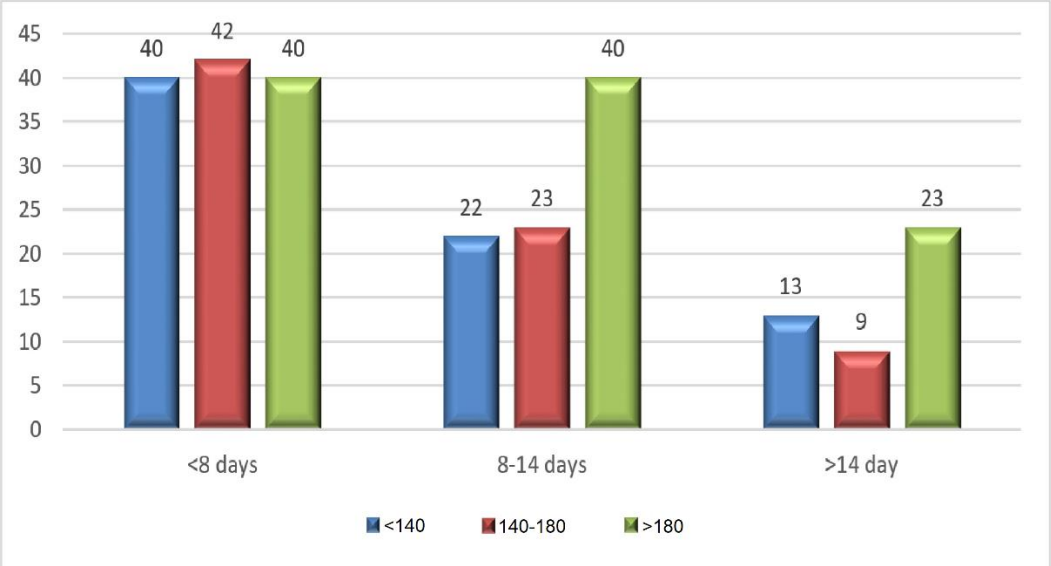

Figure 4: Length of hospital stay

There is a significant difference in CURB according to blood sugar at admission where (sig=0.00) less than (0.05) where participants who high mortality and intermediate mortality have the highest percentage of blood sugar at admission (>180).

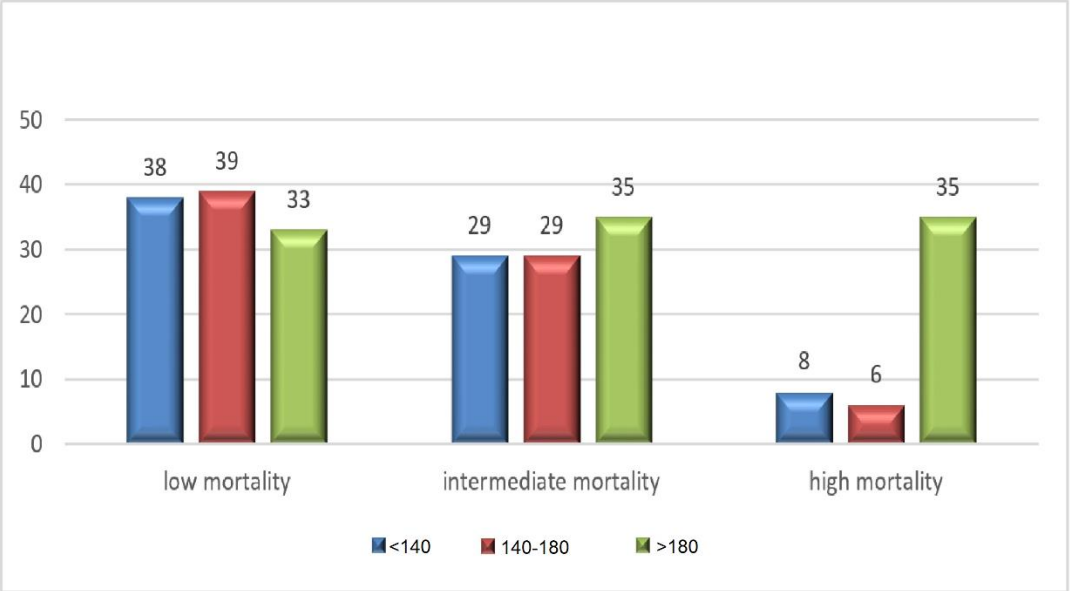

Figure 5: CURB – 65

There is a significant difference in CURB – 65 according to blood sugar at admission where (sig=0.00) less than (0.05) where participants who high mortality and intermediate mortality have the highest percentage of blood sugar at admission (>180).

Discussion

To the best of our knowledge, this is the first study to describe the prevalence and implications of hyperglycemia at admission in non-diabetic COVID-19 patients in Sudan. The data show a strong link between hyperglycemia and poor COVID-19 outcomes, including higher CURB-65 scores, more ICU admissions, and worse mortality rates. It is important to emphasize that, due to the study's cross-sectional design, we can only infer associations, not causal links. Additional longitudinal research is required to investigate the causal mechanisms behind these correlations.Approximately 252 Sudanese patients hospitalized at the Jabra Secondary Isolation Centre in Sudan had their COVID-19 infection verified; prior to this, they had no diagnosis of diabetes. In this sample, males were more likely than females to be impacted by COVID-19 (60% vs. 40%), with a ratio of 1.5:1. This finding aligns with several previous studies that noted adult male predominance.[6, 7]There is no clear explanation for the different risks of infection between men and women; however, some have proposed genetic mechanisms or sex-specific effects.[8]Just over half of the patients (51.2%) in this study were aged above 65 years. These results were comparable to those of Chinese and Italian studies (median = 62 and 67.5 years, respectively).[9,10]However, some other Chinese studies reported lower mean ages. Regarding the pneumonia severity score (CURB-65), 110 (43%) of patients were at low risk (CURB-65: 0-1), 93 (36.9%) were at intermediate risk (CURB-65: 2), and 49 (19.4%) were at high risk (CURB-65: 3 or more). These observations were comparable to a previous study, where around 15.1% of hospitalized high-risk COVID-19 patients, according to the pneumonia score, were (CURB-65 3-5).[11]

Although the mechanisms of hyperglycemia in COVID-19 are not fully understood, possible pathways include COVID-19-induced inflammation and cytokine storm (CS), characterized by significant elevations in tumor necrosis factor-alpha (TNF-) and interleukin (IL)-6 levels, leading to peripheral insulin resistance.[12]Moreover, SARS-CoV-2 infects the pancreas through ACE2, which is highly expressed in the pancreas compared to other organs, leading to pancreatic damage with

subsequent impairment of insulin secretion and development of hyperglycemia even in non-diabetic patients.[12]In the current study, the frequency of at-admission hyperglycemia (blood glucose >180 mg/dl) was 41%. The mean blood glucose level at admission was 189.79 mg/dl, ranging between 50 and 746 mg/dl. It is worth mentioning that these patients were not diabetic. Although this study did not examine the mechanism of hyperglycemia in patients, the results were similar to large studies where the rate of hyperglycemia was reported in around half of the study group.[3, 13]

In this study, at-admission hyperglycemia was significantly associated with the severity of COVID-19 infection in terms of decreased oxygen saturation to 88% and increased respiratory rate to >30 breaths/min. This echoes findings by Kumar et al.),[14]who reported an increase in admission plasma glucose levels correlating with increasing COVID-19 severity. The current study demonstrated that hyperglycemia in non-diabetic COVID-19 patients significantly increased the risk of admission to the intensive care unit (ICU) OR (2.2) 95% CI of (1.2-3.7). This is consistent with some studies [3, 15, 16]that reported increased rates of ICU admission among hyperglycemic patients. However, ICU admission did not significantly differ between patients with and without hyperglycemia in the study by Alberto C et al..[17]

Before this study, research had not reported a relationship between the severity of pneumonia using the CURB-65 scoring system and blood glucose levels in COVID-19 patients. The findings showed that at-admission hyperglycemia was significantly associated with a high CURB-65 score, with an increased rate of prolonged hospital stays of more than 14 days. These findings echo previous research by Colaneri et al.,[8] and Schurz et al.,[10] who reported a prolonged length of hospital stay (LOS) among hyperglycemic patients compared to normoglycemic ones.

Interestingly, the current study showed that at-admission hyperglycemia significantly increased the hazard of mortality. This could be explained by the likelihood of hyperglycemic patients having a severe COVID-19 infection necessitating intensive care unit treatment. The findings were consistent with many studies in which hyperglycemia in non-diabetics was associated with a higher risk of mortality compared to patients with normal blood glucose values.[3, 14, 17]Overall, many patients had not experienced hyperglycemia in their history before this COVID-19 attack. Hyperglycemia in this group was strongly correlated with severity and poor clinical outcomes, more evident in high CURB-65 pneumonia severity scores, ICU admission, and death, and in its milder conditions, it was related to more morbidity in the form of decreased oxygen saturation, tachypnea, and long hospital stays.

Conclusion

This study aimed to determine the prevalence of hyperglycemia and its effect on the prognosis of non-diabetic COVID-19 patients. A significant number of COVID-19 patients who were not diabetics had hyperglycemia upon admission. It was substantially linked to a high CURB-65 score, severe COVID-19 infection, ICU admission, and a poor prognosis for lengthy hospital stays and mortality in general.

Use of AI tools declaration

The authors declare they have not used artificial intelligence (AI) tools in the creation of this article.

Conflicts of interest

The authors affirm that there is no conflict of interest.

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