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Impact of secondary hyperglycemia in non-diabetic patients with COVID-19 in the Intensive Care Unit

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Abstract

Introduction: Patients with SARS-CoV2 present pancreatic dysfunction, leading to secondary hyperglycemia. During their evolution, the prognosis is severe. OBJECTIVE: To determine the impact of secondary hyperglycemia severity in COVID-19 patients without Diabetes Mellitus.

Material And Methods: Cross-sectional, comparative, analytical study in patients with COVID-19-associated pneumonia with blood glucose >140 mg/dl. Patients were assigned to Group I, non-diabetics with hyperglycemia, and Group II, with Diabetes Mellitus. Patient evolution with glucose and glycated hemoglobin, SOFA and APACHE II severity scales upon admission to the intensive care unit, at 24, 48, and 72 hours. Statistical analysis was performed using Student's t-test for quantitative variables, Mann-Whitney U test for qualitative variables, and chi-square test for proportions.

Results: Fifty-four patients were studied. Group I (n=23), mean age 53.22 ±15.72 years, male (69.6%); Group II (n=31), mean age 59.58 ±11.71, male (54.8%). Mortality in Group I was 30.4%, and in Group II was 41.9% (p>0.05). SOFA score: In Group I, deceased 7.6±4.8 and survivors 6.3±2.76, APACHE II: deceased 18.54±8.67 and survivors 15.26±7.04 (p>0.05). Group II SOFA: deceased 9.44 ±4.33 and survivors 6 ±3.11 (p<0.05), APACHE II: deceased 18.89±7.49 and survivors 13.58±5.51 (p <0.05).

Conclusion: Patients in the ICU with COVID-19 and secondary hyperglycemia did not have an impact on severity compared to patients with Diabetes Mellitus.

Keywords: sars-cov-2 pneumonia; diabetes mellitus; hyperglycemia

Introduction

The acute respiratory syndrome caused by the coronavirus SARS-CoV-2 and its subsequent illness, SARS-CoV-2 2019 (COVID-19), mostly presents as a mild or asymptomatic disease, but when the infection worsens, it can cause pancreatic dysfunction through immunomodulated mechanisms, as a result of the proinflammatory cytokine storm, leading to damage in the respiratory tract that can worsen to respiratory failure, septic shock, and death [1,2,3,4].

SARS-CoV-2 is an enveloped virus with a positive-sense RNA genome, approximately 90 nm3 in size, belonging to the Coronaries family of the Beta coronavirus genus. It interacts with the host cell through the receptor-binding domain (RBD) of the S subunit of the S protein, binding to the angiotensin-converting enzyme 2 (ACE2) present in epithelial cells of the respiratory tract and other extrapulmonary tissues. The virus internalizes into cells, initiating its replicative cycle through the spike subunit of SARS-CoV-2 to the host cell receptor [1,3,5].

SARS-CoV-2 can induce ketosis in non-diabetic individuals and may increase the risk of ketoacidosis in patients with diabetes; up to 17% of hospitalized patients with COVID-19 showed evidence of pancreatic injury (with elevated amylase and lipase) and hyperglycemia due to β-cell injury in the exocrine glands as well as in pancreatic islets.[7] The mechanism of virus-induced damage and whether the infection has a direct consequence on glucose homeostasis or could even trigger diabetes mellitus remain subjects of debate [8,9,10,11].bThere is evidence that individuals with pre-existing comorbidities such as hypertension, cardiovascular disease, obesity, or diabetes are at higher risk and disadvantage of dying from COVID-19. Hyperglycemia was observed in patients without a history of diabetes or glucocorticoids and is significantly associated with increased risk of intubation and higher mortality compared to patient

groups without diabetes, even with preexisting diabetes [12,13,14,15]. The objective of this study was to determine the impact of secondary hyperglycemia severity in COVID-19 patients without Diabetes Mellitus.

Materials and Methods

A cross-sectional, comparative, analytical study was conducted on patients with newly diagnosed hyperglycemia and COVID-19-associated pneumonia at the Hospital de Especialidades No.14 IMSS, with prior authorization from the Research Committee and informed consent. Patients were selected according to the following inclusion criteria: Patients over 18 years of age, diagnosed with COVID-19 pneumonia with a positive polymerase chain reaction (PCR +) test or CT scan with CORADS 4 or 5, or those admitted to the intensive care unit. Patients with COVID- 19-associated pneumonia were randomly assigned to two groups: Group I (n=23) non-diabetic with Hyperglycemia, and Group II (n=31) Diabetes Mellitus, with fasting glucose levels greater than 140 mg/dl (7.77 mmol/L), or glycosylated hemoglobin (HbA1c) levels greater than 6.5%. The evolution of patients was assessed using the SOFA and APACHE II severity scales upon admission to the unit, at 24, 48, and 72 hours, to evaluate the severity in both groups during their stay, including the paO2/Fio2 ratio, pH, HCO3, leukocytes, hemoglobin, platelets, hospital stay days, and comorbidities. Descriptive statistics were used to obtain measures of central tendency and dispersion. For inferential statistics, Student's t-test, Mann-Whitney U test, and the Chi-square test were employed with a 95% confidence interval and a significance level of $p<0.05$. IBM-SPSS 26 software was used for analysis.

Results

A total of 54 patients with a diagnosis of COVID-19 were studied. In Group I, male patients comprised 16 (69.6%) and female patients 7 (30.4%), while in Group II, male patients were 17 (54.8%) and female patients were 14 (45.2%) ($p>0.05$). The mean age in Group I was 53 ± 15.72 years and in Group II was 59.5 ± 11.71 years (NS). Hypertension was present in 10 (43.5%) patients in Group I and 21 (67.7%) in Group II ($p>0.75$). Chronic kidney disease was found in 6 (26.1%) patients in Group I, COPD in 1 (0.31%), Epilepsy in 1 (0.31%), Parkinson's disease in 1 (0.31%), and hypothyroidism in 1 (4.3%). Group II patients presented with stroke in 2 (6.5%), deep vein thrombosis in 2 (6.5%), myocardial infarction, congestive heart failure in 1 (3.2%), and prostatic hypertrophy in 1 (3.2%). The CORADS classification in Group I showed CORADS 5 in 19 cases (82.6%) and CORADS 6 in 4 cases (17.4%). In Group II, CORADS 5 was observed in 27 cases (87.1%) and CORADS 6 in 4 cases (12.9%), with no significant difference ($p>0.404$). (Table 1).

The average glucose level in Group I was 146.8 ± 30.02 mg/dl, whereas in Group II, it was 190.9 ± 51.57 mg/dl ($p<0.001$). Glycated hemoglobin in Group I was 6.19 ± 0.8%, while in Group II, it was 9.6 ± 2.37% ($p<0.0002$). The D-dimer in Group I was 6894.1 ± 7330.5 mg/ml, and in Group II, it was 5293.61 ± 5400.6 mg/ml ($p>0.05$). The nutritional status in Group I had a mean BMI of 31.9 ± 7.2, and in Group II, it was 31.95 ± 6.1 ($p>0.05$). The distribution of discharge types was as follows: mortality in Group I was 7 (30.4%) and in Group II was 13 (41.9%) ($p>0.05$). Clinical improvement was observed in 14 (60.9%) patients in Group I and in 16 (51.6%) in Group II ($p>0.05$). The need for mechanical ventilation was in 17 (31.5%) patients in Group I and 27 (87.1%) in Group II ($p>0.217$). The days per patient on mechanical ventilation in those who needed it were 7.43 ± 5.11 days in Group I and 6.90 ± 5.49 days in Group II ($p>0.05$) (Table 2).

Differences in deceased patients were evaluated; in Group I, all were male (100%), while in Group II, 6 (46%) were male ($p<0.016$). The mean age in Group I was 56.3 ± 10.3 years and in Group II was 62.2 ± 12.9 years (NS). The length of stay in Group I was 8 ± 5.9 days, and in Group II, it was 7 ± 4.6 days (NS). Glucose levels were 154.6 ± 13.8 mg/dl in Group I and 197.7 ± 44.2 mg/dl in Group II ($p<0.003$), while glycated hemoglobin was reported as 6.5 ± 0.06% in Group I and 9 ± 1.2% in Group II ($p<0.0002$). Regarding severity scales, the SOFA score in Group I was 7.6 ± 4.8 points and in Group II was 9.4 ± 4.3 points (NS), while the APACHE II score in Group I was 18.5 ± 8.6 points and in Group II was 18.8 ± 7.5 points (NS) (Table 3).

Table 1: Characteristics of non-diabetic patients with hyperglycemia and patients with Diabetes Mellitus

Variable	Group 1 Hyperglycemia (n=23)	Group 2 Diabetes Mellitus (n=31)	P-value
Age (years)	53.22±15.72	59.58±11.71	0.094*
Sex, n (%)			
Male	16(69.6)	17(54.8)	0.272**
Female	7(30.4)	14(45.2)	0.272**
Comorbidities			
Hypertension	10(43.5)	21(67.7)	0.000*
Chronic Kidney Disease	6(26.1)	0	
COPD	1()	0	
Epilepsy	1(4.3)	0	
Parkinson	1(4.3)	0	
Hypothyroidism	1(4.3)	0	
MI	0	1(3.2)	
Deep Vein Thrombosis	0	2(6.5)	
Stroke	0	2(6.5)	
Prostatic Hypertrophy	0	1(3.2)	
Heart Failure	0	1(3.2)	
CORADS			
5	19(82.6)	27(87.1)	0.646**
6	4(17.4)	4(12.9)	0.646**

Note: p-value calculated using t student for continuous variables and X2 for categorical variables

Table 2: Variables of patients with hyperglycemia and diabetes mellitus with Covid 19, at the UMAE IMSS

	Group 1 Hyperglycemia	Group 2 Diabetes Mellitus	P-value
Glucose mg/dl	146.8±30.02	190.9±	0.001*
Glucose mg/dl	6.19±0.8	9.60±2.37	0.0002*
Glycated Hemoglobin %	6894.1±7330.5	5293.61±5400.6	0.314***
D-dimer µg/ml			
Discharge Type, n (%)	7(30.4)	13(41.9)	0.387**
Death	14(60.9)	16(51.6)	0.498**
Improvement	2(8.7)	2(6.5)	0.756**
Maximum Reach			
Days of Stay	9.65±8.2 (6.1-13.2)	10.52±6.8 (8-13)	0.343***
Mechanical Ventilation	17 (73.9)	27 (87.1)	0.217**
Days of Ventilation	7.43±5.11	6.90±5.49	0.719*
* t student ** X^2 *** U de Mann Whitney			

Table 3: Difference in severity of patients who died from COVID-19.

	Group 1 Hyperglycemia	Group 2 Diabetes Mellitus	p-value
Male, n (%)	7(100)	6(46.2)	0.016*
Age (years)	56.3±10.3	62.2±12.9	
Days of Stay	8±5.9	7.0±4.6	0.757 ***
Glycated Hemoglobin %	6.5±0.06	9±1.2	0.0002 ***
Glucose mg/dl	154.6±13.8	197.7±44.2	0.003 ***
PaO2/FiO2	125.5±27.4	155.7±61.7	0.219 ***
Oxygen mmHg	73.7±17.9	63.5±16.8	0.165 ***
SOFA Points	7.6±4.8	9.4±4.3	0.394 **
APACHE Points	18.5±8.6	18.8±7.5	0.927 **
* X^2 ** t student *** U de Mann Whitey			

Discussion

Patients with COVID-19 can develop mild or even asymptomatic disease, but they can also present with atypical pneumonia causing complications and higher mortality in patients with comorbidities such as diabetes, hypertension, obesity, and other immune system diseases. During the COVID-19 pandemic, atypical pneumonia presented with various symptoms, leading to increased mortality among vulnerable groups of patients with comorbidities.[1] In the affected population, factors such as early-onset diabetes, obesity, chronic kidney disease, hypertension, and advanced age contributed to hospitalization and lethality.[2] The demographic results were very similar to those reported by Sajjad Ali,[15] with a predominance of males, an average age of over 50 years, and hypertension being the predominant comorbidity. Hyperglycemia and glycated hemoglobin were higher in patients with diabetes [16]. The clinical impact of hyperglycemia (>140 mg/dl) in COVID-19 patients without diabetes and with diabetes mellitus, as described by Fadini[10] and Copelli,[11] found that newly diagnosed hyperglycemia upon admission was considered a grave prognosis with mortality rates exceeding 30% compared to the population with diabetes mellitus. In our study, the glucose levels of patients who died in the hyperglycemia group were lower compared to the diabetes mellitus group. Wu et al. [17] found that higher glucose levels were associated with hospital mortality in critically ill patients, while our study showed a lower odds ratio for hyperglycemia (OR=0.606) and a higher odds ratio for diabetes mellitus (OR=1.651) regarding mortality.

The severity scores of the SOFA and APACHE II scales were only significant in the diabetes mellitus group, with higher scores in deceased patients compared to survivors. These findings are consistent with studies by Beigmohammadi [18] and Yang, which found that higher scores on these scales were predictors of mortality in COVID-19 patients. In patients hospitalized with COVID-19 and diabetes, Carlou [20] reported intubation rates of 29% and mortality rates of 10.6%, with discharge possible in 18% of cases, similar to our findings. Vargas-Vázquez [21] described fasting glucose as a better predictor of COVID-19 severity than glycated hemoglobin levels, while our study found higher glycated hemoglobin levels in deceased patients [19,20,21]. The findings in our study do not confirm that newly diagnosed hyperglycemia worsens or increases mortality in COVID-19 patients, as previously described by other studies. Instead, we observed that diabetes mellitus was a more significant factor in increasing severity and mortality due to the chronic damage caused by insulin resistance in tissues or microcirculation [10,11,17,20,22,24]. Limitations of our study include an insufficient sample size due to the decrease in cases as the pandemic progressed and increased immunization in the population. Additionally, many patients were not included in the study because they had previously received steroids, which predisposed them to hyperglycemia as part of initial management prior to hospitalization.

Conclusion

In conclusion, during the COVID-19 pandemic, patients admitted to the intensive care unit with hyperglycemia (>140 mg/dl) and pneumonia did not demonstrate significant repercussions in severity scales or mortality compared to patients with diabetes mellitus.

Statements

Declarations

Conflict of Interest Statement

The authors declare no conflicts of interest regarding the research, authorship, and publication of this article.

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The author declares no conflicts of interest to disclose.

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