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# HYPERGLYCEMIA ON HOSPITAL ADMISSION AS A PREDICTOR OF POOR OUTCOME IN PATIENTS HOSPITALIZED FOR COVID-19

## HIPERGLICEMIA AL INGRESO HOSPITALARIO COMO PREDICTOR DE MALA EVOLUCIÓN EN PACIENTES HOSPITALIZADOS POR COVID-19

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## ABSTRACT

**Introduction:** Hyperglycemia on hospital admission may be a useful tool to predict poor outcomes in COVID-19 patients. **Objective:** To determine if hyperglycemia on hospital admission constitutes a prognostic factor for poor outcomes. **Methods:** An observational, analytical, retrospective cohort study was conducted at the Regional Hospital of Moquegua. Medical records of 640 randomly selected patients hospitalized with confirmed COVID-19 during the first two waves of the pandemic were reviewed. Variables included poor outcomes, respiratory sequelae, admission to the Intensive Care Unit (ICU), and death. Hyperglycemia on admission was defined as blood glucose >140 mg/dL. Bivariate and multivariate analyses were performed using Poisson regression models with robust variances to find the crude and adjusted relative risks (RRa) with their respective 95% confidence intervals (CI95%). **Results:** Of the patients, 36,9% were 60 years or older, 58,9% were male, and 10,2% had diabetes mellitus. Hyperglycemia on admission was present in 34,7% of the patients. Hyperglycemia was significantly associated with poor outcomes (RRa = 5,65; CI95%: 3,72-8,62; p < 0,001), respiratory sequelae (RRa = 1,96; CI95%: 1,74-2,21; p < 0,001), ICU admission (RRa = 3,68; CI95%: 2,03-6,69; p < 0,001), and death (RRa = 1,57; CI95%: 1,22-2,02; p = 0,001). **Conclusion:** Hyperglycemia on admission is a significant prognostic factor for poor outcomes in COVID-19 patients. Careful monitoring of these patients is essential.

**Keywords:** COVID-19; Diabetes Mellitus; Hyperglycemia; Prognosis; Risk. (Source: MeSH NLM)

## RESUMEN

**Introducción:** La hiperglicemia al ingreso hospitalario podría ser una buena herramienta para predecir evolución desfavorable en pacientes con COVID-19. **Objetivo:** Determinar si la hiperglicemia al ingreso hospitalario constituye un factor pronóstico de evolución desfavorable. **Métodos:** Se realizó un estudio observacional, analítico, de cohorte retrospectivo en el Hospital Regional de Moquegua. Se revisaron de manera aleatoria historias clínicas de 640 pacientes hospitalizados con COVID-19 confirmado durante las primeras dos olas de la pandemia. Las variables incluyeron evolución desfavorable, secuelas respiratorias, ingreso a la Unidad de Cuidados Intensivos (UCI), y fallecimiento. La hiperglicemia al ingreso se definió como glicemia >140 mg/dL. Se realizaron análisis bivariados y multivariados utilizando modelos de regresión de Poisson con varianzas robustas para hallar el riesgo relativo crudo y ajustado (RRa) con sus respectivos IC95%. **Resultados:** El 36,9% tuvo 60 o más años, el 58,9% fue del sexo masculino y el 10,2% tuvo diabetes mellitus. El 34,7% de los pacientes presentaron hiperglicemia al ingreso. La hiperglicemia se asoció significativamente con una evolución desfavorable (RRa = 5,65; IC95%: 3,72-8,62; p < 0,001), secuelas respiratorias (RRa = 1,96; IC95%: 1,74-2,21; p < 0,001), ingreso a UCI (RRa = 3,68; IC95%: 2,03-6,69; p < 0,001), y fallecimiento (RRa = 1,57; IC95%: 1,22-2,02; p = 0,001). **Conclusión:** La hiperglicemia al ingreso es un factor pronóstico significativo para evolución desfavorable en pacientes con COVID-19. Es esencial monitorear cuidadosamente a estos pacientes.

**Palabras clave:** COVID-19; Diabetes Mellitus; Hiperglucemia; Pronóstico; Riesgo. (Fuente: DeCS BIREME)

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## INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 coronavirus, has created an unprecedented global health crisis since its emergence in Wuhan, China, in December 2019. This disease is characterized by a wide range of clinical manifestations, from mild symptoms to severe complications such as pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock, which can lead to multiple organ dysfunction and death [1]. In Peru, the first confirmed case of COVID-19 was reported on March 6, 2020. Despite measures implemented to contain the virus, the mortality rate reached 10.06 deaths per 10,000 inhabitants by the end of 2020, with regions like Ica, Callao, Moquegua, and Lima being the most affected [2]. In particular, the province of Mariscal Nieto in Moquegua had a high incidence of mortality, with a fatality rate of 891.9 per 100,000 inhabitants, significantly above the national average[3,4].

The unfavorable progression of COVID-19 has been linked to several risk factors, including cardiovascular disease, obesity, and diabetes mellitus [3]. Hyperglycemia, in both patients with preexisting diabetes and those without a history of the disease, has been identified as an independent predictor of mortality [5,]. SARS-CoV-2 infection can induce hyperglycemia through the exacerbation of the inflammatory response, oxidative stress, and endothelial dysfunction, which in turn compromises the patient's immune response, increasing the risk of severe complications and death.

However, although hyperglycemia has been recognized as a significant risk factor, there is an urgent need for studies that specifically examine its role as a predictor of poor outcomes in hospitalized COVID-19 patients in specific regional contexts. Most previous research has focused on international cohorts or large urban centers, leaving a gap in understanding the impact of hyperglycemia in smaller populations or less-studied areas like Moquegua, Peru. Precisely identifying hyperglycemia as a prognostic marker could improve clinical management strategies and allow for early and personalized intervention. This study aims to determine whether hyperglycemia at hospital admission constitutes a prognostic factor for unfavorable outcomes in hospitalized COVID-19 patients at the Hospital Regional de Moquegua.

## METHODS

### Design and Study Area

An observational, analytical, retrospective cohort study was conducted by reviewing the medical records of patients hospitalized in the "COVID Area" with a confirmed diagnosis through serological and radiological tests for COVID-19 at the Hospital Regional de Moquegua, located in Cercado, Mariscal Nieto, Moquegua, Peru. The study period covered the first wave (epidemiological week 10 to 48, from March 8-13, 2020 to November 29 - December 4, 2020) and the second wave of the pandemic (epidemiological week 52 to 30, from December 27-31, 2020 to July 26-31, 2021).

### Population and sample

The population consisted of 1,400 medical records of patients hospitalized in the COVID Area. Applying exclusion criteria, a total of 1,350 records were obtained, and 640 medical records were selected through simple random probabilistic sampling. The sample size was calculated with an expected relative risk of mortality of 1.23 for hyperglycemia exposure, according to a previous study[7], and a mortality rate of 46% in non-exposed individuals[8]; with a power of 80% and a confidence level of 95%.

Patients who met the following criteria were included: complete sociodemographic data, age over 18 years, blood glucose test at hospital admission, confirmed COVID-19 diagnosis with serological and/or radiological tests, and patient prognosis. Pregnant women and patients with incomplete data were excluded.

### Variables and Instruments

The study variables included unfavorable outcomes as the dependent variable, defined by the presence of respiratory sequelae (dyspnea and/or pulmonary fibrosis without a history of chronic respiratory disease), admission to the Intensive Care Unit (ICU), and/or death. Hyperglycemia at admission, defined as a blood

glucose level greater than 140 mg/dL, was the main independent variable. Covariates included sociodemographic data (age), medical history (body mass index [BMI], hypertension, and diabetes mellitus), and clinical characteristics at admission (respiratory rate, oxygen saturation, and dyspnea).

Age was measured in years, categorized as under 60 years and 60 years or older. BMI was calculated using the Quetelet index, categorized as less than 30 kg/m$^2$ and 30 kg/m$^2$ or more. Hypertension and diabetes mellitus were determined according to the patient's medical history. Respiratory rate was measured in breaths per minute, classified as less than 30 breaths per minute and 30 breaths per minute or more. Oxygen saturation was measured by pulse oximetry, categorized as greater than 92% and 92% or less. Dyspnea was clinically evaluated at the patient's admission.

**Procedures**

Patients hospitalized in the "COVID Area" of the Hospital Regional de Moquegua during the first and second waves of the pandemic were identified. The identification of patients was based on hospital records, ensuring they met the previously established inclusion criteria. Once the study population was identified, the 640 participating medical records were randomly selected using a statistical program. Relevant information was recorded on a data collection sheet at the hospital where the study was conducted.

**Statistical Analysis**

The information was processed in Excel, and statistical analysis was performed using SPSS version 27. Descriptive statistics were calculated for all variables, including frequencies and percentages for categorical variables and median for age. Bivariate analysis was used to evaluate the association between hyperglycemia at admission and unfavorable outcomes, as well as other covariates such as age, BMI, hypertension, diabetes mellitus, respiratory rate, oxygen saturation, and dyspnea. Crude (RRc) and adjusted (RRa) risk ratios and their 95% confidence intervals (Ci95%) were estimated using Poisson regression models with robust variances to determine the strength of the association between independent variables and unfavorable outcomes. Additionally, a p-value of less than 0.05 was considered significant.

**Ethical Aspects**

This study was authorized by the Research and Ethics Committee of the Faculty of Human Medicine at Universidad Ricardo Palma (Approval Certificate: PG-58-021) and the ethics committee of the Teaching and Research Support Office at the Hospital Regional de Moquegua. As it was based on the review and recording of data from medical records, it posed no risks and did not require informed consent. Patients' personal data were handled confidentially.

## RESULTS

Of the 640 participants, most patients (63.1%) were under 60 years of age, while 36.9% were 60 years or older; the median age was 53 years. 58.9% were male. 39.8% of the patients had a BMI greater than 30 kg/m$^2$. Regarding comorbidities, 14.1% had hypertension, and 10.2% had diabetes mellitus. Additionally, 90.5% of the patients were admitted with a respiratory rate of less than 30 breaths per minute, and 53.8% had an oxygen saturation of 92% or less. Finally, dyspnea was recorded in 55.9% of the patients (Table 1).

72.8% of the patients had a positive molecular test, 12.7% had an antigen test, and the rest had rapid tests. Likewise, 77.2% had chest X-rays, and 22.8% had CT scans with disease findings.

**Table 1.** Descriptive distribution of sociodemographic variables, medical history, and clinical characteristics of the patients.

| Variables | Category | Frequency | Percentage (%) |
|---|---|---|---|
| Age (years) | Under 60 | 404 | 63.1 |
| | 60 or older | 236 | 36.9 |
| Sex | Male | 378 | 58.9 |
| | Female | 263 | 41.1 |
| BMI (kg/m$^2$) | Under 30 | 285 | 60.2 |
| | 30 or higher | 255 | 39.8 |
| Hypertension | Yes | 90 | 14.1 |
| Diabetes mellitus | Yes | 65 | 10.2 |
| Respiratory rate | Under 30 | 579 | 90.5 |
| (breaths/min) | Over 30 | 61 | 9.5 |
| Oxygen saturation | Over 92 | 296 | 46.3 |
| (%) | 92 or below | 344 | 53.8 |
| Dyspnea | Yes | 358 | 55.9 |
| | No | 282 | 44.1 |

BMI: Body Mass Index

In Table 2, it can be observed that 34.7% of the patients had a blood glucose level at admission greater than 140 mg/dL, while 65.3% had a blood glucose level less than or equal to 140 mg/dL.

Regarding the prognosis variables, 57.8% of the patients experienced an unfavorable outcome, 25.5% had respiratory sequelae, 8.4% required ICU admission, and 23.9% died.

**Table 2.** Descriptive distribution of blood glucose at admission and prognosis variables in patients.

| Category | Frequency | Percentage (%) |
|---|---|---|
| Blood glucose at admission (mg/dL) | | |
| Greater than 140 | 222 | 34.7% |
| 140 or less | 418 | 65.3% |
| Prognosis variables | | |
| Unfavorable outcome | 370 | 57.8% |
| Respiratory sequelae | 163 | 25.5% |
| ICU admission | 54 | 8.4% |
| Death | 153 | 23.9% |
| Total | 640 | 100% |

ICU: Intensive Care Unit

**Table 3.** Bivariate analysis of blood glucose at admission and other factors associated with unfavorable outcomes, respiratory sequelae, ICU admission, and death in the studied patients.

| Variables | Unfavorable outcome | | | Respiratory sequelae | | | ICU admission | | | Death | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CRR | CI95% | p value | CRR | Ci95% | p value | CRR | CI95% | p value | CRR | CI95% | p value |
| Blood glucose at admission (mg/dL) | | | | | | | | | | | | |
| 140 or less | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Greater than 140 | 6.62 | 4.35-10.20 | <0.001 | 2.26 | 2.00-2.56 | <0.001 | 3.47 | 2.03-5.92 | <0.001 | 2.23 | 1.70-2.93 | <0.001 |
| Age (years) | | | | | | | | | | | | |
| Under 60 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| 60 or older | 2.51 | 1.93-3.25 | <0.001 | 1.71 | 1.51-1.94 | <0.001 | 0.44 | 0.23-0.83 | 0.012 | 4.24 | 3.11-5.79 | <0.001 |
| BMI (kg/m$^2$) | | | | | | | | | | | | |
| Under 30 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| 30 or higher | 1.00 | 0.84-1.22 | 0.925 | 1.01 | 0.88-1.15 | 0.925 | 2.04 | 1.22-3.41 | 0.007 | 0.85 | 0.63-1.13 | 0.263 |
| Hypertension | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Yes | 1.54 | 1.10-2.15 | 0.013 | 1.28 | 1.10-1.49 | <0.001 | 0.49 | 0.18-1.32 | 0.158 | 1.81 | 1.34-2.46 | <0.001 |
| Diabetes mellitus | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Yes | 1.49 | 1.01-2.20 | 0.044 | 1.26 | 1.06-1.49 | 0.009 | 0.71 | 0.26-1.90 | 0.492 | 1.11 | 0.72-1.71 | 0.650 |
| Respiratory rate (breaths/min) | | | | | | | | | | | | |
| Under 30 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| 30 or higher | 4.63 | 2.16-10.00 | <0.001 | 1.66 | 1.48-1.85 | <0.001 | 2.43 | 1.32-4.46 | 0.004 | 2.92 | 2.24-3.81 | <0.001 |
| Oxygen saturation (%) | | | | | | | | | | | | |
| Over 92 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| 92 or les | 2.25 | 1.85-2.74 | <0.001 | 1.84 | 1.58-2.14 | <0.001 | 1.35 | 0.80-2.29 | 0.260 | 4.20 | 2.84-6.22 | <0.001 |
| Dyspnea | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Yes | 1.93 | 1.60-2.33 | <0.001 | 1.66 | 1.43-1.94 | <0.001 | 1.87 | 1.07-3.29 | 0.029 | 2.08 | 1.51-2.86 | <0.001 |

ICU: Intensive Care Unit. CRR: Crude Relative Risk. 95% CI: 95% Confidence Interval. BMI: Body Mass Index.

In Table 3, it can be seen that blood glucose levels at admission greater than 140 mg/dL are significantly associated with unfavorable outcomes (CRR = 6.62, 95% CI 4.35-10.20, p < 0.001), respiratory sequelae (CRR = 2.26, 95% CI 2.00-2.56, p < 0.001), ICU admission (CRR = 3.47, 95% CI 2.03-5.92, p < 0.001), and death (CRR = 2.23, 95% CI 1.70-2.93, p < 0.001). Age 60 years or older also shows a significant association with unfavorable outcomes (CRR = 2.51, 95% CI 1.93-3.25, p < 0.001), respiratory sequelae (CRR = 1.71, 95% CI 1.51-1.94, p < 0.001), and death (CRR = 4.24, 95% CI 3.11-5.79, p < 0.001).

Respiratory rate greater than or equal to 30 breaths per minute is associated with unfavorable outcomes (CRR = 4.63, 95% CI 2.16-10.00, p < 0.001), respiratory sequelae (CRR = 1.66, 95% CI 1.48-1.85, p < 0.001), ICU admission (CRR = 2.43, 95% CI 1.32-4.46, p = 0.004), and death (CRR = 2.92, 95% CI 2.24-3.81, p < 0.001). Additionally, oxygen saturation less than or equal to 92% is related to unfavorable outcomes (CRR = 2.25, 95% CI 1.85-2.74, p < 0.001) and death (CRR = 4.20, 95% CI 2.84-6.22, p < 0.001).

On the other hand, it is observed that, in the adjusted analysis, blood glucose levels at admission greater than 140 mg/dL are significantly associated with unfavorable outcomes (ARR = 5.65, 95% CI 3.72-8.62, p < 0.001), respiratory sequelae (ARR = 1.96, 95% CI 1.74-2.21, p < 0.001), ICU admission (ARR = 3.68, 95% CI 2.03-6.69, p < 0.001), and death (ARR = 1.57, 95% CI 1.22-2.02, p = 0.001). Age 60 years or older also shows a significant association with unfavorable outcomes (ARR = 1.85, 95% CI 1.43-2.38, p < 0.001), respiratory sequelae (ARR = 1.41, 95% CI 1.25-1.60, p < 0.001), and death (ARR = 3.05, 95% CI 2.20-4.24, p < 0.001). Respiratory rate greater than or equal to 30 breaths per minute is associated with unfavorable outcomes (ARR = 2.57, 95% CI 1.27-5.21, p = 0.009) and death (ARR = 1.77, 95% CI 1.37-2.28, p < 0.001). Additionally, oxygen saturation less than or equal to 92% is related to unfavorable outcomes (ARR = 1.32, 95% CI 1.09-1.58, p = 0.004) and death (ARR = 2.36, 95% CI 1.56-3.59, p < 0.001) (Table 4).

## DISCUSSION

Blood glucose levels at admission higher than 140 mg/dL were predictors of unfavorable outcomes, respiratory sequelae, ICU admission, and death due to COVID-19 in hospitalized patients at the Hospital Regional de Moquegua during the first and second epidemiological waves of the pandemic. Gonzales Tabares et al. found that patients with a higher risk of developing complications from COVID-19 had blood glucose levels above 126 mg/dL [9]. In another study, the same author found that normoglycemic patients had a lower proportion of complications (3.2%) and deaths (0.5%) compared to hyperglycemic patients (p-value < 0.005), with lower respiratory tract infection being the most frequent complication [10].

Ruiz-Bravo and Jiménez-Valera in Spain observed that patients presenting to the emergency department with symptoms of respiratory distress had a higher probability of intubation, ICU admission, and fatal outcomes [11]. Stulin et al. reported that patients with hyperglycemia (>140 mg/dL) had higher mortality and ICU admission, considering it a marker of greater severity and poor prognosis [12]. However, in Linarez's study, no significant association was found between hyperglycemia (>140 mg/dL) and ICU admission (p-value = 0.920) and/or the use of mechanical ventilation (p-value = 0.640) [13]. Pinelo demonstrated that the presence of hyperglycemia was associated with greater severity of COVID-19 (p-value = 0.050) [14]; however, in the Cox regression model, glucose levels were not significant, unlike Cervantes et al., who determined that glucose levels ≥140 mg/dL were associated with a high mortality rate in hyperglycemic patients compared to normoglycemic patients (p-value = 0.001) [15]. Benites and Peña Sosa also demonstrated that mortality was higher in hyperglycemic patients [16,17].

Elevated blood glucose levels, especially at admission, were directly correlated with fatal outcomes. Several studies show a higher proportion of severe cases and deaths in patients with hyperglycemia compared to those without this complication [18]. Hyperglycemia can cause alterations in the immune response, endothelial damage, and increased oxidative stress, significantly increasing complications and damage to multiple organs, leading to a worse prognosis in COVID-19 patients. In hyperglycemic patients, hyperglycemia can induce dysfunction in immune cells, reducing neutrophils' ability to perform phagocytosis and increasing the production of pro-inflammatory cytokines, exacerbating the cytokine storm observed in severe COVID-19 cases.

**Tabla 4.** Análisis bivariado de la glicemia al ingreso y otros factores asociados a evolución desfavorable, secuelas respiratorias, ingreso a UCI y fallecimiento de los pacientes estudiados.

| VARIABLES | Evolución desfavorable | | | Secuelas respiratorias | | | Ingreso a UCI | | | Fallecimiento | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | RRa | IC95% | Valor de *p* | RRa | IC95% | Valor de *p* | RRa | IC95% | Valor de *p* | RRa | IC95% | Valor de *p* |
| Glicemia al ingreso (mg/dL) | | | | | | | | | | | | |
| Menor o igual de 140 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Mayor de 140 | 5,65 | 3,72-8,62 | <0,001 | 1,96 | 1,74-2,21 | <0,001 | 3,68 | 2,03-6,69 | <0,001 | 1,57 | 1,22-2,02 | 0,001 |
| Edad (años) | | | | | | | | | | | | |
| Menor de 60 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Mayor o igual de 60 | 1,85 | 1,43-2,38 | <0,001 | 1,41 | 1,25-1,60 | <0,001 | 0,41 | 0,19-0,87 | 0,021 | 3,05 | 2,20-4,24 | <0,001 |
| IMC (kg/m²) | | | | | | | | | | | | |
| Menor de 30 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Mayor o igual de 30 | 1,06 | 0,91-1,22 | 0,461 | 1,07 | 0,95-1,20 | 0,283 | 1,59 | 0,92-2,74 | 0,099 | 1,06 | 0,81-1,38 | 0,694 |
| **Hipertensión arterial** | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Si | 1,03 | 0,74-1,44 | 0,858 | 1,04 | 0,89-1,21 | 0,640 | 0,70 | 0,25-2,01 | 0,512 | 1,17 | 0,86-1,58 | 0,325 |
| **Diabetes mellitus** | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Si | 0,69 | 0,48-0,99 | 0,440 | 0,95 | 0,80-1,12 | 0,539 | 0,55 | 0,18-1,66 | 0,290 | 0,84 | 0,55-1,28 | 0,419 |
| Frecuencia respiratoria (resp/min) | | | | | | | | | | | | |
| Menor de 30 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Mayor o igual de 30 | 2,57 | 1,27-5,21 | 0,009 | 1,19 | 1,05-1,34 | 0,006 | 1,71 | 0,83-3,52 | 0,146 | 1,77 | 1,37-2,28 | <0,001 |
| Saturación de oxígeno (%) | | | | | | | | | | | | |
| Mayor de 92 | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Menor o igual de 92 | 1,32 | 1,09-1,58 | 0,004 | 1,31 | 1,14-1,51 | <0,001 | 0,93 | 0,49-1,75 | 0,817 | 2,36 | 1,56-3,59 | <0,001 |
| **Disnea** | | | | | | | | | | | | |
| No | | *Ref.* | | | *Ref.* | | | *Ref.* | | | *Ref.* | |
| Si | 1,32 | 1,12-1,56 | 0,001 | 1,32 | 1,16-1,51 | <0,001 | 1,61 | 0,88-2,95 | 0,122 | 1,36 | 1,01-1,82 | 0,042 |

UCI: Unidad de cuidados intensivos. RRc: Riesgo relativo crudo. Ic95%: Intervalo de confianza al 95%. IMC: Índice de masa corporal.

Additionally, chronic hyperglycemia causes endothelial dysfunction, contributing to a higher risk of thrombosis, which is critical in the context of COVID-19, where coagulopathy is a common complication. The oxidative stress generated by hyperglycemia also plays a key role, as it can directly damage cells and tissues through the production of reactive oxygen species (ROS), which in excess, can lead to irreversible cellular damage and multiple organ dysfunction.

These combined mechanisms may explain why patients with hyperglycemia at admission have worse clinical outcomes, including a higher need for intensive care and a higher mortality rate [5,6,18]. Advanced age (>60 years) was also associated with a higher risk of respiratory sequelae, ICU admission, and death. Llaque found that most pediatric patients infected with COVID-19 developed mild cases, with only a few presenting moderate and severe cases [19]. In Pinelo's study, age (mean of 54 years) was the most important factor for predicting patient death (OR of 1.041, p-value = 0.036) [14]. Gonzales et al. found that patients over 60 years had a nearly five times higher risk than others for developing complications from COVID-19 [9].

In contrast, Pérez-Sastré et al. observed that young adults infected with COVID-19 in Mexico developed severe cases more frequently than other age groups, possibly due to the high number of comorbidities present in this population [20]. Sánchez-Ríos linked the severity of cases in young Mexican adults primarily to a history of obesity [21]. Vila-Corcoles in Spain observed high mortality and complications in patients over 50 years old, also related to the presence of comorbidities [22,23].

Increased respiratory rate, the presence of dyspnea, and lower oxygen saturation were associated with a lower probability of favorable outcomes, but a higher risk of respiratory sequelae and death. Llaro-Sánchez found that patients from the EsSalud Sabogal Network in Peru, who presented with dyspnea or respiratory distress at admission, tended to develop more severe cases, along with a PaO2/FiO2 ratio < 300 [24]. Abril-Mera et al. observed that patients discharged after acute COVID-19 cases presented post-discharge dyspnea in 70% of cases, associated with fatigue, which aligns with our findings on the relevance of dyspnea and oxygen desaturation in the development of severe COVID-19[25]. Calvillo-Batlles developed a predictive model for ICU admission, identifying oxygen saturation at admission as a crucial criterion, with an AUC-ROC of 0.97 and an AUC-PRC of 0.78 in the context of COVID-19 [26-30]. However, in our study, ICU admission was not included in the model. Similar to our findings, these studies corroborate the importance of oxygen saturation in the progression of COVID-19.

The context of the city of Moquegua, located at 1,410 meters above sea level (masl), adds an additional factor to the morbid situation of its population. Studies conducted at moderate and high altitudes have shown that although the cutoff points for determining the severity of desaturation are different, the behavior of patients is similar to those at sea level, with decreased oxygen saturation at admission being a predictor of fatality[31]. Hypoxic hypoxia associated with altitude can exacerbate the hypoxemia caused by SARS-CoV-2, increasing the risk of respiratory failure[32]. Additionally, at higher altitudes, the partial pressure of oxygen in the air decreases, which can further compromise oxygenation capacity in COVID-19 patients, especially those with pre-existing respiratory or cardiovascular comorbidities [33]. The pathophysiology of altitude adaptation can also influence the inflammatory response and blood coagulation, critical factors in the clinical course of COVID-19.

Therefore, it is essential to consider these geographic and physiological factors when evaluating and treating COVID-19 patients in high-altitude regions like Moquegua. One of the main limitations of this research was its retrospective nature. Information on the previous metabolic state of the patients was not

available, so it could not be determined whether hyperglycemic patients had a debut of diabetes, a decompensation, or a stress-induced hyperglycemic episode. Additionally, the use of serological tests for diagnosis may have reduced diagnostic capability due to false negatives and positives.

## CONCLUSIONS

Blood glucose levels at admission higher than 140 mg/dL are a significant prognostic factor for unfavorable outcomes in hospitalized COVID-19 patients at the Hospital Regional de Moquegua during the first and second epidemiological waves. Specifically, hyperglycemia at admission was also a prognostic factor for respiratory sequelae, ICU admission, and death. These findings underscore the importance of careful monitoring and clinical surveillance for this group of patients.

We believe that although the pandemic has ended, COVID-19 cases requiring hospitalization and resulting in death still occur. Therefore, this study remains relevant for determining patient prognosis upon admission, providing crucial information for clinical management and preventing severe complications in patients with hyperglycemia at admission[34].

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