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Original Article

Clinical Parameters and In-hospital Mortality from COVID-19 in Diabetic Patients: Evidence from a Study in Angola

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Abstract: COVID-19 was first identified in China and, within a few months, declared a pandemic by the World Health Organization (WHO). Among the risk factors associated with unfavorable outcomes, diabetes mellitus stands out, often related to a higher incidence of complications and mortality. This study aimed to assess the demographic and laboratory characteristics of diabetic patients admitted to the ward and ICU with COVID-19 in Luanda, Angola, and analyze their relationship with in-hospital mortality. This is an observational, analytical, and retrospective study involving 234 patients diagnosed with COVID-19 and diabetes mellitus admitted to Clínica Sagrada Esperança between March 2020 and March 2022. The primary outcome was in-hospital mortality. The median age of the patients was 61 years, with a predominance of males (70.1%). The in-hospital mortality rate was 21%. Patients who died were significantly older (65 vs. 59 years; p = 0.016), had a shorter interval between symptom onset and hospital admission (5 vs. 7 days; p = 0.019), and a shorter length of stay (8 vs. 10 days; p = 0.032). These patients also had significantly higher levels of leukocytes, neutrophils, urea, creatinine, lactate dehydrogenase (LDH), C-reactive protein (CRP), neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR), as well as lower lymphocyte counts. In the logistic regression analysis, age, creatinine, NLR, and LDH emerged as independent risk factors for mortality, with creatinine being the main predictor (OR = 12.035). These findings reinforce the prognostic value of clinical and laboratory markers in risk stratification and clinical decision-making in diabetic patients with COVID-19, especially in a population that is still underrepresented in scientific literature.

Keywords: COVID-19; Diabetes Mellitus; Angola; Mortality; Predictors.

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1. Introduction

COVID-19 is a viral respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). [1-3] To date, SARS-CoV-2 is the seventh coronavirus identified as capable of causing disease in humans. It was first reported in December 2019 in the city of Wuhan, Hubei province, China. The rapid spread of the virus within the country and on a global scale led the World Health Organization (WHO) to declare COVID-19 a public health emergency on January 30, 2020, and it was subsequently classified as a pandemic on March 11 of the same year [4,5].

Older age and the presence of comorbidities such as diabetes mellitus, hypertension, obesity, and other underlying conditions are considered risk factors for COVID-19, as well as for the development of serious complications and a higher risk of mortality from SARS-CoV-2 infection [6-8]. In 2020, diabetes mellitus was one of the most frequently observed comorbidities in COVID-19 patients, with prevalence ranging from 5.3% to 58%

[9,10]. In a study evaluating deaths from COVID-19, diabetes mellitus accounted for 28.4% of all comorbidities identified [2]. In Angola, researchers evaluating the clinical characteristics and variables associated with morbidity and mortality from COVID-19 found that diabetic patients with a positive RT-PCR test accounted for 16.9% of cases [11].

A retrospective study carried out in Nigeria found that diabetic patients with COVID-19 had a more severe course of the disease, as well as a higher mortality rate [12]. Patients with COVID-19 and diabetes had a higher risk of clinical worsening, especially those with inadequate glycated hemoglobin (HbA1c) control [13]. This condition has been associated with higher rates of intensive care unit (ICU) admissions, higher risk of complications, prolonged hospitalizations, and increased mortality [14, 15]. Several hematological and biochemical parameters have been identified as indicators of severity and poor prognosis in COVID-19 in various regions of the world, such as Ethiopia, South Africa, Singapore, and China [16-19]; however, few studies have evaluated the prognostic value of these parameters in diabetic patients with COVID-19, and there is a scarcity of them in African countries [12, 20, 21].

The aim of this study was to assess the demographic characteristics, as well as baseline hematological and biochemical parameters, of diabetic patients diagnosed with COVID-19 and admitted to a tertiary hospital in Luanda, Angola, during the first two waves of the pandemic, correlating these data with in-hospital mortality.

2. Methods

2.1 Study design

An observational, analytical, and retrospective study was carried out of patients with COVID-19 and diabetes mellitus admitted to Clínica Sagrada Esperança-Ilha de Luanda from March 2020 to March 2022.

2.2 Population, inclusion criteria, and exclusion criteria

The study population included 234 patients diagnosed with COVID-19 and diabetes mellitus admitted to Clínica Sagrada Esperança, aged over 20, who met the definition of COVID-19 and diabetes mellitus. Patients transferred to other hospital units were excluded from the study because it was not possible to assess the outcome.

2.3 Case definition

COVID-19 disease was defined as a confirmed positive laboratory result for SARS-CoV-2, based on the detection of unique RNA sequences of the virus by nucleic acid amplification tests, such as RT-PCR, or by confirmation by rapid SARS-CoV-2 antigen detection or antibody tests. Diabetes mellitus was defined by the presence of symptoms (polyuria, polydipsia, polyphagia, weight loss) plus occasional blood glucose ≥ 200 mg/dl; HbA1c ≥6.5%; fasting blood glucose ≥126 mg/dl; 2-hour plasma glucose ≥200 mg/dl during an oral glucose tolerance test; or any diagnosis established before admission.

2.4 Variables studied

On admission, demographic and clinical variables were analyzed: age and gender; hematological variables: hemoglobin value, percentage values of lymphocytes and neutrophils and absolute values of leukocytes and platelets, the neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were calculated; biochemical variables: blood glucose, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and C-reactive protein (CRP) values. D-dimer values, prothrombin time, and INR; length of hospital stay; and time from symptom onset to patient admission were also analyzed.

2.5 Data collection source and procedure

The data was obtained from the hospital data management software (2soft) at Clínica Sagrada Esperança—Ilha de Luanda. In this study, data was collected by filling out a form previously prepared for this purpose in the Google Forms survey management application from the clinical files of all patients with COVID-19 and diabetes mellitus admitted during the study period and being temporarily stored in the Google Sheets spreadsheet program.

2.6 Outcome

The primary outcome of this study was in-hospital mortality. Patients were divided into two groups according to the outcome: those who were discharged alive (discharged) and those who died (died)

2.7 Statistical Analysis

The data was analyzed according to the main outcome. The normality of the distribution of variables was assessed using the Shapiro-Wilk test. Qualitative variables were presented as absolute and relative frequencies, while quantitative variables were described as mean ± standard deviation (SD) or, where appropriate, as median and interquartile range (IQR). The value of $p < 0.05$ was considered statistically significant. For comparison between groups, the Mann-Whitney, Student's t, and chi-squared tests were used, as appropriate. Multivariate analysis was carried out by binomial logistic regression, using the conditional backward method, based on the Hosmer-Lemeshow test and the Nagelkerke R^2 statistic, in order to identify variables associated with poor prognosis in patients with COVID-19 and diabetes mellitus. Statistical analyses were carried out using SPSS software, version 27.0 for Windows (IBM-SPSS, Armonk, NY).

3. Results

3.1 Patient demographics

Table 1 summarizes the results of patient demographics, comorbidities, as well as length of hospital stay (LOS) and time since symptom onset (TOS) distributed by outcome (discharge alive/death). In this cohort, 234 diabetic and COVID-19 patients were admitted to the CSE from March 2020 to March 2022. The median age was 61.0 years (IIQ: 58.0-68.0). Those who died had a significantly higher median age (65.0 vs. 59.0 years, p=0.016) than those who were discharged (Table 1). More men than women were admitted during this period: 70.1% vs. 29.9%. There was no significant difference in mortality between the sexes (p=0.079).

Table 1. Demographic and clinical characteristics in diabetic patients with COVID-19 distributed by outcome.

Parameters	Participants	Total	Alives	Deceased	p-value
Age	234	61.00	59.00	65.00	.016
Median (IQR)		(52.00-68.00)	(51.00-67.75)	(58.00-69.00)	
Sex n (%)	234				.079
Male		164(70.1)	134(72.8)	30(60.0)	
Female		70(29.9)	50(27.2)	20(40.0)	
LOS, in days (Median (IIQ))	233	10(7-15)	10(8-15)	8(4-14)	.032
TOS, in days (Median (IIQ))	210	7(4-9)	7(4-10)	5(3-7)	.019

Legend. IQR. Interquartile range. LOS. Length of hospital stay. TOS. Time of onset of symptoms.

Twenty-one percent (50/234) of the patients admitted died. The median length of stay was 10 days (IQR: 7-15), with a significant difference in those who died, who stayed

2 days less (8 vs. 10 days, p = 0.032). The median time from symptom onset (TOS) to hospitalization was 7 days (IQR: 4-9). The median TOS was significantly lower in those who died (5 vs. 7 days, p= 0.019).

3.2 Hematological parameters

The association between baseline hematological and biochemical parameters between the deceased and discharged patients is shown in Table 2. There was a statistically significant difference in the leukocyte count (9.50 vs. 6.70, p = 0.001), neutrophils (8.31 vs. 4.57, p < 0.001), and lymphocytes (0.96 vs. 1.20, p = 0.012), as well as a higher NLR (8.1 vs. 4.0, p = 0.012) and PLR (198 vs. 155, p = 0.043) among those who died. The median values for urea (49 vs 32, p = 0.010), creatinine (1.2 vs 1.0, p = 0.043), LDH (542 vs 381, p = 0.019), and CRP (16.0 vs. 8.2, p < 0.001) were significantly higher in those who died compared to those who were discharged. The other hematological and biochemical parameters showed no significant difference between the groups (p>0.05).

Table 2. Laboratory parameters in diabetic patients with COVID-19 distributed by outcome.

Parameters	Total		Alive	Deceased	P-Value
	Participants	Median (IQR)	Median (IQR)	Median (IQR)	
Leukocytes (10^9/L)	213	7,30 (5,50–10,40)	6,70 (5,30–9,40)	9,50 (7,05–12,55)	0,001
Neutrophils (10^9/L)	203	4,93 (3,64–8,08)	4,57 (3,43–7,14)	8,31 (5,94–10,91)	<0,001
Lymphocytes (10^9/L)	195	1,17 (0,80–1,61)	1,20 (0,83–1,70)	0,96 (0,66–1,37)	0,012
Platelets (10^9/L)	210	201,5 (146,0–294,0)	203,5 (145,0–297,0)	189,5 (151,0–268,7)	0,524
PLR	190	162 (112–278)	155 (106–255)	198 (135–324)	0,043
NLR	188	4,4 (2,6–7,9)	4,0 (2,5–6,2)	8,1 (5,0–12,0)	<0,001
Hemoglobin (♂), g/dL	156	13,6 (12,0–14,7)	13,7 (12,4–14,8)	12,9 (11,7–14,0)	0,071
Hemoglobin (♀), g/dL	65	11,9 (10,5–13,0)	11,8 (10,5–13,0)	11,9 (9,60–13,0)	—
Blood glucose (mg/dL)	234	189 (125–285)	172 (121–261)	265 (132–336)	0,061
AST (U/L)	154	37,3 (25–59)	37,9 (25–58)	34,0 (27–77)	0,649
ALT (U/L)	163	31,7 (20–55)	32,6 (20–55)	28,5 (22–68)	0,64
INR	79	1,02 (0,98–1,13)	1,02 (0,99–1,13)	1,04 (0,94–1,15)	0,874
Urea (mg/dL)	184	33 (23–58)	32 (22–53)	49 (28–85)	0,01
Creatinine (mg/dL)	190	1,1 (0,8–1,6)	1,0 (0,8–1,4)	1,2 (0,9–2,5)	0,043
D-dimer (ng/mL)	80	1430 (702–3205)	1390 (655–2937)	1557 (1023–7153)	0,101
CRP (mg/L)	201	9,0 (3,5–20)	8,2 (2,5–16)	16,0 (7–26)	<0,001
LDH (U/L)	109	408 (288–556)	381 (264–536)	542 (365–690)	0,019

Legend. ALT. Alanine aminotransferase. AST. Aspartate aminotransferase. Hb. Hemoglobin. LDH. Lactate dehydrogenase. IQR. Interquartile range. INR. International Normalized Ratio. C-RP. C-reactive protein. NLR. Neutrophil/lymphocyte ratio. PLR. Platelet/lymphocyte ratio.

3.3 Association between laboratory parameters and mortality

As shown in Table 3, the parameters with p < 0.05 in Table 1 and Table 2 were included in the logistic regression model, i.e., age, TIH, TIS, leukocyte count, neutrophils, lymphocytes, NLR, PLR, CRP, LDH, serum urea, and creatinine values. A reverse conditional method was used for binary logistic regression analysis. The logistic regression model was statistically significant, $\chi^2(4) = 28.577$, p = 0.001. The model explained 51.1% (Nagelkerke R2) of the variance in mortality and correctly classified 84.7% of cases. The results showed that serum creatinine, NLR, age, and LDH values were independent risk factors for mortality, and their odds ratio (OR) values were 12.035, 1.523, 1.143, and 1.002, respectively.

Table 3. Binary logistic regression analysis of factors associated with outcome in diabetic patients with COVID-19.

	B	Wald	p-Value*	OR	95% C.I. for OR	
					Lower	Upper
Creatinine	2.488	5.122	**.024**	12.035	1.395	103.793
N/LR	.421	5.021	**.025**	1.523	1.054	2.200
Age	.134	5.729	**.017**	1.143	1.025	1.276
LDH	.002	4.178	**.041**	1.002	1.000	1.004
Constant	-14.119	7.589	**.006**	.000		

Dependent variable: Covid 19. B: Unstandardized Regression Coefficient. *p-value referring to the Multiple Linear Regression analysis by the Backward: Conditional method (4º step). Significant values when $p < 0.05$.

4. Discussion

In this study, our aim was to evaluate predictors of in-hospital mortality in diabetic patients in Angola. Of the total of 234 diabetic patients with COVID-19, 21% died, and a significantly higher median age (65.0 vs. 59.0 years, p=0.016) was observed in patients who were discharged (Table 1). Similar findings were observed in a recent study carried out in the UK, in which the mean age was significantly higher in diabetic and COVID-19 patients who died [22]. In this cohort, there was no statistically significant difference between the sexes, although there was a greater predominance of males [22]; however, the opposite data was found in other studies [23], in which there was a greater propensity for males to die in patients with severe COVID-19 and diabetes ($p < 0.05$), which could be explained by the fact that male gender and advanced age have been described as risk factors for COVID-19 infection, as well as severe forms of the disease, increasing the risk of mortality and ICU admission [24].

According to our study, the time from symptom onset (TIS) to hospitalization (5 vs. 7 days, p = 0.019) was significantly shorter among patients who died. These findings suggest that disease severity may be an important determinant of healthcare-seeking behavior, as more pronounced clinical manifestations are likely to heighten the perception of risk and, consequently, prompt earlier hospital presentation. The median length of hospital stays (8 vs. 10 days, p = 0.032) was also significantly shorter in patients who died, underscoring the rapid progression of the disease in this subgroup. By contrast, Alkundi et al. [22], in their evaluation of clinical characteristics and outcomes of diabetic patients hospitalized with COVID-19, reported no statistically significant difference in the mean length of hospital stay between survivors and non-survivors (15 vs. 13.7 days, p = 0.530) [22].

The most described leukocyte changes in COVID-19 patients are leukocytosis, with neutrophilia and lymphopenia, and several theories have been described to explain the occurrence of these findings. One of them has been attributed to systemic inflammation, which leads to neutrophilia, due to the major role played by neutrophils acting as the body's first line of defense while it prepares a more specific defense [25]. On the other hand, the presence of neutrophilia in diabetic patients with COVID-19 may indicate their susceptibility to bacterial infections, since viral infection can create a favorable environment for this to happen. In the acute phase of COVID-19, lymphocytes are recruited from the blood to the tissues in response to the infection, thus decreasing their count in the peripheral blood. In addition, some studies have revealed the presence of ACE2 receptors on lymphocytes. Therefore, the virus can infect these cells, and after using them to multiply, it induces apoptosis, with a consequent decrease in the count of this cell group [25].

Several studies evaluating the clinical characteristics of diabetic patients with COVID-19 have shown that in this group of patients, such changes occur more intensely [13, 26, 27]. In the current study, there was a statistically significant difference in leukocyte count (9.50 vs. 6.70, $p = 0.001$), neutrophils (8.31 vs. 4.57, $p < 0.001$), and lymphocytes (0.96 vs. 1.20, $p = 0.012$), as well as a higher NLR (8.1 vs. 4.0, $p = 0.012$) and PLR (198 vs. 155, $p = 0.043$) between patients with COVID-19 and diabetes mellitus who died. Similarly, in a South African study evaluating hematological predictors of favorable outcome among ICU patients with COVID-19, there was a statistically significant difference in neutrophil count, as well as a higher NLR among non-surviving patients, 50.2% of whom were diabetic [17]. These findings suggest the influence of these parameters on patient outcomes and could be seen as markers of poor prognosis.

Likewise, the median value of urea (49 vs 32, $p = 0.010$), creatinine (1.2 vs 1.0, $p = 0.043$), LDH (542 vs 381, $p = 0.019$), and CRP (16.0 vs 8.2, $p < p<0.001$) was significantly higher in those who died compared to those who were discharged, results which coincidentally were found in the study by Rastad et al. [20], in which there was a lower lymphocyte count, a higher leukocyte and neutrophil count, as well as elevated serum creatinine, CRP, and LDH concentrations in the group of non-surviving COVID-19 diabetic patients [20]. During the acute inflammatory process, there is a high hepatic production of C-reactive protein due to the stimulation of IL-6 in hepatocytes [28]. The rise in serum creatinine in these patients could be explained by the fact that COVID-19 patients can develop sepsis, which can lead to acute kidney injury, as well as dysfunction of other organs. On the other hand, the presence of acute kidney injury in these patients could be justified by the wide distribution of ACE2 receptors in various organs, including the kidney, leading to the involvement of multiple systems and not just the respiratory system. Conversely, Sebastião et al. [29] showed a significant decrease in serum creatinine values between surviving and non-surviving COVID-19 patients (1.06 vs. 0.50, $p = 0.025$), in which 20% of diabetic patients were identified in the non-surviving group [29].

In the current study, binary logistic regression analysis showed that creatinine, NLR, age, and LDH were relevant factors for the worst clinical outcomes. Like previous studies, advanced age has been identified as a predictor of mortality in diabetic patients with COVID-19 [20,30]. According to Liu et al. [31], in their study evaluating the role of the neutrophil-lymphocyte ratio in the prognosis of type 2 diabetic patients with COVID-19, the multivariate logistic regression model found that type 2 diabetic patients with COVID-19 who had higher NLR values had greater severity, longer hospital stays, and more hospital expenses [31]. These findings were coincidentally evidenced in the current study (NLR, $P < 0.025$; OR: 1.523), allowing us to suggest that NLR can be seen as a prognostic marker in diabetic patients with COVID-19.

LDH is an enzyme that catalyzes the reversible conversion of pyruvate into lactate for energy production in cells under anaerobic conditions. This enzyme is present in various cells in the body: liver, striated muscles, heart, kidneys, lungs, brain, and red blood cells [32]. When cell damage occurs, LDH is released from inside the cells, leading to an increase in its blood concentration, which occurs in various clinical conditions such as infections, sepsis, neoplasms, hemolytic diseases, liver diseases, and others [19]. Because of this, LDH has been identified as an inflammatory marker in many clinical conditions. In a meta-analysis carried out by Fialek et al., it was concluded that high LDH levels were associated with poor outcomes in COVID-19 patients [33]. Likewise, in the present study, this parameter was similarly shown to be associated with a negative outcome, with an OR of 1.002 (CI: 1.00-1.004).

Overall, the magnitude of risk factors identified in our cohort was comparable to that reported in other regions. Age remained an independent predictor of mortality (OR 1.14 per year), corroborating findings from studies conducted in Iran and China, which demonstrated approximately a twofold higher risk in individuals aged ≥65 or ≥70 years [20,30]. The neutrophil-to-lymphocyte ratio (NLR) was also significantly associated with mortality (OR 1.52), consistent with Chinese studies reporting a 4- to 6-fold increased risk in diabetic patients with COVID-19 [31]. Creatinine exhibited a more pronounced effect in our cohort (OR 12.0) compared with values around 3 reported in other series, possibly reflecting contextual differences and sample size limitations [20]. Lactate dehydrogenase (LDH) showed only a modest incremental effect (OR 1.002), yet this finding aligns with international meta-analyses that documented higher LDH levels in non-survivors [33].

This study has some limitations mainly related to its retrospective, single-center design. Because the analysis relied on secondary data from clinical records, the completeness and accuracy of some information could not be guaranteed, and important variables such as diabetes type, glycated hemoglobin (HbA1c), body mass index, hypertension, chronic kidney disease, therapeutic interventions (corticosteroids, antivirals, anticoagulation, dialysis), and COVID-19 vaccination status were not systematically available. We therefore performed complete case analyses, which reduced the sample size for some parameters. Laboratory tests followed the hospital's routine protocols without additional standardization for this study, which may have introduced variability over time. Despite these limitations, the retrospective approach made it possible to capture a considerable number of cases during critical phases of the pandemic, providing relevant insights into the local context. Future multicenter, prospective studies are recommended to validate and extend these findings.

4. Conclusion

The results of this study reinforce the prognostic value of laboratory parameters such as age, creatinine, neutrophil-lymphocyte ratio (NLR), and lactate dehydrogenase (LDH) in predicting in-hospital mortality in diabetic patients with COVID-19 in an African context that is still poorly represented in the literature. These findings could contribute to early risk stratification and support more assertive clinical decisions. It is recommended that future studies explore early laboratory monitoring strategies, personalized preventive measures, and targeted interventions to optimize the care of these patients, especially in resource-limited settings.

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Research Ethics Committee Approval: This study was carried out after approval of the research project by the Department of Teaching and Research in Medicine of the Faculty of Medicine of the Agostinho Neto University, ensuring compliance with ethical assumptions and the principles of scientific validity. The study was also carried out with the prior authorization of the Management Board of Clínica Sagrada Esperança — Ilha de Luanda. The ethical precepts observed are in line with the principles of the Declaration of Helsinki, guaranteeing the legitimacy of the data, the privacy of the participants, and the confidentiality of the information whenever necessary. The results of this research are in public domain and have been considered at all stages of the work.

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