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Hyperglycemia and elevated C-reactive protein are independent predictors of hospital mortality in hospitalized COVID-19 patients in South-Kivu, eastern Democratic Republic of the Congo: A cross-sectional study

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Abstract

Background and Aim: The coronavirus disease 2019 (COVID-19) pandemic was a priority public health problem because of its high mortality rate. This study mainly aimed to determine factors associated with a poor outcome in COVID-19 hospitalized patients in South-Kivu, an eastern province of the Democratic Republic of the Congo (DRC).

Methods: This observational study retrospectively evaluated medical records of patients consecutively admitted for probable or confirmed COVID-19 between May 01 and July 31, 2020 at the Hôpital Provincial Général de Référence de Bukavu (HPGRB), a tertiary hospital located in South-Kivu. A binary logistic regression model was performed to determine the predictors of mortality.

Results: A total of 157 hospitalized COVID-19 patients aged 57.7 (13.2) years were included in this study. Male gender (69.4%), older age (52.9%), medical history of diabetes (38.2%), and arterial hypertension (35.1%) were the most frequent risk factors. Most patients presented with fever (73.3%), cough (72.6%), and dyspnea (66.2%). Overall, 45.1% of patients died. Intrahospital mortality was significantly associated with advanced age [odds ratio, OR (95% confidence interval, CI) = 2.34 (1.06–5.38)], hypoxemia [OR (95% CI) = 4.67 (2.02–10.77)], hyperglycemia [OR (95% CI) = 2.14 (1.06–4.31)], kidney failure [OR (95% CI) = 2.82 (1.4–5.68)], hyperleukocytosis [OR (95% CI) = 3.33 (1.67–6.66)], and higher C-reactive protein (CRP) levels [OR (95% CI) = 3.93 (1.93–8.01)]. After adjustment for various covariates, only

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higher CRP levels [OR (95% CI) = 3.23 (1.23–8.5)] and hyperglycemia [OR (95% CI) = 2.5 (1.02–6.11)] at admission were independently associated with mortality.

Conclusion: Hyperglycemia and marked inflammatory syndrome were the major predictors of poor outcomes in patients hospitalized for COVID-19 in South-Kivu. These two factors should be quantified at hospital admission to establish the patient's prognosis.

KEYWORDS

COVID-19, hospital mortality, hyperglycemia, inflammation, prognosis, South-Kivu

1 | INTRODUCTION

In the past 3 years, the world has been facing the coronavirus disease 2019 (COVID-19) pandemic. The new coronavirus, severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the causal agent of this pandemic, was identified in China in January 2020, after a cluster of atypic pneumonia observed in Wuhan since December 2019.[1] It has rapidly spread in the world and reached Africa since February 2020.[2]

This pandemic has made its particular history in Africa. At its beginning, the previsions made by the World Health Organization (WHO) were alarmist for this part of the world.[3] In fact, alleging the weakness of the health systems in Africa, the persistence of other epidemic and endemic diseases such as Ebola, human immunodeficiency virus infection, malaria, and the double burden of infectious and noninfectious, several scientists were fearing the worst for Africa.[4–7]

Even though the effects of the pandemic have actually been less terrible than expected, the early management of the pandemic was challenging for several African countries. Of note, a resistance of the population against quarantine and other preventive measures was observed.[8] In addition, during the year 2020, most African countries were confronted with COVID-19 diagnostic challenges, explaining the difficulties in biologically confirming the disease.[9,10] The WHO published criteria for the suspect cases of COVID-19 according to clinical and epidemiological characteristics.[11] These criteria had the advantage of allowing rapid screening of cases and, in the context of diagnostic challenges, they helped to promptly offer appropriate care to COVID-19 patients.

Several risk factors have been identified that are associated with the severity and mortality of COVID-19 patients. These include older age, modifiable CVRFs such as smoking and obesity, and chronic comorbidities such as diabetes mellitus, arterial hypertension, kidney injury, cancer, and chronic obstructive pulmonary disease. Additionally, some biological factors like increased D-dimer levels, elevated C-reactive protein (CRP), and decreased levels of serum albumin have been found to contribute to the severity of COVID-19.[12,13] Delayed diagnosis and management of COVID-19 was recognized to be associated with a high fatality.[14] Hence, in resource-limited settings, it was crucial to have simple and affordable tools to promptly screen for suspected cases of COVID-19 based on clinical criteria,[11,15,16] and more importantly, to identify patients at high risk of mortality and prognostic factors that may be helpful in decision-making related to the care of COVID-19 patients.

This study aimed to assess the in-hospital mortality and its associated factors in patients consecutively admitted for suspected or confirmed COVID-19 at the Hôpital Provincial Général de Référence de Bukavu (HPGRB), a tertiary university hospital located in Bukavu, the capital city of the South-Kivu province, in the eastern DRC, during the first wave of the pandemic.

2 | METHODS

2.1 | Study design, setting, and population

This cross-sectional study was conducted in the Emergency ward and the Center for Care and Isolation of COVID-19 patients of the HPGRB. It included all patients admitted for suspected or confirmed COVID-19, between May 01 and July 31, 2020. COVID-19 was defined according to WHO criteria[11] as:

1. A person who meets the clinical criteria (acute onset of fever and cough; or acute onset of any three or more of the following signs or symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status) and epidemiological criteria (residing or working in an area with a high risk of transmission of virus anytime within the 14 days before symptom onset; or residing on travel to an area with community transmission anytime within the 14 days before symptom onset; or working in any health care setting anytime within the 14 days before symptom onset)
2. A patient with severe acute respiratory illness (acute respiratory infection with a history of fever or measured fever of ≥38°C; and cough; with onset within the last 10 days; and requires hospitalization)

According to these definition criteria, 157 patients who fulfilled the inclusion criteria during the study period were recruited for this study.

2.2 | Data collection and study parameters

Data were retrospectively collected from patients' records, using an established questionnaire. Following data were collected: sociodemographic characteristics (age and sex), modifiable cardiovascular risk factors (CVRF) (self-reported history of arterial hypertension, diabetes mellitus, and smoking), clinical parameters (blood pressure, heart rhythm, temperature, and oxygen saturation (SaO_2) on the pulse), biological parameters (capillary glycemia, glycated hemoglobin, white blood cell count, hemoglobin, platelets, creatinine, potassium, sodium, calcium, chloride, magnesium, CRP, procalcitonin), and vital outcome at discharge from the hospital (defined as a dichotomous variable: "improvement" (for patients who showed an improvement and were discharged alive from the hospital) or "death" (for patients who died during their hospital stay), in accordance with the information retrieved from the medical records.

2.3 | Statistical analyses

Categorical variables were presented as frequencies and percentages. We assessed the distribution of quantitative variables using the Shapiro–Wilk test. As most continuous variables were not normally distributed, they were summarized using the median and interquartile range (IQR). Data analysis and interpretation of the study results followed the prescribed protocols described by Assel et al.[17] Comparisons between patients who died and those who survived were made using the two-tailed Pearson's χ^2 test (or Fisher's exact test when at least one expected cell size was <5) for categorical data, and quantitative data were compared using the two-tailed Mann–Whitney test. Binary and multivariable logistic regression models were built to identify the predictors of COVID-19-related mortality. All statistical analyses were performed using Epi info software version 7.2.4.0 (CDC) and GraphPad Prism version 9.0.0 for Windows (GraphPad Software), at a significance level of 5%.

TABLE 1 Prevalence of different comorbidities/medical conditions.

Medical conditions	Frequency (%)
Based on medical history	
History of diabetes mellitus	60 (38.2)
History of arterial hypertension	52 (33.1)
Older age (age > 70 years)	29 (18.5)
History of cardiopathy	17 (10.8)
History of chronic kidney disease	9 (5.7)
History of tuberculosis	6 (3.8)
Human immunodeficiency virus infection	5 (3.2)
History of smoking	3 (1.9)
Based on clinical and biological findings	
Hypoxemia (oxygen saturation on pulse oximeter < 90%)	102 (69.9)
Impaired renal function (GFR < 60 mL/min/1.73 m^2)	87 (58.8)
Hyperglycemia (blood sugar > 200 mg/dL)	63 (46.7)
High blood pressure (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg)	57 (39.0)
Anemia (hemoglobin < 12 g/dL for women or <13 g/dL for men)	35 (22.9)

Abbreviations: DBP, diastolic blood pressure; GFR, glomerular filtration rate; SBP, systolic blood pressure.

TABLE 2 Clinical and biological parameters of the studied population.

Parameters	Median	Interquartile range
Clinical examination parameters		
Temperature (°C), *n* = 128	37.0	36.4–38.1
Systolic blood pressure (mmHg), *n* = 146	134.0	117.0–149.0
Diastolic blood pressure (mmHg), *n* = 145	80.0	67.0–89.0
Oxygen saturation on pulse oximeter (%), *n* = 146	86.5	74.0–98.0
Heart rate (bpm), *n* = 143	105.0	92.0–120.0
Breath rate (breaths/min), *n* = 113	28.0	24.0–32.0
Biological parameters		
Glycemia (mg/dL), *n* = 135	185.0	139.0–331.0
Glycosylated hemoglobin (%), *n* = 76	6.98	5.23–9.04
C-reactive protein (mg/L), *n* = 143	55.9	35.6–176.2
White blood cell count (×10^3 cells/μL), *n* = 153	7.90	5.70–11.90
Lymphocytes (×10^3 cells/μL), *n* = 152	1.30	0.97–1.75
Neutrophils (×10^3 cells/μL), *n* = 152	5.62	3.62–9.30
Platelets (×10^3 cells/μL), *n* = 152	225.5	182.5–279.5
Hemoglobin (g/dL), *n* = 153	14.1	12.9–15.3
Creatinine (mg/dL), *n* = 148	1.54	1.24–2.22
Glomerular filtration rate (mL/min/1.73 m^2), *n* = 148	55.9	34.9–71.4
Serum sodium (mmol/L), *n* = 133	135.0	130.0–137.0
Serum chloride (mmol/L), *n* = 130	99.0	97.0–102.0
Serum potassium (mmol/L), *n* = 131	4.10	3.80–4.40
Serum ionized calcium (mmol/L), *n* = 133	1.22	1.17–1.27
Serum magnesium (mg/dL), *n* = 79	1.90	1.60–2.20

Abbreviation: bpm, beats per minute.

2.4 | Ethical considerations

This study was approved by the institutional Health Ethics Committee (Comité Institutionnel d'Ethique de la Santé [CIES]) of the Université Catholique de Bukavu. All procedures performed were in accordance with the ethical standards of the institutional ethical committee and with the 1964 Declaration of Helsinki and its later amendments. Furthermore, patients admitted to the university hospital consent that their clinical and imaging data can be used for publication or education purpose.

3 | RESULTS

A total of 157 patients (median age: 60.0 years, IQR: 50.0–67 years; 69.4% male) were included in this study. Diabetes mellitus was the most frequent comorbidity, reported by 38.2% of patients (60/157), followed by history of arterial hypertension (33.1% of patients: 52/157), older age (>70 years: 18.5% of patients: 29/157), and history of cardiopathies (10.8% of patients: 17/157). Other comorbidities were rare: only 5.7% (9/157), 3.8% (6/157), 3.2% (5/157), and 1.9% (3/157) of patients reported history of chronic kidney disease, tuberculosis, HIV infection, and smoking, respectively (Table 1).

The studied patients had a median (IQR) body temperature of 37.0 (36.4–38.1)°C, and a systolic blood pressure (SBP) and diastolic blood pressure (DBP) of 134.0 (117.0–149.0) mmHg and 80.0 (67.0–89.0) mmHg, respectively. The median heart rate (median: 105.0; IQR: 92.0–120.0 beats/min [bpm]) and respiratory rate (28.0; IQR: 24.0–32.0 breaths/min) were high, while the median SaO_2 was low: 86.5% (IQR: 75.0%–98.0%), with 102 patients (69.9%) having a SaO_2 below 90% (Table 2).

Biological parameters of the studied population are summarized in Table 2. Briefly, the median (IQR) capillary glycemia at admission was high: 185.0 (139.0–331.0) mg/dL, with 63/135 patients (46.7%) having values above 200 mg/dL. Only 76 patients (48.4%) had available hemoglobin A1C (HbA1c) values. The median (IQR) HbA1c was 6.98 (5.23–9.04)%, with approximately half of the patients having an HbA1c above 7%. The median (IQR) CRP level was elevated: 55.9 (35.6–176.2) mg/L, as well as the serum creatinine: 1.54 (1.24–2.22) mg/dL, corresponding to a median glomerular filtration rate (GFR) of 55.9 (34.9–71.4) mL/min/1.73 m^2. Over half of the patients (87/148 patients, 58.8%) had impaired renal

TABLE 3 Characteristics of patients who died compared with those who survived (improved).

Characteristic	Death (*n* = 69)	Improvement (*n* = 84)	*p* Value
Demographic parameters			
Age (years)[a]	61.0 (53.0–70.0)	58.0 (46.0–65.0)	0.036
Age ≥70 years[b]			0.041
Yes	18 (62.1)	11 (37.9)	
No	51 (41.1)	73 (58.9)	
Sex[b]			
Female	17 (36.2)	30 (63.8)	0.139
Male	52 (49.1)	54 (50.9)	
Clinical and biological parameters[a]			
Systolic blood pressure (mmHg)	135.0 (114.0–154.0)	133.0 (117.0–144.0)	0.419
Diastolic blood pressure (mmHg)	81.0 (67.0–88.0)	80.0 (66.0–90.0)	0.746
Heart rate (bpm)	113.0 (97.0–122.0)	100.0 (90.0–114.0)	0.021
Breath rate (breaths/min)	28.0 (24.0–36.0)	26.0 (24.0–30.0)	0.032
Pulse oxygen saturation (%)	76.0 (62.0–87.0)	89.0 (85.0–92.0)	<0.001
Glycemia on admission (mg/dL)	235.0 (159.0–361.0)	175.5 (126.0–250.0)	0.002
White blood cell count (×10^3 cells/μL)	10.20 (6.80–13.40)	6.50 (4.70–10.10)	<0.001
C-reactive protein (mg/L)	148.6 (71.9–205.8)	62.6 (25.1–133.3)	<0.001
Glomerular filtration rate (mL/min/1.73 m^2)	49.3 (32.5–64.1)	61.2 (43.3–72.3)	0.011
Medical conditions/comorbidities[b]			
History of arterial hypertension			0.301
Yes	20 (39.2)	31 (60.8)	
No	49 (48.0)	53 (52.0)	

TABLE 3 (Continued)

Characteristic	Death (*n* = 69)	Improvement (*n* = 84)	*p* Value
Elevated blood pressure[c]			0.456
Yes	27 (48.2)	29 (51.8)	
No	36 (41.9)	50 (58.1)	
History of cardiopathy			0.677
Yes	8 (50.0)	8 (50.0)	
No	61 (44.5)	76 (55.5)	
History of diabetes mellitus			0.470
Yes	24 (41.4)	34 (58.6)	
No	45 (47.4)	50 (52.6)	
Hyperglycemia (>200 mg/dL)			0.032
Yes	35 (57.4)	27 (38.6)	
No	35 (56.5)	27 (43.6)	
Hypoxemia (SaO_2 < 90%)			<0.001
Yes	56 (56.0)	44 (44.0)	
No	9 (21.4)	33 (78.6)	
Elevated C-reactive protein (≥100 mg/L)			<0.001
Yes	41 (59.4)	28 (40.6)	
No	19 (27.1)	51 (72.9)	
Hyperleukocytosis (≥10,000 WBC/μL)			<0.001
Yes	35 (62.5)	21 (37.5)	
No	31 (33.3)	62 (66.7)	
Impaired renal function[d]			0.003
Yes	46 (54.8)	38 (45.2.2)	
No	18 (30.0)	42 (70.0)	

Abbreviations: bpm, beats per minute; WBC, white blood cell.

[a]Data are median (interquartile range), and comparisons (*p* values) are based on Mann–Whitney test.

[b]Data are *n* (%), and comparisons (*p* values) are based on χ^2 test.

[c]Elevated blood pressure was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg.

[d]Impaired renal function was defined as a glomerular filtration rate <60 mL/min/1.73 m^2.

function (defined by a GFR below 60 mL/min/1.73 m^2). The white blood cell count was within normal ranges: 7900 (5700–11,900) cells/μL, of which 5620 (3620–9300) neutrophils/μL and 1300 (970–750) ymphocytes/μL).

Overall, 69/153 patients (45.1%) died during their hospitalization. Compared to those who survived, the patients who died were significantly older (61.0 (53.0–70.0) vs. 58.0 (46.0–65.0) years old, $p = 0.036$), had significantly higher heart rate (113.0 (97.0–122.0) vs. 100.0 (90.0–114.0) bpm, $p = 0.021$), respiratory rate (28.0 (24.0–36.0) vs. 26.0 (24.0–30.0) cycles/min, $p = 0.032$), capillary glycemia at admission (235.0 (159.0–361.0) vs. 175.5 (126.0–250.0) mg/dL, $p = 0.002$), CRP (148.6 (71.9–205.8) vs. 62.6 (25.1–133.3) mg/L, $p < 0.001$), and white blood cell count (10,200 (6800–13,400) vs. 6500 (4700–10,100) cells/μL, $p < 0.001$), and lower SaO_2 (76.0 (62.0–87.0) vs. 89.0% (85.0%–92.0%), $p < 0.001$), and GFR (49.3 (32.5–64.1) vs. 61.2 (43.3–72.3) mL/min/1.73 m^2, $p = 0.011$) (see Table 3).

In binary logistic regression, factors significantly associated with mortality included advanced age [odds ratio, OR (95% confidence interval, CI) = 2.34 (1.06–5.38)], hypoxemia [OR (95% CI) = 4.67 (2.02–10.77)], hyperglycemia [OR (95% CI) = 2.14 (1.06–4.31)], impaired renal function [OR (95% CI) = 2.82 (1.4–5.68)], hyperleukocytosis [OR (95% CI) = 3.33 (1.67–6.66)], and higher CRP levels [OR (95% CI) = 3.93 (1.93–8.01)]. In multiple logistic regression model, only elevated CRP [adjusted OR (95% CI) = 3.23 (1.23–8.5)] and hyperglycemia at admission [adjusted OR (95% CI) = 2.5 (1.02–6.11)] remained independently associated with in-hospital mortality after controlling for other covariates (Figure 1).

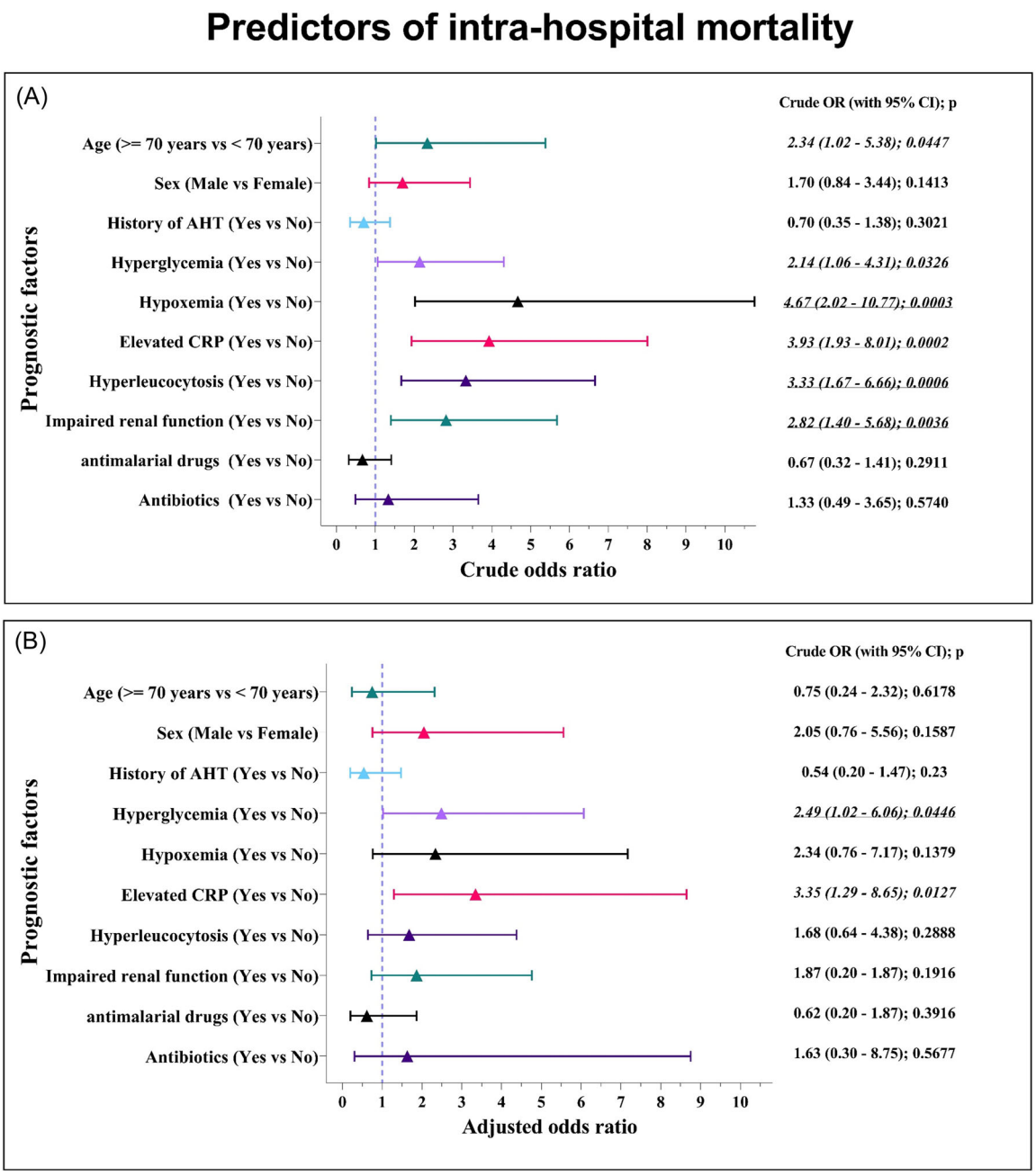

FIGURE 1 Predictors of intrahospital mortality. (A) Simple logistic regression analyses, presenting crude odds ratio (OR) with 95% confidence intervals (CIs). (B) Multiple logistic regression analyses showing adjusted odds ratio with 95% confidence intervals. AHT, arterial hypertension; CRP, C-reactive protein; DM, diabetes mellitus.

Finally, considering only the 30 patients who had a molecular confirmation (by a positive PCR test) of the SARS-CoV-2 infection, the in-hospital mortality rate was 46.7% (14 patients). Like the general group, the patients who died in this subgroup had significantly higher CRP (188.1 (118.3–210.5) vs. 82.5 (36.9–143.3) mg/L, $p = 0.016$) compared to those who survived. Also, they were relatively older (64.5 (55.0–72.0) vs. 52.5 (40.0–66.0) years old, $p = 0.06$) and their glycemia at admission was relatively higher (257.0 (142.6) vs. 223.8 (115.5) mg/dL, $p = 0.53$) but without reaching statistical significance (Table S1).

4 | DISCUSSION

This study was designed to assess the in-hospital mortality and its associated factors in patients suspected of COVID-19 admitted at a tertiary university hospital in Bukavu (eastern DRC). Its findings showed high COVID-19-associated hospital mortality (43.9%) during the first wave of COVID-19 infections in South-Kivu. Identified prognostic factors included: older age, hypoxemia, elevated blood glucose, impaired renal function, and marked inflammatory syndrome (hyperleukocytosis and elevated CRP). After controlling for other

covariates, only elevated CRP levels and elevated blood glucose at admission were found to be significantly and independently associated with hospital mortality.

Overall, prognostic factors identified in this study are in accordance with the findings of most previous studies. In fact, since the beginning of the pandemic, advanced age, hypoxemia, kidney diseases, elevated white blood cell count, and elevated CRP were identified among the most important COVID-19 prognostic factors.[18] Of note, unlike most previous studies,[19–25] medical history of arterial hypertension and diabetes mellitus were not significantly associated with a poor outcome in this study. However, patients with hyperglycemia at admission were more likely to die during their hospitalization, regardless of their diabetes mellitus status.

In fact, hyperglycemia at admission was found to be a major independent prognostic factor in this study. Approximately half of patients (46.7%) of COVID-19 patients included in this study had capillary blood glucose levels above 200 mg/dL at admission. This observation may be, at least partly, explained by the stress status induced by the SARS-CoV-2 infection, leading to a release of hyperglycemic hormones (glucagon, cortisol, catecholamines, etc.), responsible for insulin resistance and impaired glucose regulation,[26] both in diabetic and in nondiabetic patients. In addition, it has been reported that SARS-CoV-2 infection may cause damage to the pancreas islets of Langerhans, inducing impaired β-cell function, thus leading to hyperglycemia in patients with unknown diabetes and to a poor prognosis in patients with known diabetes.[27–30]

In addition to hyperglycemia, severely diseased COVID-19 patients may present also elevated levels of serum lactate, procalcitonin, and CRP, suggesting a marked systemic inflammatory response.[31] The conjunction of marked systemic inflammatory syndrome and hyperglycemia is associated with the activation of a cascade of harmful systemic reactions, including oxidative stress,[32] coagulation impairment,[33–39] and immune dysregulation,[40,41] altogether perpetuating and worsening the critical condition of patients.

Finally, one should consider the limitations of this study while interpreting its findings. Owing to its retrospective design, some prognostic factors reported in other studies (such as obesity, dyslipidemia, blood group, etc.) could not be investigated since they were not routinely collected in hospitalized patients. Another major limitation is that only 20% of patients had a COVID-19 diagnosis confirmed by a positive PCR test. Most patients were diagnosed based only on the WHO clinical criteria, and this may have induced a selection bias. This limits the generalization of these results. However, analyses of data from the subgroup of patients with COVID-19 diagnosis confirmed by a positive PCR test gave results that were similar to the one obtained in the general study population. Despite the above-mentioned limitations, this has some strengths. The major strength is that this study identified simple and easily recognizable prognostic factors that can be used even in resource-limited settings for helping decision-making related to the care of patients infected with COVID-19 and hopefully for reducing COVID-19-related mortality.

5 | CONCLUSION

In conclusion, the first wave of COVID-19 was associated with high hospital mortality in South-Kivu. Elevated CRP and hyperglycemia on admission were the two factors independently associated with hospital mortality in this region. Given the interplay between glucose dysregulation and inflammatory syndrome, clinicians should pay particular attention to COVID-19 patients who present with or develop, during their hospitalization, elevated blood glucose or CRP.

AUTHOR CONTRIBUTIONS

Christian Tshongo: Conceptualization; investigation; methodology; resources; writing—original draft; writing—review and editing. **Marius Baguma**: Conceptualization; data curation; formal analysis; investigation; methodology; resources; supervision; validation; visualization; writing—original draft; writing—review and editing. **Guy-Quesney Mateso**: Conceptualization; investigation; resources; writing—original draft; writing—review and editing. **Samuel Lwamushi Makali**: Conceptualization; data curation; formal analysis; investigation; methodology; validation; writing—original draft; writing—review and editing. **Aline Bedha**: Investigation; writing—review and editing. **Pacifique Mwene-Batu**: Investigation; methodology; writing—review and editing. **Martine Mihigo**: Investigation; writing—review and editing. **Fabrice Nzabara**: Investigation; writing—review and editing. **Cordule Balola**: Investigation; writing—review and editing. **Pierre Kabuya**: Investigation; writing—review and editing. **Achille Bapolisi**: Investigation; writing—review and editing. **Mannix Masimango**: Investigation; writing—review and editing. **Esto Bahizire**: Investigation; writing—review and editing. **Ghislain Maheshe-Balemba**: Investigation; writing—review and editing. **Tony A. Shindano**: Investigation; writing—review and editing. **Cikomola Cirhuza**: Conceptualization; investigation; methodology; project administration; supervision; validation; writing—original draft; writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The first author (Christian Tshongo), the corresponding author (Marius Baguma), and the lead author (Cikomola Cirhuza) had full access to all of the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

The lead author Cikomola Cirhuza affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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