

# Revista Prevenção de Infecção e Saúde

The Official Journal of the Human Exposome and Infectious Diseases Network

**ORIGINAL ARTICLE** 

DOI: https://doi.org/10.26694/repis.v8i1.4535

# Clinical outcome of patients with diabetes mellitus infected by SARS-COV-2

Desfecho clínico de pacientes com diabetes mellitus infectadas pelo SARS-COV-2

Evolución clínica de pacientes con diabetes mellitus infectados por SARS-COV-2

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#### How to cite this article:

Barros NRB, Mascarenhas NA, Barros Junior, FS, Vasconcelos BB, Sousa TMO, Carvalho ARB. Clinical outcome of patients with diabetes mellitus infected by SARS-CoV-2. Rev Pre Infec e Saúde [Internet]. 2023;8:4535. Available from: http://periodicos.ufpi.br/index.php/repis/article/view/4535. DOI: https://doi.org/10.26694/repis.v8i1.4535

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# ABSTRACT

Introduction: Diabetes, a chronic metabolic disease with high prevalence in Brazil, is a risk factor for severe SARS COV-2 infection. The relationship between previous glycemic control and the prognosis of patients hospitalized with COVID-19 is not fully understood. **Objective:** analyze the clinical outcome of patients with diabetes mellitus infected by SARS-COV-2. Outlining: A retrospective analysis of medical records was carried out using the Trakcare electronic system of all diabetic patients hospitalized with a confirmatory diagnosis of pneumonia due to COVID-19 in the medical clinic ward of HRAN, from June to August 2021, who, upon admission, performed the glycated hemoglobin test and analyzed it using the SPSS software (20.0). Results: A sample of 52 patients was obtained during the study period. Most patients are female, with a mean age of approximately 58 years. The comorbidity most associated with the participants was systemic arterial hypertension, with most diabetics presenting good prior glycemic control, represented by HbA1c < 7%. The lethality found was 7.7%. Implications: The study shows a high lethality of diabetic patients infected by COVID-19, but no statistical significance was found for HbA1c levels with the increase in length of stay, use of non-rebreathing mask, need for invasive mechanical ventilation or lethality.

#### DESCRIPTORS

COVID-19; SARS-CoV-2; Diabetes Mellitus; Diabetes Complications.

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Submitted: 2023-07-11 Accepted: 2023-07-17 Published: 2023-07-18

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# INTRODUCTION

The COVID-19 disease, caused by the pathogen SARS-CoV-2, has considerably affected several sectors, including healthcare. It has become one of the biggest public health problems in the 21st century, of ongoing international importance.<sup>1</sup>

There are risk groups that, given the high vulnerability of this disease, require specialized care.<sup>2</sup> Among them are patients with comorbid Diabetes Mellitus (DM), as the World Health Organization (WHO) indicated.<sup>3</sup>

According to global estimates, 9.3% of the world's population (463 million people) suffers from this disease, numbers that may increase by the year 2030 (10.2%) and 2045 (10.9%).<sup>4</sup>

Cumulative clinical studies have suggested that patients with DM and respiratory infections from COVID-19 often have COVID-19-associated hospitalization rates and higher lethality rates compared with patients without comorbidities.<sup>5,6</sup>

Infection with SARS-CoV-2 occurs by entry into the cell, primarily through binding of the virus' Spike protein to the Angiotensin Converting Enzyme 2 (ACE2) receptor. These receptors are found in large quantities in the lung tissue, the site of virus tropism, and the endothelium of vessels. Individuals with DM have increased expression of the ACE2 receptor, which can amplify the chance of infection and even influence the severity of the disease.<sup>7,8</sup>

Thus, the inflammatory environment created by SARS-CoV-2 infection leads to the release of cytokines, an activating condition of the coagulation cascade and the cause of thrombotic phenomena.<sup>9</sup> In individuals with DM, this pro-clotting environment already exists, due to the significant increase in markers of hypercoagulation and fibrinolysis, in addition to increased platelet activity and adhesion to the endothelial wall, making the body a favorable environment for the occurrence of thromboembolic events.6,8

Therefore, DM, with the advent of the pandemic of COVID-19, places itself as one of the

main comorbidities for the increased risk of complications, hospitalizations, prolonged intubation, and death.<sup>10</sup>

Considering the higher risk of non-positive outcomes for people with diabetes affected by SARS-CoV-2,<sup>5,6</sup> measures for follow-up of patients hospitalized in this condition need to be implemented to reduce negative impacts on the patient's hospitalization. The study aims to analyze the clinical outcome of patients with diabetes mellitus infected with SARS-COV-2.

# METHOD

This is an analytical, cross-sectional, retrospective study with a quantitative approach, which followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).<sup>11</sup> The study site was a Regional Hospital in Brasilia-DF, considering data from June to August 2021.

Data were extracted from medical records via the Trakcare electronic system of all diabetic patients admitted with a confirmatory diagnosis of COVID-19 pneumonia to the medical ward at the study site, who were tested for glycated hemoglobin on admission.

The selection of the medical records followed a simple random sampling, obtaining a sample of 52 patients in the period studied. Excluded: medical records of patients vaccinated against the new coronavirus (COVID-19), patients with anemia, evidenced by the admission blood count, with the reference value of 13 to 17 g/dl for men and 12 to 16 g/dl for women, with uremia, defined by urea values above 55 mg/dl, history of alcoholism or bleeding. Prior use of corticosteroids, opioids, dapsone, or antiretrovirals. Presence of hemoglobinopathies that could interfere in the determination of glycated hemoglobin. Excluded pregnant patients had incomplete data on laboratory, clinical, or radiological exams required in the electronic medical record, which could present data that could compromise the result of the study.

The following variables were collected: age, gender, diabetes-related comorbidities, use of oral antidiabetics or insulin, admission pulmonary impairment evidenced by non-contrast chest computed tomography (CT), and admission laboratory tests for inflammatory evidence (lymphocytes, lactate dehydrogenase, c-reactive protein, and ferritin). The patients were divided into groups according to the glycated hemoglobin levels of < 7%, 7% - 9%, 9% - 10%, and>10%.

The groups' data were related to the study outcomes: length of stay, use of non-rebreather mask (NRM) oxygen therapy, need for invasive mechanical ventilation (IMV), and mortality.

For data analysis and data treatment, exploratory descriptive statistics were applied. Categorical variables were analyzed using absolute (n) and relative (%) frequency, and quantitative variables were analyzed using means and standard deviation. Fisher's exact and Mann-Whitney's U tests were used for inferential analysis. The data were analyzed in SPSS software version 20.0. Furthermore, the significance level adopted was  $p \le 0.05$ .

The project was submitted to the Research Ethics Committee of the health service involved in the study and, subsequently, to Plataforma Brasil, obtaining approval under opinion number: 4.718.205 on May 18, 2021, meeting the recommendations of Resolution No. 466/12, of the National Health Council.

# RESULTS

Between June to August 2021, after applying the inclusion and exclusion criteria, 52 diabetic patients with a diagnosis of COVID-19 infection were obtained. Of the total selected patients, about 44.2% were male (n=23) and 55.8% were female (n=29), and the mean age was  $58.3 \pm 11.7$  years (Table 1).

In the analysis of the clinical profile of the participants, the most frequent comorbidity associated with diabetes was systemic arterial hypertension (SAH), with 73.1% (n=38), followed by obesity at 17.3% (n=9). Of the diabetic patients, 78.8% (n=41) used oral antidiabetics, and 13.5% (n=7) used insulin as a therapeutic measure.

At hospital admission, it was found that the demand for medical care occurred with a mean of  $9.65 \pm 3.32$  days of symptoms and oxygen saturation of  $87.02 \pm 6.09$  %. Most patients, 53.8% (n=28), were stratified with COVID-19 pneumonia, with 25 to 50% pulmonary involvement, as evidenced by non-contrast chest CT on admission.

Regarding biochemical markers, 25% (n=13) showed lymphopenia, 84.6% (n=44) increased lactate dehydrogenase (LDH), 97.7% (n=42) increased c-reactive protein (CRP), where 53.5% (n=23) of these patients showed values ten times higher than normal. 81.5% (n=31) showed increased ferritin, with 52.6% (n=20) of them values three times higher than the laboratory reference (Table 1).

	N(%)	CI-95%	Average (CI-95%)	SD
	S	Social Profile		
Age Group			58.33(55.07-61.58)	11.70
20-59 years	27(51.9)	(38.5-65.1)		
≥60 years	25(48.1)	(34.9-61.5)		
Sex		, , , , , , , , , , , , , , , , , , ,		
Female	29(55.8)	(42.3-68.7)		
Male	23(44.2)	(31.3-57.7)		
	C	linical Profile		

 Table 1 - Characterization of the social and clinical profile of diabetes mellitus patients diagnosed with SARS-CoV-2

Prior Comorbidity

Systemic Arterial Hypertension				
(SAH)				
No	14(26.9)	(16.3-40.0)		
Yes	38(73.1)	(60.0-83.7)		
Diabetes Mellitus				
No	0(0.0)			
Yes	52(100.0)			
Obesity				
No	43(82.7)	(70.8-91.1)		
Yes	9(17.3)	(8.9-29.2)		
Other				
No	7(13.5)	(6.2-24.6)		
Yes	45(86.5)	(75.4-93.8)		
Quantity of medications			1.15(0.96-1.35)	0.70
Oral Antidiabetic				
No	11(21.2)	(11.8-33.6)		
Yes	41(78.8)	(66.4-88.2)		
Insulin				
No	45(86.5)	(75.4-93.8)		
Yes	7(13.5)	(6.2-24.6)		
Days of symptoms			9.65(8.71-10.58)	3.32
Non-contrast chest CT				
≤ <b>25</b> %	20(38.5)	(26.2-52.0)		
25% -50%	28(53.8)	(40.4-66.9)		
50%   -75%	3(5.8)	(1.7-14.6)		
≥ <b>75</b> %	1(1.9)	(0.2-8.6)		
Oxygen saturation on admission (%)			87.02(85.32-88.71)	6.09
Lymphocytes			1426.92(1254.85-1598.99)	618.07
< 1000	13(25.0)	(14.8-37.9)		
1000 -4500	39(75.0)	(62.1-85.2)		
LDH			689.63(616.51-762.6)	262.66
< 460	8(15.4)	(7.6-26.9)		
460 -1380	43(82.7)	(70.8-91.1)		
≥1380	1(1.9)	(0.2-8.6)		
CRP			76.00(54.19-97.81)	70.87
< 5	1(2.3)	(0.3-10.4)		
5 -50	19(44.2)	(30.1-59.0)		
≥50	23(53.5)	(38.8-67.8)		
Ferritin			1773.50(721.40-2825.60)	3200.88
< 275	7(18.4)	(8.6-32.8)		
275 -825	11(28.9)	(16.5-44.5)		
≥825	20(52.6)	(37.1-67.8)		
Legend: 95%CI = 95% confidence interv	al; SD = stanc	lard deviation.		

**Legend:** 95%CI = 95% confidence interval; SD = standard deviation. **Source:** Research data

In the subdivision of the groups as to glycated hemoglobin, group 1 (HB1Ac:  $\leq$  7%) consists of 34.6% (n=18) of the participants, group 2 (HB1Ac: > 7 to  $\leq$ 9%) 30.8% (n=16), group 3 (HB1Ac: > 9 to  $\leq$  10%) 11.5% (n=6) and in group 4 (HB1Ac: > 10%) 23.1% (n=12) (Figure 1).

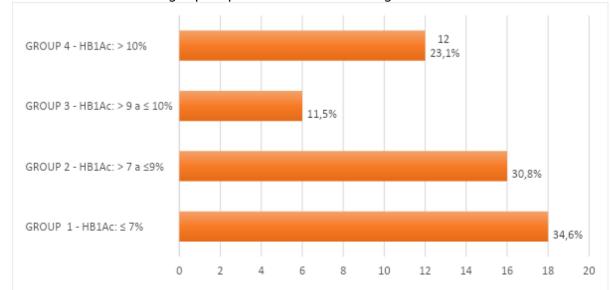


Figure 1 - Characterization of the groups of patients with diabetes diagnosed with SARS-CoV-2 infection.

Source: Research data.

In the context of inflammatory evidence, most patients with lymphopenia 30.8% (n=4), altered LDH, 34.9% (n=15), and ferritin 35% (n=7) were found in group 1 (HB1Ac:  $\leq$ 7%). In opposition, 66.7% (n=2) of patients who had 50 to 75% lung involvement evidenced by chest CT were in group 4 (HB1Ac: > 10%), and the only one with involvement greater than 75% was found in group 2 (HB1Ac: > 7 to  $\leq$  9%) (Table 2).

	GROUP 1 (Hb1Ac ≤ 7%)		GROUP	GROUP 2-Hb1Ac: >7 a ≤9 %		GROUP 3-Hb1Ac: >9 a ≤10 %		GROUP 4 - Hb1Ac: > 10 %	
	N(%)	Average ± SD	N(%)	Average SD	±	N(%)	Average ± SD	N(%)	Average± SD
				Social	Pro	ofile			
Age Group		58.3±12.2		60.44±12.2	25		64.17±8.50		52.67±10.4 3
20-59 years	10(37.0)		7 (25.9)			2(7.4)		8 (29.6)	
≥60 years	8(32.0)		9 (36.0)			4(16.0)		4 (16.0)	
Sex									
Female	10(34.5)		11 (37.9)			1(3.4)		7 (24.1)	
Male	8(34.8)		5 (21.7)			5(21.7)		5 (21.7)	
				Clinica	l Pr	ofile			
Prior Comorbidity SAH	,								
No	6(42.9)		1(7.1)			2(14.3)		5 (35.7)	
Yes	12(31.6)		15 (39.5)			4(10.5)		7 (18.4)	
DM									
No	0(0.0)		0(0.0)			0(0.0)		0 (0.0)	
Yes	18(34.6)		16 (30.8)			6(11.5)		12 (23.1)	

 Table 2 - Association of the social and clinical profile concerning the groups of patients with diabetes mellitus diagnosed with SARS-CoV-2 infection regarding the glycated hemoglobin values (H1Ac).

No       17(39.5)       13 (30.2)       6(14.0)       7(6.3) (76.3)         Yes       1(1.1)       33 (33.3)       0(0.0)       (5.5)         Other       (33.3)       0(0.0)       (14.3) (41.4)       14.4         Yes       13(28.9)       13(3.3)       0(0.0)       (14.1)       12.4         Quantity of medications       1.22.90       1.092.073       1.672.082       4         No       2(18.2)       4(36.4)       1(9.1)       (36.4)       1.092.073       1.672.082       4         Ves       16(30.0)       (22.3)       5(12.2)       (20.6)       (20.6)       3       1.092.012	Obesity								
Yes       1(11.1)       3       0(0.0)       5         Other	No	17(39.5)				6(14.0)			
Other         Instant and the second se	Yes	1(11.1)		3		0(0.0)		5	
No         5/(1.4)         114.3 (13.3)         00.0 (14.3) (24.4)         (14.3) (24.4)           Quantity of medications Oral Antidiabet/ Ves         1.240.6         1.00±0.73         1.67±0.82         1.08±0.67           No         2(18.2)         4(36.4)         1(9.1)         4 (36.4)         4 (19.1)         4 (36.4)           Yes         16(39.0)         12 (29.3)         5(12.2)         (19.5)         1           Insulin         14 (31.1)         4(8.9)         9 (20.0)         1         4 (32.9)         9.50±4.09         10.33±3.20           Non-contract chest CT         9.6±3.2         9.20±3.55         9.50±4.09         10.33±3.20           Somo-contract hest CT         7(35.0)         8(40.0)         1(5.0)         4 (21.4)           25%         7(35.0)         8(40.0)         10(0.0)         0(0.0)         0(0.0)           Oxygen saturation         88.172 3.50         89.38±4.18         83.50±8.02         83.92±8.51           1000         4(30.8)         3(23.1)         3(23.1)         3(23.1)         3(23.1)         2(3.1)           1000         4(30.8)         3(23.1)         3(23.1)         3(23.1)         2(3.1)         2(3.1)           250         6(31.6)         11(10) <t< td=""><td>Other</td><td></td><td></td><td>(33.3)</td><td></td><td></td><td></td><td></td><td></td></t<>	Other			(33.3)					
$\begin{array}{ c c c c c } \mbox{rescaled} rescale$	No	5(71.4)		1(14.3)		0(0.0)			
$ \begin{array}{ c c c c } \hline \begin{tabular}{ c c c c c } \hline \begin{tabular}{ c c c c c c c } \hline \begin{tabular}{ c c c c c c c c } \hline \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	Yes	13(28.9)				6(13.3)		11	
NO       2(18.2)       4(30.4)       1(9.1)       (36.4)         Yes       16(39.0)       12       5(12.2)       8         Insulin       14       4(8.9)       9       2(20.0)         Yes       0(0.0)       2(28.6)       2(28.6)       2(28.6)       3(32.9)         Days of symptoms       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Non-contrast chest CT       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Som-contrast chest CT       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Som-contrast chest CT       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Som-contrast chest CT       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Som Contrast chest CT       7(35.0)       8(40.0)       1(5.0) $\binom{4}{(20.0)}$ Som Contrast chest CT       8.17±       300.00       00.00       00.00         Oxygen saturation on admission (%)       38.17±       89.38±4.18       83.50±8.02       83.92±8.51         Lymphocytes       1455.56       6156.25±       1166.67±       120.83±         Collocitation on admission (%)       225.61       51(1.6)       (27.9)       24.25		ations	1.2±0.6	(33.3)	1.00±0.73		1.67±0.82		1.08±0.67
Yes       16(39.0)       (29.3)       5(12.2)       (19.5)         Insulin       (14, (31.1)       4(8.9) $\frac{9}{(20.0)}$ Yes       0(0.0)       2(28.6)       2(28.6)       (42.9)         Days of symptoms       9.6±3.2       9.20±3.55       9.50±4.09       10.33±3.20         Non-contrast chest CT       7(25.0)       5(17.9)       (21.4)       (20.0)       22         25%       7(35.0)       8(40.0)       1(5.0) $\frac{4}{(20.0)}$ 22       25%       0(0.0)       0(0.0)       0(0.0)       0(0.0)       0(0.0)       0(0.0)       20       27       275%       0(0.0)       88.17±       89.38±4.18       83.50±8.0C       83.92±8.51       83.92±8.51         dumission (%)       3.55       1655.25±       1166.67±       1208.33±       536.76         < 1000       4(30.8)       3(23.1)       3(7.7)       9       9.51.25±       136.75       145.5±       156.75±       1166.67±       1208.33±       1208.75±       136.75       1208.33±       1208.75±       136.75       1208.35±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1208.75±       1	No	2(18.2)		4(36.4)		1(9.1)			
$ \begin{array}{                                    $	Yes	16(39.0)				5(12.2)			
NO       18(40.0)       (31.1)       4(8.9)       (20.0)         Yes       0(0.0)       2(28.6)       2(28.6) $(42.9)$ Days of symptoms       9.643.2       9.20±3.55       9.50±4.09       10.33±3.20         Non-contrast chest CT       8(40.0)       1(5.0) $\begin{pmatrix} 4\\(21.4)\\(20.0)\\(21.4)\\(20.0)\\(21.4)\\($	Insulin								
Yes $0(0.0)$ $2(28.6)$ $2(28.6)$ $(42.9)$ Days of symptoms Non-contrast chest CT $9.6\pm 3.2$ $9.20\pm 3.55$ $9.50\pm 4.09$ $10.33\pm 3.20$ 225% $7(35.0)$ $8(40.0)$ $1(5.0)$ $\frac{4}{(20.0)}$ 25%   -50% $10(35.7)$ $7(25.0)$ $5(17.9)$ $\frac{6}{(21.4)}$ $50\%   -75\%$ $1(33.3)$ $0(0.0)$ $0(0.0)$ $0(0.0)$ $0(0.0)$ $(66.7)$ $00xygen$ saturation on $3.50$ $89.38\pm 4.18$ $83.50\pm 8.02$ $83.92\pm 8.51$ Lymphocytes $1455.56$ $1656.25\pm$ $1166.67\pm$ $1208.33\pm$ Lymphocytes $1435.56$ $1656.25\pm$ $687.70$ $728.23+$ OUO $4(30.8)$ $3(23.1)$ $3(23.1)$ $3(23.1)$ $9$ DHL $27.89\pm$ $713.44\pm$ $682.17\pm$ $754.25\pm$ $1300$ $0(0.0)$ $1(100)$ $0(0.0)$ $119.75$ $<460$ $3(37.5)$ $4(50.0)$ $1(12.5)$ $0(0.0)$ $111.92\pm$ $21380$ $0(0.0)$ $0(0.0)$ $1(100.0)$ $0(0.0)$ $0(0.0)$ $3(5.$	No			(31.1)				(20.0)	
Non-contrast chest CT         4 $25\%$ 7(35.0)         8(40.0)         1(5.0) $\begin{pmatrix} 4\\ 20.0 \\ 6\\ 21.4 \end{pmatrix}$ $50\%$ 10(35.7)         7(25.0)         5(17.9) $\begin{pmatrix} 6\\ 21.4 \\ 2\\ 66.7 \end{pmatrix}$ $50\%$ 1(33.3)         0(0.0)         0(0.0) $\begin{pmatrix} 66.7 \\ 66.7 \end{pmatrix}$ $275\%$ 0(0.0)         1(100)         0(0.0)         0(0.0)           Oxygen saturation on (%)         88.17±         89.38±4.18         83.50±8.02         83.92±8.51           Lymphocytes         1455.56         1656.25±         637.70         1208.33±           1000 -4500         4(30.8)         3(23.1)         3(23.1)         3(23.1)           1000 -4500         14(35.9)         13 (33.3)         3(7.7)         9(23.1)           1000 -4500         14(35.9)         13 (33.3)         3(7.7)         9(23.1)           PHL         627.89±         713.44±         682.17±         754.25±           1460 -1380         15(34.9)         11         111.92±         90.51           1380         0(0.0)         1(100)         0(0.0)         100.0           151.50         6(6.7)         9(1.41         99.51         90.51 $55$ 0	Yes	0(0.0)		2(28.6)		2(28.6)		-	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			9.6±3.2		9.20±3.55		9.50±4.09	4	10.33±3.20
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	≤ <b>25</b> %	7(35.0)		8(40.0)		1(5.0)		(20.0)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	25% -50%	10(35.7)		7(25.0)		5(17.9)		(21.4)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	50% -75%	1(33.3)		0(0.0)		0(0.0)			
admission (%)3.5069.364.16 $63.30\pm0.02$ $63.92\pm0.7$ Lymphocytes1455.561656.25±1166.67±1208.33± $\pm 563.83$ 685.5637.70536.76< 1000		· · ·	<b>88 17</b> +	1(100)		0(0.0)		0(0.0)	
Lymphocycles $\pm 563.83$ $685.5$ $637.70$ $536.76$ < 1000			3.50						
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Lymphocytes							Э	
1000[-450014(35.9)(33.3) $3(7.7)$ (23.1)DHL $627.89\pm \\ 248.39$ 713.44± $682.17\pm \\ 314.50$ 754.25± \\ 198.75< 460	< 1000	4(30.8)				3(23.1)		(23.1)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	1000 -4500	14(35.9)				3(7.7)			
< 4603(37.5)4(50.0)1(12.5)0(0.0)460 -138015(34.9)115(11.6)12≥13800(0.0)1(100)0(0.0)0(0.0)CRP $68.22\pm$ 66.7142.90±36.9491.43±68.74 $111.92\pm$ 90.51< 5	DHL			()				( )	
$460 -1380$ $15(34.9)$ $(25.6)$ $5(11.6)$ $(27.9)$ $\geq 1380$ $0(0.0)$ $1(100)$ $0(0.0)$ $0(0.0)$ CRP $68.22\pm \\ 66.71$ $42.90\pm 36.94$ $91.43\pm 68.74$ $111.92\pm \\ 90.51$ $< 5$ $0(0.0)$ $0(0.0)$ $1(100.0)$ $0(0.0)$ $5 -50$ $6(31.6)$ $9(47.4)$ $1(5.3)$ $3 \\ (15.8)$ $\geq 50$ $6(26.1)$ $4(17.4)$ $4(17.4)$ $9 \\ (39.1)$ Ferritin $1916.92 \\ \pm 2274.9$ $2618.00\pm \\ 5484.9$ $1360.80\pm \\ 629.37$ $878.80\pm \\ 564.87$ $< 275$ $4(57.1)$ $1(14.3)$ $0(0.0)$ $2 \\ (28.6)$ $275 -825$ $1(9.1)$ $4(36.4)$ $2(18.2)$ $4 \\ (36.4)$ $> 825$ $7(35.0)$ $6(30.0)$ $3(15.0)$ $4 \\ 140.00$	< 460	3(37.5)	240.39		300.03	1(12.5)	514.50		190.70
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	460 -1380	15(34.9)				5(11.6)			
CRP $66.71$ $42.90\pm36.94$ $91.43\pm08.74$ $90.51$ < 5	≥1380	0(0.0)	( <b>a a a</b>			0(0.0)			
< 5 $0(0.0)$ $0(0.0)$ $1(100.0)$ $0(0.0)$ $5 -50$ $6(31.6)$ $9(47.4)$ $1(5.3)$ $3$ $\geq 50$ $6(26.1)$ $4(17.4)$ $4(17.4)$ $9$ Ferritin $1916.92$ $\pm 2274.9$ $2618.00\pm$ $5484.9$ $1360.80\pm$ $629.37$ $878.80\pm$ $564.87$ < 275	CRP				42.90±36.94		91.43±68.74		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	< 5	0(0.0)		0(0.0)		1(100.0)			
$ \stackrel{\geq}{=} 50 \qquad 6(26.1) \qquad 4(17.4) \qquad 4(17.4) \qquad (39.1) \\                                   $	5 -50	6(31.6)		9(47.4)		1(5.3)		(15.8)	
Ferritin $\pm 2274.9$ 5484.9629.37564.87< 275	≥ 50	6(26.1)		4(17.4)		4(17.4)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Ferritin								
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	< 275	4(57.1)		1(14.3)		0(0.0)			
				A(2( A)		2(18.2)		4	
	2/5 -825	1(9.1)		4(36.4)		2(10.2)			

**Legend:** 95%CI = 95% confidence interval; SD = standard deviation. **Source:** Research data

	Regar	ding	the	clinic	al	evolution	during
hospi	talizati	ion, th	ie mea	n len	gth o	of stay was	s 15.94 ±
10.3	days,	48.1%	(n=25	5) of	the	diabetic	patients

required a higher intake of oxygen therapy and the use of NRM, 13.5% (n=7) underwent IMV, and 7.7% (n=4) died (Table 3).

Table 3- Characterization of th	he outcome of patients wit	h diabetes mellitus diagnosed w	vith SARS-CoV-2 infection.
	(01)		

	N(%)	CI-95%	Average (IC-95%)	SD
Used NRM				
No	27(51.9)	(38.5-65.1)		
Yes	25(48.1)	(34.9-61.5)		
<b>Invasive Mechar</b>	nical Ventilation (IMV)			
No	45(86.5)	(75.4-93.8)		
Yes	7(13.5)	(6.2-24.6)		
Hospitalization <sup>•</sup>	time		15.94(13.08-18.81)	10.30
Died				
No	48(92.3)	(82.7-97.3)		
Yes	4(7.7)	(2.7-17.3)		
evend: $95\%$ (1 =	95% confidence interval	· SD = standard deviati	ion	

**Legend:** 95%CI = 95% confidence interval; SD = standard deviation. **Source:** Research data.

In the correlation of outcomes with HB1Ac stratification, the use of NRM was higher in group 4, 32% (n=8), p-value=0.07, and mechanical ventilation,

49.9% (n=3), p-value=0.101. The group that presented fewer deaths was Group 1, with 37.5% (n=18), p=0.068 (Table 4).

 Table 4 - Outcome association to the groups of patients with diabetes mellitus diagnosed with SARS-CoV-2 infection regarding glycated hemoglobin (H1Ac) values.

	GROUP	GROUP 1 (Hb1Ac ≤ GROUP 2-Hb1Ac: > 7 a 7%) ≤9 %		GROUP	3-Hb1Ac: >9 a ≤10 %	GROUP			
	N(%)	Average ± SD	N(%)	Average ± SD	N(%)	Average ± SD	N(%)	Average ± SD	P-valu e
Used NRM									0.074
No	12 (44.4)		10(37.0)		1(3.7)		4(14.8)		
Yes IMV	6(24.0)		6(24.0)		5(20.0)		8(32.0)		0.101
No	18 (40.0)		14(31.1)		4(8.9)		9(20.0)		
Yes	Ò(0.0)		2(28.6)		2(28.6)		3(42.9)		
Hospitali time	zation	14.67±11.1		14.50±7.92		13.17±7.81		21.17±12.1	0.255
Died									0.068
No	18 (37.5)		15(31.3)		4(8.3)		11 (22.9)		
Yes	Ò(0.0)		1(25.0)		2(50.0)		1(25.0)		

**Legend:** 95%CI = 95% confidence interval; SD = standard deviation. **Source:** Research data.

# DISCUSSION

This study highlighted the effects of DM during the hospital stay, which can reflect complications for these patients with COVID-19.

According to the epidemiological bulletin of the Ministry of Health (MS) in May 2021, in Brazil, the age group with the highest hospitalization for COVID-19 is between 60 and 69 years.<sup>12</sup> This study showed a reduced age range compared to national data, with a mean age of 58.3 +/- 11.7 years, ranging from 46 to 70 years. The study sample was represented by 55.8% females, a divergence from Brazil, which has a predominance of hospitalizations for COVID-19 in males, with 55% of the cases.

The profile of patients with diabetes justifies the profile found in the study, a pathology more

prevalent in women, represented by 56.2% of diabetics in Brazil, according to the Brazilian Diabetes Society.<sup>13</sup>

A relevant finding is a change in the management flowcharts for patients with COVID-19 during the evolution of the pandemic. The orientation the Ministry of Health exposed at the beginning of the pandemic was to proceed with orotracheal intubation in patients using supplemental oxygen therapy with a flow higher than 5l/min. This management was justified by the pathophysiology of COVID-19, which developed as an acute respiratory distress syndrome (ARDS).<sup>14</sup>

It is a consolidated concept that early mechanical ventilation and mechanical ventilation with protective ventilatory parameters benefit the evolution of these patients in the intensive care unit.<sup>15</sup> However, after the exhaustion of public resources and the growing number of cases, the Ministry of Health changed the flowchart, guiding the rational use of oxygen therapy, with the indication of IMV only after the use of the maximum flow of oxygen, that is, the indication of orotracheal intubation was only for patients with SpO2 saturation < 90%, even with the use of 15L/min in NRM.<sup>16</sup>

In this study, the instruction to delay orotracheal intubation was reproduced, 48.1% of participants required the use of NRM, but only 13.5% progressed to IMV. Spontaneous respiratory effort due to hypoxia causes increased inspiration culminating in increased negative pressure generated within the thorax. This manifestation perpetuates inflammation and may cause alveolar edema and pulmonary fibrosis, worsening the prognosis of these patients. The orientation to delay the start of mechanical ventilation may be associated with increased mortality.<sup>7,8</sup>

The national and worldwide lethality of the disease in the general population is around 2.8%, but the study showed a higher lethality of 7.7%.<sup>9</sup> In this context, patients with diabetes showed a higher lethality rate than general patients infected with

COVID-19 in Brazil. Data from the World Health Organization (WHO) 2019, found increased lethality for COVID-19 in this study population of 9.2%.<sup>17</sup>

Biochemical analysis of diabetic patients infected with COVID-19 showed an increased prevalence of lymphopenia and elevated levels of LDH, CRP, and ferritin; similar results have been widely found in the literature. However, it is in group 1, composed of people with diabetes with good prior glycemic control, where most participants were found with lymphopenia, increased LDH, and ferritin on hospital admission compared to groups 2, 3, and 4.

Studies state that diabetes is a chronic inflammatory disease. Its maintained glycemic uncontrol perpetuates a pro-inflammatory environment in the body, culminating in an immune-metabolic adaptive milieu in the face of COVID-19 infection.<sup>18,19</sup>

In the correlation of the clinical data, the individuals who evolved to an unfavorable outcome, with longer hospital stays and the need for NRM and IMV, are found in the majority in group 4, but without statistical significance. This study demonstrates that better glycemic controls, quantified by HbA1C measurement, do not predict good prognosis in hospitalized patients with COVID-19.

Among the 52 patients studied, there was no statistically significant increase in development in the primary endpoints. It is important to highlight that no patient in group 1 evolved to death. The study carried out in New York, with 506 diabetic patients with COVID-19 infection, tried to demonstrate the correlation of HB1Ac levels on admission, with the same outcomes studied in our study, obtaining no statistical significance.<sup>20</sup>

A meta-analysis performed on 179 COVID-19-infected patients grouped into HB1Ac stratification levels also showed no statistical significance compared to COVID-19 severity.<sup>21</sup>

The conclusions regarding the results are limited in scope, as other studies suggest that the severity of the COVID-19 condition is related to glycemic and metabolic control, as measured by Glycated Hemoglobin (HbA1c).<sup>20,22,23</sup>

In addition, another factor influencing the severity of COVID-19 includes the presence of other comorbidities, and due to the use of secondary data, information on adjacent comorbidities was inadequately populated.

# CONCLUSION

The study shows a high lethality of diabetic patients infected with COVID-19 but did not find statistical significance of HbA1c levels with increased length of stay, use of non-rebreathing mask, need for ventilation, and invasive mechanics.

However, the high lethality of 7.7% found in diabetic patients with SARS-CoV-2, seen at the study site, represents almost three times the overall national lethality, this raises concern for this risk group.

Knowledge of the variables influencing the outcome of these patients can guide health services in the creation of protocols that can improve the care and management of these patients, to reduce the number of deaths and their complications.

# RESUMO

Introdução: O diabetes Mellitus, uma doença metabólica crônica com grande prevalência no Brasil, é fator de risco de gravidade na infecção por SARS COV-2. A relação do controle glicêmico prévio com o prognóstico dos pacientes internados com COVID-19 não é totalmente compreendida. Objetivo: analisar o desfecho clínico de pacientes com diabetes mellitus infectadas pelo SARS-COV-2. Delineamento: Realizou análise retrospectiva de prontuários através do sistema eletrônico Trakcare de todos os pacientes diabéticos internados com diagnóstico confirmatório de pneumonia por COVID-19 na enfermaria de clínica médica em um Hospital Regional em Brasília de junho a agosto de 2021, os quais, no ato da admissão, realizaram o exame de hemoglobina glicada e analisados no *software* SPSS (20.0). Resultados: Foram obtidos uma amostra 52 pacientes no período estudado. A maioria dos pacientes é do sexo feminino, com idade média aproximada 58 anos. A comorbidade mais associada aos participantes diabéticos foi a hipertensão arterial sistêmica, apresentando um bom controle glicêmico prévio, representado por HbA1c  $\leq$  7%. A letalidade encontrada foi de 7,7%. Implicações: O estudo evidencia uma elevada letalidade dos pacientes diabéticos infectados pela COVID-19, porém não se encontrou significância estatística dos níveis de HbA1c com o aumento no tempo de internação, uso de máscara não reinalante, necessidade de ventilação mecânica invasiva.

# DESCRITORES

COVID-19; SARS-CoV-2; Diabetes Mellitus; Complicações do Diabetes.

#### RESUMEN

Introducción: La diabetes mellitus, una enfermedad metabólica crónica con alta prevalencia en Brasil, es un factor de riesgo de gravedad en la infección por COVID-19. La relación del control glucémico previo con el pronóstico de los pacientes hospitalizados por COVID-19 no es totalmente conocida. **Objetivo**: Analizar el resultado clínico de los pacientes con diabetes mellitus infectados por SARS-COV-2. **Delineación**: Análisis retrospectivo de las historias clínicas a través del sistema electrónico Trakcare de todos los pacientes diabéticos ingresados con diagnóstico confirmatorio de neumonía por COVID-19 en la sala de clínica médica de un Hospital Regional de Brasilia de junio a agosto de 2021, a los que, en el momento del ingreso, se les realizó la prueba de hemoglobina glicosilada y se analizaron mediante el software SPSS (20.0). **Resultados**: Se obtuvo una muestra de 52 pacientes en el período estudiado. La mayoría de los pacientes eran mujeres, con una edad media aproximada de 58 años. La comorbilidad más asociada a los participantes diabéticos fue la hipertensión arterial sistémica, presentando un buen control glucémico previo, representado por una HbA1c  $\leq$  7%. La letalidad encontrada fue del 7,7%. **Implicaciones**: El estudio muestra una alta letalidad de los pacientes diabéticos infectados por COVID-19, pero no se encontró significación estadística de los niveles de HbA1c con el aumento del tiempo de hospitalización, uso de mascarilla no respiratoria, necesidad de ventilación mecánica invasiva.

#### DESCRIPTORES

COVID-19; SARS-CoV-2; Diabetes Mellitus; Complicaciones de la Diabetes.

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### **COLLABORATIONS**

BNRB, MNA, BJFS: contributed to the study conception, data collection, data interpretation, manuscript preparation, and approval of the final version. VBB, STMO, CARB: contributed to the study conception and design, evaluation of the stages, manuscript drafting, critical content review, and approval of the final version. The authors are responsible for all aspects of the work, ensuring its accuracy and integrity. All authors agree and take responsibility for the content of this version of the manuscript to be published.

# ACKNOWLEDGMENTS

Not applicable.

### **AVAILABILITY OF DATA**

The original data can be found in the medical records archived in the selected hospital units.

#### FUNDING SOURCE

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

# CONFLICTS OF INTEREST

There are no conflicts of interest to declare.