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NUTRITIONAL RISK AND ASSOCIATED FACTORS IN HOSPITALIZED PATIENTS WITH COVID-19

Risco nutricional e fatores associados em pacientes hospitalizados com COVID-19

Riesgo nutricional y factores asociados en pacientes hospitalizados con COVID-19

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ABSTRACT

Introduction: a new type of coronavirus causing an outbreak was identified and named COVID-19 by the WHO. **Objective:** to identify the nutritional risk and associated factors in patients with COVID-19 who received care at a public hospital unit of reference in the Oeste da Bahia region. **Method:** a retrospective study, based on data contained in the medical records of patients with a positive diagnosis for SARS-CoV-2, during the period from 2020 to 2022. Information was collected on demographic, epidemiological, biochemical and nutritional aspects of the patients. The association between the independent variables and nutritional risk was tested using Poisson regression models. **Results:** of the 553 patients evaluated, there was a predominance of males and individuals without nutritional risk, the mean age was 52.9 years, and the mean length of stay was 6.2 days. Nutritional risk on admission was inversely associated with serum concentrations of lymphocyte count (0.99, 95%CI, 0.98-0.99) and fasting glucose (0.96, 95%CI, 0.93-0.99) after simultaneous adjustment for age and length of stay. **Conclusion:** serum lymphocyte concentration and fasting blood glucose were inversely associated with nutritional risk on admission in patients with COVID-19 treated at a public hospital of reference for the disease.

Keywords: COVID-19; Nutritional status; Risk factors; Hospitalization.

RESUMO

Introdução: um novo tipo de coronavírus causador de um surto foi identificado e denominado COVID-19 pela OMS. **Objetivo:** identificar o risco nutricional e fatores associados em pacientes com COVID-19 atendidos em unidade hospitalar pública de referência da região Oeste da Bahia. **Método:** estudo retrospectivo, baseado em dados contidos em prontuários de pacientes com diagnóstico positivo para SARS-CoV-2, no período de 2020 a 2022. Foram coletadas informações sobre aspectos demográficos, epidemiológicos, bioquímicos e nutricionais dos pacientes. A associação entre as variáveis independentes e o risco nutricional foi testada por meio de modelos de regressão de Poisson. **Resultados:** dos 553 pacientes avaliados houve predomínio de doenças e indivíduos sem risco nutricional, a média de idade foi de 52,9 anos e o tempo médio de internação foi de 6,2 dias. O risco nutricional na admissão foi inversamente associado às concentrações séricas de contagem de linfócitos (0,99, IC 95%, 0,98-0,99) e glicemia de jejum (0,96, IC 95%, 0,93-0,99) após ajuste simultâneo para idade e tempo de internação. **Conclusão:** a concentração sérica de linfócitos e a glicemia de jejum estiveram inversamente associadas ao risco nutricional na admissão em pacientes com COVID-19 atendidos em hospital público de referência para a doença.

Palavras-chave: COVID 19; Estado nutricional; Fatores de risco; Hospitalização.

RESUMEN

Introducción: la OMS identificó un nuevo tipo de coronavirus que provocó un brote y lo denominó COVID-19. **Objetivo**: identificar riesgo nutricional y factores asociados en pacientes con COVID-19 atendidos en un hospital público de referencia de la región occidental de Bahía. Método: estudio retrospectivo, a partir de datos contenidos en historias clínicas de pacientes diagnosticados positivos a SARS-CoV-2, del 2020 al 2022. Se recopiló información sobre aspectos demográficos, epidemiológicos, bioquímicos y nutricionales de los pacientes. La asociación entre variables independientes y riesgo nutricional se probó mediante modelos de regresión de Poisson. **Resultados**: de los 553 pacientes evaluados hubo predominio de enfermedades e individuos sin riesgo nutricional, la edad promedio fue de 52,9 años y el tiempo de estancia promedio fue de 6,2 días. El riesgo nutricional al ingreso se asoció inversamente con las concentraciones séricas de linfocitos (0,99, IC del 95%, 0,98-0,99) y la glucosa en sangre en ayunas (0,96, IC del 95%, 0,93-0,99) después del ajuste simultáneo por edad y duración de la estancia. **Conclusión**: la concentración de linfocitos séricos y la glucemia en ayunas se asociaron inversamente con el riesgo nutricional al ingreso en pacientes con COVID-19 atendidos en un hospital público de referencia para la enfermedad.

Palabras clave: COVID 19; Estados nutricionales; Factores de riesgo; Hospitalización.

INTRODUCTION

In early 2020, a new type of coronavirus causing an outbreak was identified and named COVID-19 by the WHO.[1] It was a severe acute respiratory syndrome caused by Sars-Cov-2, a virus that belongs to the Coronaviridae family, responsible for causing diseases in the respiratory tract.[2]

COVID-19 is characterized by increased secretion of pro-inflammatory cytokines associated with an exaggerated immune response.[3] In this sense, biochemical alterations are observed in critically ill patients infected with the virus.[4] The systematic review and meta-analysis carried out by Kazemi et al.[5] identified that critically ill patients showed a significant increase in C-reactive protein (CRP). And some studies have shown that there is a relationship between patients diagnosed with COVID-19 and glycemic changes.[4,5] Bode et al.[6] evaluated 1,122 patients admitted to 88 American hospitals with COVID-19, of whom 451 were diagnosed with diabetes mellitus or transient hyperglycemia and 671 had no glycemic changes. The authors found that patients with transient hyperglycemia had a higher risk of mortality and a longer length of stay.[6]

A systematic review and meta-analysis carried out by Feng et al.[7] of 3,614 patients hospitalized in wards and intensive care units worldwide found that the prevalence of malnutrition risk varied from 70.7% to 92.2% in hospitalized patients with COVID-19, suggesting the need for screening and nutritional support during hospitalization. Screening tools are used to detect protein and energy malnutrition and help determine the patient's prognosis.[8] The European Society for Clinical Nutrition and Metabolism (ESPEN) and the Brazilian Nutrition Association (ASBRAN) recommend the use of the Nutritional Risk Screening (NRS-2002) to identify nutritional risk during the first hours of a patient's admission.[9]

Silveiro et al.[3] state that nutritional status and diet modulate inflammation and immune function and can be adjusted to influence the evolution of COVID-19. For this reason, nutritional therapy should be considered one of the fundamental pillars of hospital care in relation to the therapeutic measures applied to patients infected with Sars-Cov-2.[10]

In the hospital setting, a number of risk factors for nutritional status can affect critically ill patients: systemic inflammation and metabolic alterations, reduced mobility, and inappetence.[11] Therefore, it is essential that these patients are screened, diagnosed, and treated using nutritional assessment methods.[10] In this context, the aim of this study was to identify the nutritional risk and associated factors in patients with COVID-19 who received care at a hospital unit.

METHODS

This study is part of a larger project entitled "Demographic, epidemiological, clinical, and nutritional profile of patients with Sars-Cov-2: A retrospective study with adult and elderly patients admitted to a hospital unit in the municipality of Barrreiras - Bahia." It consists of research based on the collection of data contained in the medical records of patients diagnosed with COVID-19 who received care at a public hospital in the municipality of Barreiras in the state of Bahia, a center of reference for the treatment of COVID-19 in the Oeste da Bahia region, during the period from March 2020 to December 2022. The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of the Universidade Federal do Oeste da Bahia (CAEE 56068221.0.0000.8060).

The data were collected during the months of June 2022 and February 2023, and the database was built based on the medical records of patients with a positive diagnosis for SARS-CoV-2 who were admitted to the reference hospital for treatment of this disease. Information on the demographic, epidemiological, biochemical, and nutritional aspects of the patients was collected.

The inclusion criteria for this study were the medical records of patients over the age of 18 that had information on the Nutritional Risk Screening (NRS) tool. Patients or their guardians were contacted for their consent to participate in the study and after they signed the informed consent form, the data were included in the study. Medical records of patients under 18 years of age, who did not have information on the NRS and who did not approve the use of their data were excluded.

With regard to the demographic data collected, age was recorded in full years and sex was categorized as male or female. The epidemiological aspects included the medical diagnosis of chronic non-communicable diseases (diabetes mellitus or systemic arterial hypertension), length of hospital stay in days, and clinical outcome (discharge or death/transfer due to deterioration). In addition, information was collected on the biochemical tests (lymphocyte count, leukocytes, platelets, hemoglobin, CRP, and fasting glucose) carried out on admission of the patient.

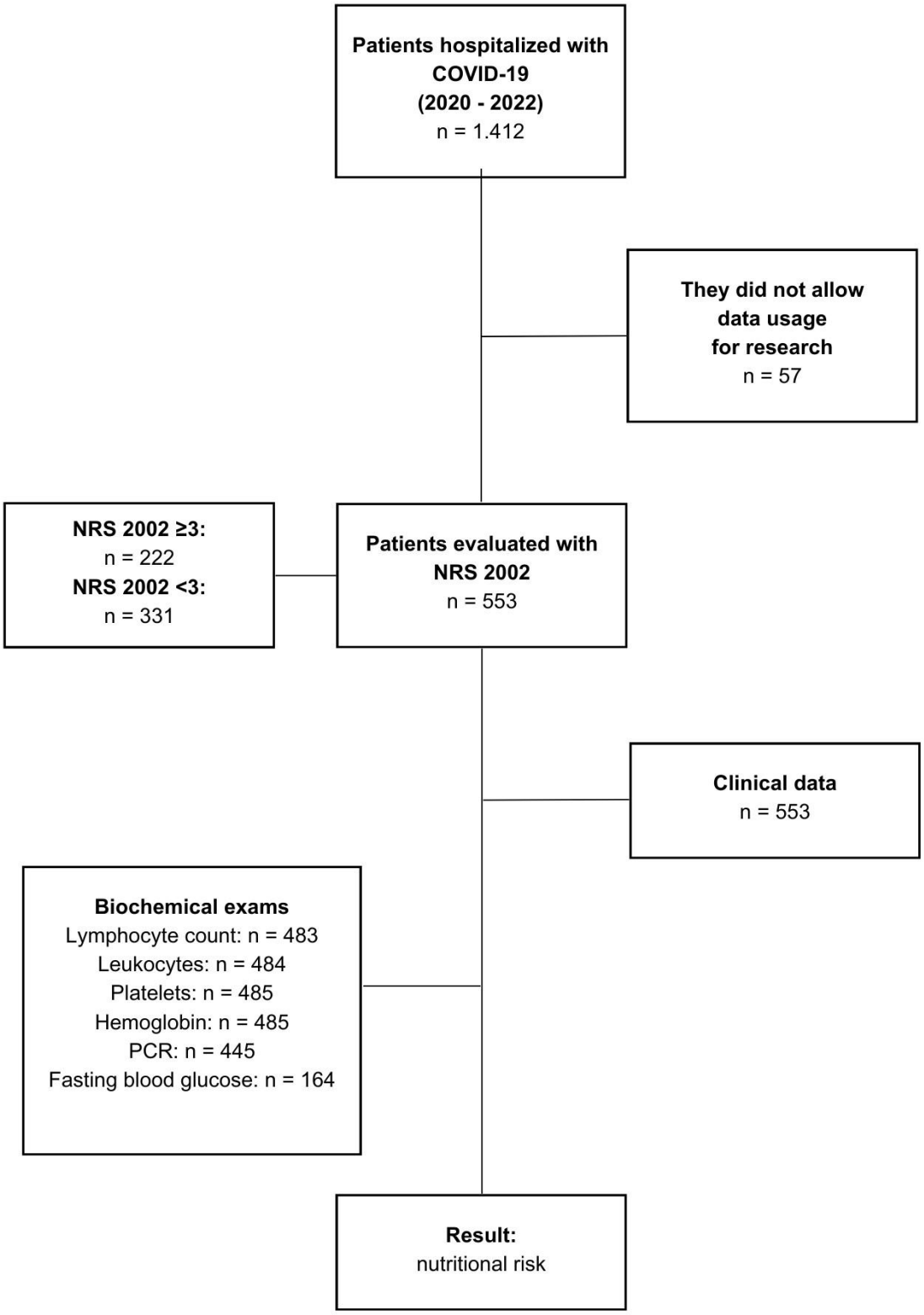
With regard to the nutritional variable, information on nutritional risk was obtained using the NRS instrument. This instrument investigates the patient's nutritional status in relation to malnutrition or the risk of developing it during hospitalization, classifying patients according to the level of nutritional status and the severity of the disease, adjusted for age, if over 70 years old, with a score ≥ 3 considered as nutritional risk and <3 as no nutritional risk.[9]

The data were analyzed using Stata 13.1 software. The normality of the variables was assessed using the Shapiro-Wilk test. First, descriptive statistics (frequency and mean) were used for the statistical treatment. Student's t-test or the Mann-Whitney test was used to compare means between the NRS cut-off points. The chi-squared test was used to verify the association between the NRS cut-off points and the variables of gender and clinical outcome. The association between the independent variables and nutritional risk was tested using Poisson regression models. In the multiple model, variables with $p<0.20$ in the bivariate analysis were considered, and only those with $p<0.05$ remained in the model.

RESULTS

The hospital admitted 1,412 patients with COVID-19 between 2020 and 2022, of which 57 family members or patients did not allow their data to be used for the research. For this study, data from 553 medical records containing information on the use of the NRS were used. The data are shown in Figure 1.

Figure 1 – Flowchart with information about research participants.



Of the 553 patients evaluated, 61.5% were male with an average age of 52.9 years. Of these patients, 19.4% died or were transferred to other units due to the severity of their disease, and the average length of stay was 6.2 days. Regarding the biochemical tests carried out on admission, the average results obtained were: lymphocyte count (n=483) 1,124 mm³, leukocytes (n=484) 9,899mm³, platelets (n=485) 341,178µL, hemoglobin (n=485) 14.1g/dL, CRP (n=445) 66.9mg/dL, and fasting glucose (n=164) 137.2mg/dL (Table 1).

Table 1 – Characteristics of the study population according to nutritional risk on admission. Barreiras - BA, 2020 - 2022.

Variables	NRS 2002			
	All patients (N = 553)	Nutritional risk (N = 222)	Without nutritional risk (N = 331)	P-value
Age, years[1]	52.9	54.9 (±17.5)	51.6 (±14.7)	**0.01**
Male sex (%)[2]	61.5	55.8	65.3	**0.02**
Hospitalization time (days)[1]	6.2	6.1 (±4.3)	6.3 (±3.5)	0.58
Deaths + transfers due to deterioration (%)[2]	19.4	19.0	19.8	**0.04**
Lymphocyte count (mm³)(N = 483)[3]	1.224	1.109 (±603)	1.300 (±1.264)	0.10
Leukocytes (mm³) (N = 484)[3]	9.899	9.723 (±8.313)	10.016 (±7.271)	0.07
Platelets (µL) (N = 485)[1]	341.178	332.696 (±141.000)	346.784 (±133.961)	0.26
Hemoglobin (g/dL)(N = 485)[1]	14.1	13.9 (±1.9)	14.1 (±1.7)	0.21
C-reactive protein (mg/dL) (N = 445)[1]	66.9	73.4 (±60.7)	61.9 (± 56.1)	**0.04**
Fasting blood sugar (mg/dL) (N = 164)[3]	137.2	122.4 (±63.1)	145.9 (±77.7)	**0.02**

Without nutritional risk: less than 3 points. Nutritional risk: greater than or equal to 3 points. [1]t-test / [2]Chi-squared / [3]Mann-Whitney test. Values with significant p are in bold.

The prevalence of diabetes mellitus and systemic arterial hypertension was 16.70% and 35.40%, respectively. Regarding the questions of the nutritional screening tool, 95.30% of the patients had a body mass index greater than 20.50kg/m², 60.04% reported weight loss in the previous 3 months, 66.73% reported a reduction in food intake, and 90.78% of the patients did not have a serious illness, poor general condition, or were in an intensive care unit.

On admission, there was a predominance of patients without nutritional risk (59.85%). It was observed that an older age (p=0.01) and the male sex (p=0.02) were significantly associated with nutritional risk on admission. The frequency of death and transfer due to deterioration was higher in patients with lower nutritional risk (p=0.04). Regarding the biochemical tests, serum CRP concentration was higher in patients with nutritional risk (p=0.04). In addition, fasting serum glucose concentration was higher in patients without nutritional risk (p=0.02).

The association between nutritional risk on admission and demographic, clinical, and biochemical variables is shown in Table 2. The bivariate analyses showed positive associations between nutritional risk on admission and age, sex, and serum CRP concentrations, whereas lymphocyte concentrations and fasting glucose showed inverse associations. In the final model for the outcome nutritional risk on admission, after simultaneous adjustment for the variables age and length of stay, it was found that serum concentrations of lymphocyte count (0.99, 95%CI, 0.98-0.99) and fasting glucose (0.96, 95%CI, 0.93-0.99) were inversely associated with the outcome nutritional risk on admission.

Table 2 – Univariate and multivariate analysis of nutritional risk on admission of patients hospitalized for COVID-19 according to demographic, clinical, and biochemical variables. Barreiras - BA, 2020 - 2022.

Variables	Crude Prevalence Ratio (95%CI)	P	Adjusted Prevalence Ratio (95%CI)	P
Age	1.08 (1.02; 1.14)	**0.01**		
Sex	1.0	**0.01**		
Female	1.26 (1.04; 1.52)			
Hospitalization time (days)	1.00 (0.98; 1.02)	0.54		
Clinical outcome		0.80		
Deaths + transfers due to deterioration (%)	1.03 (0.81; 1.30)			
Lymphocyte count (mm³)	0.99 (0.98; 0.99)	**0.03**	0.99 (0.98; 0.99)	**0.01**
Leukocytes (mm³)	0.99 (0.99; 1.00)	0.65		
Platelets (µL)	0.99 (0.99; 1.00)	0.22		
Hemoglobin (g/dL)	0.96 (0.91; 1.01)	0.17		
C-reactive protein (mg/dL)	1.01 (1.00; 1.03)	**0.02**		
Blood sugar (mg/dL)	0.96 (0.93; 0.99)	0.02	0.96 (0.93; 0.99)	0.04

P value: Poisson regression assuming significance at $p < 0.05$.
Model adjusted for age and length of stay. Values with significant p are in bold.

DISCUSSION

This study sought to verify the relationship between nutritional risk and associated factors in patients with COVID-19 who received care at a public hospital unit in the municipality of Barreiras, Bahia. The results showed that on admission, there was a predominance of patients without nutritional risk. An older age and higher serum CRP concentration were positively associated with nutritional risk. The higher frequency of male patients, deaths or transfers due to deterioration, and higher serum glucose concentration were associated with the absence of nutritional risk on admission. Serum concentrations of lymphocyte count and fasting glucose were inversely associated with nutritional risk on admission.

According to the nutritional screening carried out on the admission of the hospitalized patients, we found that 59.85% were not at nutritional risk. This result corroborates research carried out by Silva et al.,[12] in which 76.70% of patients admitted to the contingency unit for the treatment of COVID-19 in Rio Grande do Norte were not at risk. A multicenter study conducted in Egypt assessed the nutritional risk of hospitalized patients with COVID-19 at the time of admission using two different methods. The results showed that only 5.10% of admitted patients were classified as severe nutritional risk according to the NRS, while the Malnutrition Universal Screening Tool (MUST) identified nutritional risk in 14.90% of patients.[13] These data show similarities in the hospitalization profile with the present study, even though it was conducted in a different geographical context.

According to Seres,[14] due to the severity of COVID-19 infection, it is likely that malnutrition is less prevalent in patients when they are first admitted to hospital. In this sense, it is possible that malnutrition may occur throughout the hospitalization process [13] and in the post-COVID-19 stage.[13] Therefore, reassessing nutritional risk throughout the hospitalization process is essential.[12] The study conducted by Youssef et al.[13] highlighted a significant increase in the risk of malnutrition throughout the hospitalization period. The results showed that the malnutrition rate increased from 14% at admission to 26.30% at discharge. In addition, malnutrition was found to be more prevalent in patients admitted to intensive care units compared to those who recovered during the hospitalization period.

A study conducted by Zhao et al.[15] at the West Campus of Union Hospital (Wuhan, China), a hospital designated to treat COVID-19 patients, found that 92% of patients were considered to be at nutritional risk and had a worse disease progression. It can be noted that the assessment of nutritional status by subjective methods may underestimate malnutrition in some contexts, such as in this study.[16] However, this tool has shown better predictive validity for prolonged hospitalization.[17]

Of the 553 patients evaluated in this study, 61.50% were male with a mean age of 52.90 years, and these findings were significantly associated with nutritional risk on admission. In the study conducted by Li. et al.[18] in the city of Wuhan, when they analyzed the profile of 549 hospitalized patients with COVID-19, they found that 42.20% (n=231) were between 45 and 64 years old and 50.90% (n=279) of the patients were male. More recent studies[19, 20] carried out in regional hospitals in the Federal District public health network have shown that the highest prevalence of hospitalization remained in the 41-80 age group and in males.

Zhang et al.[21] and Silverio et al.[3] cite that the elderly are more susceptible to infection by the COVID-19 virus and more likely to develop the severe form of the disease than people under 50, which may be due to the process of immunosenescence. These patients often experience increased secretion of pro-inflammatory cytokines associated with an overreaction of the immune system. As a result, there is an increased risk of infection, progression of disease severity and, consequently, greater nutritional risk.

Regarding biochemical aspects, the serum concentration of CRP was higher in patients at nutritional risk (p=0.04). This protein is produced by the liver and plays an important role as an early marker of infection and inflammation.[22] However, it can increase significantly in the acute phase of the disease, within 6 to 8 hours, and shows a higher peak within 48 hours after the onset of infection.[23] The results of the present study confirm the hypothesis that CRP is predictive of the severity of COVID-19, which was also demonstrated in the retrospective multicenter cohort study conducted by Yang et al.[24] in the city of Wenzhou, Zhejiang, China, which found that 55% of patients had high serum CRP levels on admission and a positive correlation with disease severity. It should be noted that Zhang et al.[21] and Liu et al.[25] found that the prognosis of COVID-19 could be predicted by lymphopenia, leukocytosis, neutrophilia, low albumin values, as well as high CRP levels.

The association between high levels of CRP and severe cases of COVID-19 is mainly explained by the ability of SARS-CoV-2 infection to provoke an intense immune response characterized by marked cell activation and excessive production of inflammatory cytokines, resulting in a greater risk of complications for the patient.[22, 26]

The highest percentage of deaths and transfers due to deterioration occurred in patients with lower nutritional risk (p=0.04). The study carried out by Zhou et al.[27] observed the mechanism of action of the Sars-Cov-2 virus and found that in addition to lung and heart tissues, angiostensin-converting enzyme (ACE2) expression was found in the kidneys, testis, bladder, liver, stomach, intestinal epithelium, and vascular endothelium, providing a mechanism for the multiple organ dysfunction observed in COVID-19, which may explain the association of the increased rate of deaths and transfers in patients with low nutritional risk.

Fasting serum glucose concentrations were also inversely associated with the outcome nutritional risk on admission. Hyperglycemia in critically ill patients is considered an adaptive metabolic manifestation of stress and is associated with increased mortality in critically ill patients, as in the case of COVID-19 infection.[6, 28]

The experimental study by Morse et al.[29] demonstrated that the virus can infect pancreatic b-cells, causing a state of hyperglycemia or de novo diabetes. Analysis of pancreatic tissue from COVID-19 revealed an association between the SARS-CoV-2 virus and b-cells, as well as an overexpression of the protein known as neuropilin 1 (NRP1), present in pancreatic cells, which facilitates viral entry into the cells and inhibits insulin secretion.[29, 30]

This study also found that nutritional risk on admission of COVID-19 patients was inversely associated with serum lymphocyte concentrations. Changes in lymphocyte counts are associated with oxygen demand.[4] The results found in this study corroborate the analysis of Kazemi et al.[5], who found that the average lymphocyte count of patients with a mild/moderate diagnosis of the disease was higher than that of critically and severely ill patients, showing an inverse relationship between this biochemical parameter and the severity of the disease.

The clinical spectrum of COVID-19, as well as its association with nutritional risk in hospitalized patients, has been shown to be quite varied and broad, ranging from mild or asymptomatic infection to severe clinical manifestations that can lead to severe acute respiratory distress syndrome (SARS) and death.[31] It has been suggested that the prognosis of severe cases is related to risk factors such as age, sex, presence of comorbidities, and chronic non-communicable diseases (hypertension, diabetes, cardiovascular diseases, among others), although various aspects of the disease pathophysiology, clinical evolution, and immune response pattern have not been fully elucidated.[28, 31]

Some limitations of the study should be considered. The collection of medical records may have compromised the results, given the difficulty in understanding the way the multidisciplinary team wrote up the clinical information and patient progression, as well as the lack of information on patients' clinical outcomes after hospital transfer. In addition, there are limitations inherent to the fact that this is a retrospective study.

To overcome these limitations, an attempt was made to evaluate each medical record in its entirety, from the recording of data at the time of admission to the patient's clinical outcome in the hospital setting in question. A strong point of this study is its originality, as it is the first study carried out in Oeste da Bahia to investigate the nutritional risk in hospitalized patients with COVID-19, between March 2020 and December 2022. It is worth mentioning that the hospital unit where the research was carried out was a reference center for the treatment of COVID-19, serving 18 municipalities in the Barreiras - Bahia region.

CONCLUSION

It was found that serum lymphocyte concentration and fasting blood glucose were inversely associated with nutritional risk on admission of patients with COVID-19 who received care at a public hospital of reference for the disease. These results highlight the need for future studies to investigate the relationship between nutritional risk and the clinical outcomes of COVID-19.

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