

Flaviani Diogo Reis Augusto¹
Aline Duarte de Souza¹
Cláudia Porto Sabino Pinho²

¹ Universidade Federal de Pernambuco, Hospital das Clínicas de Pernambuco. Recife, PE, Brasil.

² Universidade Federal de Pernambuco, Hospital das Clínicas de Pernambuco, Programa de Residência em Nutrição Clínica. Recife, PE, Brasil.

Correspondence Cláudia Porto Sabino Pinho claudiasabinopinho@hotmail.com

Assessment of risk and nutritional status in hospitalized Covid-19 patients

Avaliação do risco e estado nutricional em pacientes com Covid-19 hospitalizados

Abstract

Introduction: Initial data connect infection by the novel coronavirus with nutritional status. Malnutrition seems to be a risk factor for Covid-19, and once the infection is installed, both malnutrition, overweight or obesity are an important predictor of unfavorable evolution. Aim: To evaluate the risk and nutritional status in hospitalized patients with Covid-19. Methods: Crosssectional study involving patients with Covid-19 infection admitted to a university hospital in Recife-PE. The sample consisted of individuals aged \geq 20 years who tested positive for Covid-19, through the RT-PCR molecular test, through nasopharyngeal secretion swab. Nutritional risk was assessed through recommended screening for this group of patients, and nutritional status, through the Body Mass Index (BMI) and biochemical tests. Demographic variables, length of hospital stay and clinical outcome (discharge, transfer to ICU and death) were also considered. Results: 71 patients were evaluated, with a mean age of 52.3 ±13.4 years. Nutritional risk was observed in 95.8% of patients, low weight and overweight were found in 12.7% and 56.3% of the sample, respectively. Low hemoglobin levels were found in 70% of patients and about 75% of patients had depletion according to the total lymphocyte count (TLC) parameter. There was no association of nutritional status with worse outcome. Conclusion: A high percentage of nutritional risk, overweight, low levels of TLC and anemia were observed in patients with Covid-19. Nutritional extremes (malnutrition and obesity) were not associated with a worse clinical outcome and longer hospital stay.

Keywords: Coronavirus Infections. SARS virus. Nutritional status. Malnutrition Obesity.

Resumo

Introdução: Dados iniciais conectam a infecção pelo novo coronavírus com o status nutricional. A desnutrição parece ser um fator de risco para a Covid-19, e uma vez a infecção instalada, tanto a desnutrição, quanto o sobrepeso ou obesidade constituem importante preditor de evolução desfavorável. *Objetivo*: Avaliar o risco e estado nutricional em pacientes com Covid-19 hospitalizados. *Métodos*: Estudo de corte transversal, envolvendo pacientes com infecção por Covid-19 internados em um hospital universitário na cidade de Recife-PE. A amostra foi constituída por indivíduos com idade ≥20 anos que tiveram resultado positivo para Covid-19, através do teste molecular RT-PCR, através de

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swab de secreção naso-orofaringe. O risco nutricional foi avaliado através de triagem recomendada para este grupo de pacientes, e o estado nutricional, por meio do Índice de Massa Corpórea (IMC) e exames bioquímicos. Consideraram-se ainda variáveis demográficas, tempo de internamento e desfecho clínica (alta, transferência para UTI e óbito). Resultados: Foram avaliados 71 pacientes, com média de idade de 52,3 ±13,4 anos. O risco nutricional foi observado em 95,8% dos pacientes, o baixo peso e o excesso de peso foram constatados em 12,7% e 56,3% da amostra, respectivamente. Baixos níveis de hemoglobina foram encontrados em 70% dos pacientes e cerca de 75% dos pacientes apresentaram depleção de acordo com o parâmetro de contagem total de linfócitos (CTL). Não houve associação do estado nutricional com pior desfecho. Conclusão: Foi verificado elevado percentual de risco nutricional, excesso de peso, baixos níveis de CTL e de anemia nos pacientes com Covid-19. Os extremos nutricionais (desnutrição e obesidade) não foram associados a um pior desfecho clínico e maior tempo de internamento.

Palavras-chave: Infecções por Coronavírus. Vírus da SARS. Estado Nutricional. Desnutrição. Obesidade.

INTRODUCTION

The infection caused by the new coronavirus was declared a pandemic situation by the World Health Organization (WHO).¹ Several studies were impressively conducted and published in a short period of time to identify factors related to a worse outcome and prognosis.²

Initial data connect infection by the novel coronavirus with nutritional status. Malnutrition seems to be a risk factor for Covid-19, and once the infection is installed, both malnutrition and overweight or obesity are an important predictor of unfavorable evolution.^{2,3}

Exploratory studies indicate that patients infected with the novel coronavirus (SARS-COV-2) experience several symptoms that can negatively affect their nutritional status, leading to body weight loss and malnutrition,⁴ such as fever, dyspnea, fatigue, diarrhea, nausea, vomiting, inappetence, anosmia, ageusia, in addition to an intense inflammatory response that characterizes the infection.^{5,6}

One of the only studies available on the magnitude of malnutrition in patients affected by infection with the new coronavirus, developed in Wuhan, China, described a prevalence of 27.5% of nutritional risk and 52.7% of malnutrition, evaluating 182 elderly people by Mini Nutritional Assessment (MNA).⁵ According to Liu et al.,⁷ malnutrition was frequent and severe in the elderly, with reports of malnutrition in up to 65% of hospitalized elderly patients and about 60% of institutionalized elderly infected with SARS-COV-2.

Patients with high BMI evolve with worse prognosis, which can be pointed out as a possible role of sarcopenic obesity or comorbidities associated with excess body fat.⁸ The relationship between Covid-19 and obesity can be explained by the fact that excess body fat is associated with overactivation of the complement system, leading to an inflammatory storm and associated complications.^{7,9}

Some authors^{2,10,11} suggest that early identification and correction of malnutrition have the potential to improve the outcome of patients, making it evident the importance of tracking the risk and assessing the nutritional status of infected patients. In this context, the present study aims to investigate the risk and nutritional status of patients diagnosed with Covid-19 hospitalized.

METHODS

This is a retrospective, cross-sectional study in which a prospective analysis variable (length of stay and outcome) was coupled, involving patients with Covid-19 admitted to the clinical ward of a university hospital in the city of Recife-PE, from April to August 2020.

The research sample was obtained by convenience, and included all individuals aged 20 years or older who tested positive for Covid-19 infection by molecular test RT-PCR, through nasopharyngeal secretion swab. Patients who were unable to report updated weight and/or height data and patients from the Intensive Care Unit were excluded to avoid the effects of hospitalization on anthropometric measurements.

When performing nutritional risk screening, nutritional risk eligibility criteria were used based on comorbidities related to a worse prognosis, indicators and symptoms associated with malnutrition, proposed by Piovacari et al.,¹⁰ which establish nutritional risk when at least one of the following criteria is present: elderly (\geq 65 years), adults with BMI <20.0 kg/m², patients with high risk or pressure injury, immunosuppressed patients, inappetent, persistent diarrhea, history of weight loss, chronic obstructive pulmonary disease (COPD), asthma, structural lung diseases, heart diseases, including major arterial hypertension, insulindependent diabetes, renal failure and pregnant women.

In the assessment of nutritional status, weight and height data reported on admission were used, BMI was calculated and its classification was established according to the proposed cut-off points for adults¹² and the elderly.¹³

We also evaluated demographic data (gender, age), clinical data regarding the presence of comorbidities (systemic arterial hypertension, diabetes mellitus and chronic kidney disease), type of nutritional therapy (oral, enteral and parenteral), length of stay and outcome (discharge, transfer to ICU or death) and biochemical data such as hematocrit, hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and total lymphocyte count (TLC). All biochemical tests were transcribed from the medical records, considering the first examination of hospitalization.

Anemia was diagnosed according to hemoglobin (Hb) concentrations, being determined when values below 12g/dL were observed for women and below 13g/dL for men, as defined by the Ministry of Health.¹⁴ Microcytic anemia was considered when the MCV was below 80.0 (fl), and hypochromic anemia when the MCH value was below 27.0 (pg).¹⁴

The TLC was obtained by the formula TLC= (%dlymphocytes x leukocytes) /100, adopting the classification: severe depletion for values below 800mm³; moderate depletion for values between 800 and 1199mm³; mild depletion when values were between 1,200 and 2,000mm³, and normal for values above 2,000mm^{3.15}

The research protocol was based on the ethical principles established by the Resolution of the National Health Council/Ministério da Saúde (Ministry of Health) No. 466/2012, and was evaluated by the Ethics and Research Committee on Human Beings of the institution and approved under CAAE number 32782620.0.0000.887.

Data analysis

Data were analyzed using the Statistical Package for Social Sciences program – SPSS version 13.0 (SPSS Inc., Chicago, IL., USA). Continuous quantitative variables were tested for normality by the Kolmogorov-Smirnov test and as they presented normal distribution were described as mean and standard deviation, being compared by the Anova One Way test and Bonferroni afterwards. Categorical variables were described by simple frequency, and proportions were compared by Pearson's Chi-square test or Fisher's exact test. Statistical significance was considered at p<0.05.

RESULTS

During the study period, 71 eligible patients with Covid-19 were hospitalized. The mean age was 52.3 \pm 13.4 years and there was a homogeneous distribution between the sexes (50.7% of men).

Regarding the clinical profile, the frequency of SAH and DM was 66% and 42%, respectively. Nutritional risk was observed in 95.8% of patients and low weight in 12.7% of the sample. More than half of the patients were overweight (56%).

Low hemoglobin levels were observed in 70% of the sample, 18.6% with microcytic anemia and 18.6% with hypochromic anemia. According to the total lymphocyte count parameter, 73.6% had some degree of nutritional depletion.

It was also found a mean length of stay of 10.5 ± 7.7 days, and that approximately 6% of patients were referred to the Intensive Care Unit and 3% died (Table 1).

Sex		
Male	35	49.3
Female	36	50.7
Age group		
Adult	49	69.0
Elderly	22	31.0
Comorbidities		
Systemic Arterial Hypertension	47	66.2
Diabetes <i>mellitus</i>	30	42.3
Chronic kidney disease	14	19.7
Nutritional risk	68	95.8
Nutritional Status		
Low weight	9	12.7
Eutrophy	22	31.0
Overweight	40	56.3
Type of nutritional therapy		
Oral	64	91.4
Enteral	3	4.3
Parenteral	3	4.3
Anemia	49	70.0
Hematocrit		
Low	55	78.6
Normal	15	21.4
Hight	0	0
VCM		
Low	13	18.6
Normal	53	75.7
Hight	4	5.7
НСМ		
Low	13	18.6
Normal	55	78.6
Hight	2	2.9
CTL		
<800	8	15.1
800-1.200	7	13.2
1.200-2.000	24	45.3
>2.000	14	26.4
Outcome		
Hospital discharge	62	91.2
ICU	4	5.9
Death	2	29

Table 1. Demographic, clinical and nutritional characteristics of hospitalized COVID-19 infectedpatients. Recife-PE, Brasil (n=71).

MCV – Mean Corpuscular Volume; HCM – Mean Corpuscular Hemoglobin; CTL – Total Lymphocyte Count; ICU - Intensive Care Therapy.

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Analyzing the demographic, clinical and nutritional variables, according to nutritional status, a higher mean age was found among malnourished individuals (p<0.001). Lower means of MCV and MCH were observed among individuals with excess weight (p<0.05), as well as a higher percentage of SAH (p=0.011). Nutritional status was not associated with a worse outcome (p=0.289) and longer hospital stay (p= 0.743) (Table 2).

Variable	Low weight M (SD)	Eutrophy M (SD)	Overweight M (SD)	p-value*
Age	67.4(8.6) ^a	52.3(14.9) ^b	48.8(11.0) ^c	<0.001
Hemoglobin	10.2(3.1)	10.7(2.2)	11.4(2.2)	0.258
Hematócrit	30.8(8.9)	31.9(6.5)	34.2(6.5)	0.269
VCM	93.9(10.5) ^a	86.8(6.5) ^a	85.4(7.2) ^b	0.012
НСМ	30.9(3.0) ^a	29.0(2.1) ^a	28.5(2.5) ^b	0.030
Hospitalization time	8.8(4.5)	11.2(8.0)	10.6(8.3)	0.743
(days)				
SAH				0.011
Yes	7(14.9)	9(19.1)	31(66.0)	
No	2(8.3)	13(54.2)	9(37.5)	
DM				0.797
Yes	4(13.3)	8(26.7)	18(60.0)	
No	5(12.2)	4(34.1)	22(53.7)	
DRC				0.546
Yes	3(21.4)	4(28.6)	7(50.0)	
No	6(10.5)	18(31.6)	33(57.9)	
Type of NT				0.942
Oral	8(12.5)	20(31.3)	36(56.3)	
Enteral or Parenteral	1(16.7)	2(33.3)	3(50.0)	
Outcome				0.289
Hospital discharge	7(11.3)	20(32.3)	35(56.5)	
ICU or Death	2(33.3)	1(16.7)	3(50.0)	

Table 2. Demographic, clinical and nutritional variables according to nutritional status in hospitalizedpatients infected with COVID-19. Recife-PE, Brasil (n=71).

** One way ANOVA test and a posteriori Bonferroni test; **Chi Pearson's Square. ^{a,b,c}Different letters mean statistical differences.Caption: MCV – Mean Corpuscular Volume; HCM – Mean Corpuscular Hemoglobin; SAH - Systemic Arterial Hypertension; DM- Diabetes Mellitus; CKD - Chronic Kidney Disease; TN - Nutritional Therapy; ICU - Intensive Care Therapy

DISCUSSION

The high prevalence of nutritional risk among patients infected with the new coronavirus (95.8%) corroborates the findings reported by Liu et al.,⁷ who identified 85.8% of nutritional risk in elderly patients with Covid screened by the Nutritional Risk Score (2002). Another investigation developed by Li et al.,⁵ involving elderly hospitalized for infection by the new coronavirus in Wuhan, China, reported only 27.5% of nutritional risk, considering the Mini Nutritional Assessment (MNA) tool.

This result much lower than the findings of the present investigation can be attributed to a possible selection bias, since the center and the participants evaluated were designated by the Chinese government.

Thus, the differences found may refer to the criteria adopted to track the nutritional risk and the characteristics of the evaluated population.

The present study adopted the criteria proposed by Piovacari et al., ¹⁰ recommended by the Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN), which considers nutritional risk when there is a condition associated with a worse clinical outcome in patients with Covid-19, and was proposed in this context of pandemic due to the limitation of face-to-face assessment. It should be considered that this proposal can increase the screening of individuals at risk, but when weight loss cannot be documented and that nutritional assessment represents a risk for the professional, it can be a useful strategy to direct the indication of nutritional therapy.

Some authors have demonstrated the importance of nutritional risk screening tools in patients affected by Covid-19 infection. Zhang et al.¹¹ applied the NUTRIC Score tool in critical patients infected with the new coronavirus and found that mortality was significantly higher in the high nutritional risk group. In addition, these patients had a higher frequency of acute respiratory distress syndrome, acute myocardial injury, secondary infection, shock and use of vasopressors. Liu et al.⁷ also reported longer hospitalization and worsening of diseases in elderly patients who presented nutritional risk screened by four screening tools (NRS 2002, Malnutrition Universal Screening Tool (MUST), Mini Nutritional Assessment (MNA-sf) and Nutritional Risk Index (NRI). Thus, the use of screening tools in patients with Covid-19 was useful to screen for a worse outcome.

Low weight was found in a relatively small portion of the sample of this study (12.7%), a result that corroborates the study by Kim et al.,¹⁶ who reported only 2.2% of malnutrition according to BMI, adopting the cut-off point proposed by the WHO, in adult patients admitted to a hospital in New York. However, data from a study involving elderly hospitalized in Wuhan, China, identified 52.7% of malnutrition, considering the Mini-Nutritional Assessment method.⁵

It should be considered that only the BMI was adopted to determine the nutritional condition and this was obtained from the reported measures. This was the strategy adopted in this investigation, to avoid physical contact with patients infected with Covid-19, reducing the possibility of contamination by health professionals and minimizing the risk of spreading the virus, being a practice recommended by numerous national and international guidelines.¹⁷⁻¹⁹

Although the use of reported measures is a limitation, some studies have shown that these measures performed better than the estimated measures.^{20,21} Nevertheless, caution is required when considering the reported measures for patients with Covid-19, as they are inserted in a situation of acute malnutrition, with an intense risk of weight loss, due to the inflammatory storm to which they are submitted, the presence of underlying diseases and gastrointestinal symptoms related to the infection.^{22,23} It has also been shown that patients infected with Covid-19 have a significant reduction in food intake during the days prior to hospitalization, which may contribute to the referred weight does not adequately reflect the current weight of these patients.²⁴

The effect of impaired nutritional status on the evolution of Covid-19 infection is not totally understood, but some authors have already pointed out that nutritional status may influence the individual risk for the progression of SARS-CoV-2.²⁵ Kim et al.¹⁶ found that patients with low weight had a higher risk of mechanical ventilation and death.

The present results indicated that more than half of the sample (56%) was overweight, and this high prevalence may be related to the fact that obese patients have a higher risk of hospitalization due to

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numerous factors. This result corroborates the study by Kim et al.,¹⁶ who found 74.7% of overweight patients according to BMI, adopting the cut-off point proposed by the WHO, in adult patients admitted to a hospital in New York. Al-Salameh et al.,²⁶ in their study of adult patients hospitalized with Covid-19 in France, found a high prevalence of overweight, representing 65.1% of the sample.

Obesity has also been listed as an important predictor of poor prognosis in patients with Covid-19.^{2,27} Huh et al.,²⁸ in an investigation to assess whether BMI and metabolic factors were associated with a poor clinical outcome in the infection by the novel coronavirus, found that overweight in women was associated with a more severe evolution of the disease and a higher risk of death. Smati et al.,²⁹ in a multicenter study conducted in France, involving patients with type 2 diabetes mellitus (T2DM) hospitalized due to Covid-19, found that excess weight was an independent risk factor for poor early prognosis, increased need for mechanical ventilation and/or death.

Obesity directly compromises lung function, being multifactorial and being related to the mechanical and inflammatory aspects of the condition itself.³⁰ Immune dysregulation and prolonged inflammation may be the main drivers of poor clinical outcomes in obese patients with Covid-19.³¹ Changes in the mechanics of the lungs and chest wall are observed in obesity,³⁰ causing a reduction in lung operating volume and, consequently, the patient is experiencing narrowing and closing of the airways.³²

In addition, excess weight is a factor that leads to increased production of inflammatory cytokines, which in turn is associated with decreased defense cells, especially T cells. Furthermore, obese patients have increased expression of the angiotensin-converting enzyme 2 (ACE2) in the lung and the increase in circulating proteases are involved in facilitating the entry of the virus, which may exacerbate SARS-CoV-2 infection.³³

According to the total lymphocyte count parameter, about 75% of the patients presented depletion. Although this is a valid marker of malnutrition and nutritional risk, because it is related to immune reserves and cellular defense conditions, its usefulness in the presence of infection is limited, being much more adequate to reflect the severity of the disease. This result is similar to what was found by Pingzheng et al.,³⁴ who described that 73.5% of adult patients infected with Covid-19 in Wuhan had low levels of TLC, and by Zhang et al.,¹¹ who when evaluating immunological parameters in infected patients detected that 75.4% had lymphopenia. Lymphopenia was associated with increased risk of hospitalization and infection-related death in the general population.³⁵

A high percentage of anemia was found in this study (70%), similar to what was found by Bellmann-Weiler et al.,³⁶ who evaluated prevalence, predictive value of anemia and deregulated iron homeostasis in patients with Covid-19 infection and found that, among 259 patients, 24.7% had inflammatory anemia during admission, a percentage that progressively increased to 68.8% on the seventh day of hospitalization. Huang et al.,³⁷ evaluated clinical characteristics of positive cases of Covid-19 in Wuhan and found low levels of hemoglobin in 38.2% of hospitalized patients.

Inflammatory anemia (IA), which is also known as chronic disease anemia, is considered the most prevalent anemia in chronic diseases and hospitalized patients.³⁸ During inflammatory / infectious processes, anemia is caused by pro-inflammatory cytokines such as interleukin (1 β and 6) and tumor necrosis factor α (TNF- α .), which may directly affect iron homeostasis.³⁹ The release of these cytokines, mainly IL-6, results in upregulation of the iron regulatory hormone hepcidin (HAMP), produced mainly by hepatocytes and released into the blood flow to regulate systemic iron homeostasis. Systemic HAMP blocks the export of cellular iron through ferroportin 1 (FPN1), resulting in reduced intestinal absorption of iron, increased iron retention in

hepatocytes and macrophages, causing a reduced availability of the metal for erythropoiesis, compromising the production of hemoglobin, resulting in the development of anemia.⁴⁰

The lowest mean of MCV and MCH observed among overweight individuals differs from the results reported by Tashima et al.,⁴¹ who did not find differences in hematimetric parameters in obese women. Hypochromic and microcytic anemia, which characterizes the profile of iron deficiency anemia, reinforces the malnutrition of obese patients, in which dietary excesses are commonly accompanied by poor dietary choices.

The higher mean age among malnourished patients observed in these results reinforces the greater vulnerability of the elderly to nutritional impairment. This greater exposure in elderly patients infected with Covid-19 may be related to the greater impairment of the mucosal epithelium caused by the virus, affecting gastrointestinal symptoms, decreased appetite and weight loss,⁷ in addition to the poorly diversified nature of their dietary patterns.⁵ The present results did not indicate longer hospital stay and worse clinical outcome in malnourished and obese patients, although consistent results reveal a higher risk of poor prognosis in these individuals.¹⁶

Some limitations should be considered in the interpretation of our findings, such as the small sample size and the fact that the patients were from a single health unit, which may reflect selection bias and limit the generalization of the results. In addition, it should be considered that only BMI was adopted for nutritional diagnosis, which does not distinguish body components (fat and muscle mass), and this was based on self-reported measures of weight and height.

CONCLUSION

A high percentage of nutritional risk, overweight, low levels of TLC and anemia were observed in patients with Covid-19. Nutritional extremes (malnutrition and obesity) were not associated with a worse clinical outcome and longer hospital stay.

The presented results reinforce the importance of risk screening and nutritional assessment of hospitalized patients with Covid-19, especially in more vulnerable groups, such as the elderly, so that prevention and intervention strategies can be proposed early. Further studies need to be developed to broaden the knowledge about the impact of Covid-19 infection on nutritional status and the effects of previous nutritional condition on the evolution of the disease.

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Contributors

Augusto FR worked at all stages, from the conception of the study to the writing of the final version of the article; Souza AD participated in the data collection and final review of the article; Pinho CPS participated in the conception of the study, the analysis and interpretation of the data and the revision of the final version of the article.

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