

## Características clínicas e nutricionais de pacientes críticos com Covid-19

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**Resumo:** A pandemia pela Covid-19 representou um desafio para os sistemas de saúde principalmente pela alta mortalidade, manifestações clínicas multiformes e prognóstico relacionado ao diagnóstico nutricional e perfil bioquímico dos pacientes. **Objetivo:** Correlacionar as características clínicas dos pacientes com Covid-19 admitidos em uma Unidade de Terapia Intensiva (UTI) com exames laboratoriais, dados antropométricos e desfecho clínico da doença. **Metodologia:** Estudo epidemiológico e transversal em banco de dados secundários, analisando parâmetros laboratoriais (hemoglobina, hematócrito, leucócitos, bastonetes, plaquetas, creatinina, d-dímero, transaminase oxalacética, transaminase pirúvica e proteína C reativa) e nutricionais (circunferência do braço, circunferência da panturrilha e índice de massa corporal) de pacientes com Covid-19 admitidos na UTI entre março de 2020 e março de 2021. Os prontuários médicos dos pacientes foram revisados e foram coletados dados referentes à identificação dos pacientes, data de internação, data do desfecho (alta ou óbito), tempo de internação, bem como a presença de doenças crônicas e o uso contínuo de medicamentos, além dos exames laboratoriais da admissão e parâmetros nutricionais referentes ao diagnóstico nutricional inicial. **Resultados:** Foram observadas correlações inversas entre idade e indicadores antropométricos. O uso de um maior número de medicamentos (média 2,1) esteve associado a menores valores de índice de massa corporal (média 29,2 kg/m<sup>2</sup>) e circunferência do braço finais (média 32,3cm). Pacientes que foram à óbito tinham maior idade, tinham menor tempo de internação, maiores valores de creatinina e menores indicadores antropométricos iniciais. **Conclusões:** Quanto maior a idade, menores os valores antropométricos. Pacientes idosos e com doenças crônicas apresentaram pior prognóstico na evolução da Covid-19.

**Palavras-chave:** Covid-19; Diagnóstico Nutricional; Prognóstico.

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## Prognostic analysis and clinical and nutritional characteristics of critical Covid-19 patients

**Abstract:** *The Covid-19 pandemic represented a challenge for health systems, in large part due to the high mortality rate of the disease in older population, multiform clinical manifestations and prognosis related to nutritional diagnosis and biochemical profile of patients. Objective: to correlate Covid-19 patients admitted to an Intensive Care Unit (ICU) with laboratory tests, anthropometric data and the clinical outcome of the disease. Methodology: an epidemiological and cross-sectional study was performed using secondary databases, analyzing the laboratory (hemoglobin, hematocrit, leukocytes, rods, platelets, creatinine, d-dimer, oxaloacetic transaminase, pyruvic transaminase and C-reactive protein) and nutritional (upper arm circumference, calf circumference and body mass index) parameters of Covid-19 patients admitted to the ICU between March 2020 and March 2021. Sociodemographic, laboratory and clinical data were collected from hospitalized Covid-19 patients in the hospital. Results: inverse correlations were observed between age and anthropometric indicators. The use of a greater number of medications (average 2.1) was associated with lower final Body Mass Index (average 29.2 kg/m<sup>2</sup>) and arm circumference (average 32.3 cm) values. Patients who died were older, had shorter hospital stays, higher creatinine levels and lower baseline anthropometric indicators. Conclusions: older patients had lower anthropometric values. Patients with chronic diseases had a worse prognosis in the evolution of Covid-19.*

**Key-words:** Covid-19; Nutritional Diagnosis; Prognosis.

### Introdução

Covid-19, a disease caused by infection with the novel coronavirus (SARSCoV-2), first began to infect the global population at the end of 2019, according to the Pan American Health Organization (BRASIL, 2020). The disease caused concern due to its rapid spread, the absence of specific treatment, a high degree of lethality in the older population and the fact that it affects multimorbid and malnourished individuals more seriously (BARAZZONI et al., 2020; TEIXEIRA et al., 2021).

Critically ill patients over the age of 60 and those with underlying medical conditions (such as hypertension, diabetes, cardiovascular disease, and chronic respiratory disease) are at high risk of mortality and are critically important in clinical care and critical care (ZHAO et al., 2020). Age seems to be the most important factor linking to a more severe course of COVID19 (HASSELI et al., 2021), once disease manifestations in Covid-19 patients range from asymptomatic to fatal, with more severe consequences as individuals age (SIMOPOULOS et al., 2021).

A healthy nutritional status is a fundamental aspect in the fight against Covid-19 (LIMA, 2020), since a weakened immune system is a significant risk factor for respiratory viral infections. Proper diet and nutrition are believed to be important factors for an optimal immune response to prevent infection (IM et al., 2020). Older patients and those with comorbidities (e.g. diabetes, cardiovascular disease, chronic respiratory disease) are most likely to die and at higher risk of

malnutrition/malnutrition (SONG et al., 2021). COVID-19 patients also exhibited signs of protein wasting, such as reduced albumin levels and organ dysfunction, highlighting the role of nutritional risk screening and prognostic value of COVID-19 patients (SONG et al., 2021).

Iron metabolism and anemia may play an important role in the multiple organ dysfunction syndrome of coronavirus disease 2019 (COVID-19). Hemoglobin concentration is one of the most important determinants of the oxygen-carrying capacity of blood. Low hemoglobin in COVID-19 patients, especially in populations at risk of complications and mortality, may be due to patients suffering from a reduced ability of hemoglobin to meet the increased oxygen demand of peripheral tissues due to a hypermetabolic state during infection coverage (TANERI et al., 2020).

In addition, many laboratory parameters are affected by the disease, and can be considered significant predictors of adverse clinical outcomes (LIPPI et al., 2020). The changes in the four stages of the disease stand out, in addition to the blood count, inflammatory response markers such as C-reactive protein (CRP), D-dimer, lactate dehydrogenase and liver enzymes, such as oxaloacetic transaminase and pyruvic transaminase.

The present study is justified by the importance of understanding the profile of hospitalized Covid-19 patients, as well as their nutritional parameters, nutritional diagnosis and biochemical profiles, as there is little data in literature on the subject, especially with regard to the region under study. The objective of the study is to correlate Covid-19 patients admitted to an Intensive Care Unit (ICU) in a high-complexity hospital in the southwest of the state of Paraná with laboratory tests, anthropometric data and outcomes of discharge or death.

## **Methodology**

### **Outline and participants**

An epidemiological and cross-sectional study was performed using secondary databases. It was undertaken at the Hospital Regional do Sudoeste Walter Alberto Pecóits (the Walter Alberto Pecóits Southwest Regional Hospital (HRSWAP)), in Francisco Beltrão, Paraná, through the review of medical records of patients with a confirmed diagnosis of Covid-19. Data collection was performed following authorization from the Technical Directory of HRSWAP and approval from the Ethics Committee in Research with Human Beings of the Universidade Estadual do Oeste do Paraná (West Paraná State University) (UNIOESTE) under number CAAE Nº 51802421.3.0000.0107.

## Procedures

Patients admitted to the HRSWAP ICU between March 2020 and March 2021, with a confirmed diagnosis of Covid-19, were considered for the study. Patients with incomplete data recorded in the database were excluded.

## Data Collection

Data relating to general information (age, sex, pre-existing chronic diseases and use of continuous medication), the chronology of the clinical condition studied (date of admission, date of discharge/death and length of hospitalization), laboratory tests performed at admission, information regarding anthropometric indicators (ideal and estimated weight, estimated height, estimated body mass index, arm and calf circumference) at time of ICU admission, nutritional diagnosis, and outcome (discharge or death) were retrospectively collected from electronic medical records.

Body Mass Index (BMI) values less than or equal to  $18.4 \text{ kg/m}^2$  were considered underweight, those between  $18.5$  and  $24.9 \text{ kg/m}^2$  of normal weight, those between  $25$  and  $29.9 \text{ kg/m}^2$  pre-obese, and those greater than  $30 \text{ kg/m}^2$  obese (EBSERH, 2019; WHO, 1995).

For laboratory tests, the reference values for hemoglobin and hematocrit were considered according to sex, ranging from  $13$  to  $16.9 \text{ g/dL}$  for men and from  $11.5$  to  $14.9 \text{ g/dL}$  for women for hemoglobin, and from  $39.7\%$  to  $52\%$  for men and  $35.3$  to  $46.1\%$  for women for hematocrit, respectively. Normal platelet counts were considered to be from  $128.177$  to  $299,774/\text{mm}^3$  for men and  $135.606$  to  $343.044/\text{mm}^3$  for women. Creatinine was considered normal at between  $0.7$  and  $1.3 \text{ mg/dL}$  for men and  $0.55$  and  $1.2 \text{ mg/dL}$  for women. Normal d-dimer was considered less than  $500 \text{ ng/mL}$ . Normal GOT was between  $15$  and  $37 \text{ U/L}$ , and normal GPT was between  $16$ - $63 \text{ U/L}$  for men and  $14$ - $59 \text{ U/L}$  for women.

The reference values were based on those adopted by the Carlos Chagas Laboratory, between 2021 and 2022, in accordance with the standard of excellence of the National Quality Control Program (PNCQ) and the National Accreditation System (DICQ), sponsored by the Brazilian Society of Clinical Analysis (SBAC).

## Statistical Analysis

To characterize the sample, the variables were described as mean, median, standard deviation, interquartile range, minimum and maximum values. The normality of data distribution was tested by the Shapiro-Wilk test. Since the continuous variables were not normally distributed, Spearman's correlation coefficients were used to verify the relationship between general patient variables and anthropometric parameters. The comparison between the characteristics of patients who were discharged and those who died was performed using the Mann-Whitney U test. All analyzes were performed using the SPSS 25.0 statistical program and a significance level of  $p < 0.05$  was adopted.

## Results

In the present study, 58 medical records of patients from ICU with a mean age of 62.1 years were evaluated. Most patients were male (67.24%) and the mean length of hospitalization was 20.5 days. The main chronic diseases were systemic arterial hypertension (SAH) (62.07%), diabetes mellitus (DM) (27.59%), obesity (24.14%), and chronic obstructive pulmonary disease (COPD) (12.07%).

In relation to medication, 48.28% used continuous medication at time of admission. Table 01 displays the general characteristics of the sample. The median age and length of hospitalization were 63 years and 16 days, respectively. The median number of diseases was two, while for the use of medication it was zero. In general, a large range of variation is observed for most of the variables analyzed.

**Table 01.** General characteristics of sample (n = 58).

Variable	Mean	Median	Standard deviation	Minimum	Maximum
Age (years)	62.1	63.0	14.3	23	86
Length of hospitalization (days)	20.5	16.0	13.5	5	67
Comorbidities (n)	2.1	2.0	1.3	0	5
Use of medication (n)	2.1	0.0	2.9	0	13
Hemoglobin (g/dL)	12.3	12.7	1.7	7.9	15.4
Hematocrit (%)	36.6	37.9	5.1	23.5	47.6
Leukocytes (/mm <sup>3</sup> )	11641	10450	5738	3200	28700
Band cells (%)	5.3	3.0	6.9	0	44
Platelets (/mm <sup>3</sup> )	259534	248000	97154	91000	613000
Creatinine (mg/dL)	1.49	1.39	0.76	0.52	4.73
D-dimer (ng/mL))	3398	1270	7356	137	53806
GOT (U/L)	52.1	44.1	30.8	12.3	182.8
GPT (U/L)	47.6	38.6	38.3	6.7	225.4
CRP (mg/dL)	14.1	13.5	8.6	0.9	41.1
BMI (kg/m <sup>2</sup> )	29.2	28.7	5.3	16.0	43.1
AC (cm)	32.3	31.5	4.6	22.0	44.0
CC (cm)	36.5	36.0	4.8	28.0	49.0

**Nota.** GOT= Oxaloacetic Transaminase; GPT = Pyruvic Transaminase; BMI = Body Mass Index; AC = Arm Circumference; CC = Calf Circumference

Regarding the initial nutritional diagnosis, low body mass index (3.45%), normal body mass index (15.52%), pre-obesity (37.93%), and obesity (43.10%) were recorded.

The correlations between the characteristics of the patients and the anthropometric parameters are shown in Table 02. Moderate and inverse correlations were observed between age and D-dimer and the three anthropometric parameters (BMI, AC and AC). Therefore, greater age and higher D-dimer levels correlated with lower initial BMI and initial and final circumferences, or in other words, anthropometric indicators declined as age increased. The levels

of hemoglobin and hematocrit were positively associated with anthropometric parameters (with the exception of hemoglobin with BMI). The other correlations were not statistically significant.

According to the results of this study, there is an inverse correlation between final BMI and initial arm circumference (AC) and calf circumference (CC) with age, where the indicators decline as age increases.

Medication use was inversely related to BMI and AC. It was also possible to relate the increase in inflammatory activity to increased values of D-dimer.

**Table 02.** Correlation between the general characteristics of the patients in the study and the initial and final anthropometric parameters (n = 58).

Variable	BMI (kg/m <sup>2</sup> )	AC (cm)	CC (cm)
Age years)	<b>-0.209</b>	<b>-0.312</b>	<b>-0.448</b>
Length of hospitalization (days)	0.196	0.129	0.183
Diseases (n)	0.032	0.061	0.005
Use of medication (n)	-0.150	-0.089	-0.180
Hemoglobin (g/dL)	0.256	<b>0.289</b>	<b>0.337</b>
Hematocrit (%)	<b>0.271</b>	<b>0.296</b>	<b>0.347</b>
Leukocytes (/mm <sup>3</sup> )	-0.066	-0.103	-0.010
Band cells (%)	-0.084	-0.105	-0.136
Platelets (/mm <sup>3</sup> )	-0.173	-0.118	-0.130
Creatinine (mg/dL)	0.007	-0.005	-0.084
D-dimer (ng/mL))	<b>-0.360</b>	<b>-0.412</b>	<b>-0.389</b>
GOT (U/L)	-0.054	-0.095	-0.119
GPT (U/L)	0.004	-0.062	-0.116
CRP (mg/dL)	0.091	0.039	0.125

**Note.** GOT= Oxaloacetic Transaminase; GPT = Pyruvic Transaminase; BMI = Body Mass Index; AC = Arm Circumference; CC = Calf Circumference. Values in bold indicate  $p < 0,05$ .

Table 03 shows the statistical analyzes between the characteristics of the patients who were discharged and those who died. Statistically significant differences were observed regarding age, length of hospitalization, platelets, creatinine and GOT. Patients included in the statistical analysis who were discharged were younger ( $p=0.033$ ), with longer periods of hospitalization ( $p=0.024$ ), higher platelet levels ( $p=0.048$ ), lower creatinine levels ( $p=0.002$ ), and lower GOT ( $p=0.010$ ).

**Table 03.** Comparison of patient characteristics according to outcome - discharge/death.

Variable	Discharge	(n = 23)	Death	(n = 35)	P
	Mean	Median (IQ)	Mean (SD)	Median (IQ)	
Age (years)	57.1 (15.1)	60.0 (22.0)	65.5 (13.0)	67.0 (17.0)	0.033
Length of hospitalization (days)	27.4 (17.3)	26.0 (28.0)	16.0 (7.5)	14.0 (10.0)	0.024
Diseases (n)	1.8 (1.1)	2.0 (1.0)	2.3 (1.3)	2.0 (2.0)	0.097
Use of medication (n)	1.7 (2.5)	0.0 (4.0)	2.3 (3.1)	0.0 (4.0)	0.656
Hemoglobin (g/dL)	12.1 (1.3)	12.3 (2.0)	12.5 (1.8)	12.9 (2.0)	0.171
Hematocrit (%)	36.0 (3.7)	37.9 (5.1)	36.9 (5.8)	38.0 (6.4)	0.294
Leukocytes (/mm <sup>3</sup> )	10817 (5735)	9900 (3700)	12183 (5759)	10700 (9000)	0.273
Canes (%)	5.0 (5.8)	3.0 (4.0)	5.5 (7.7)	3.0 (4.0)	0.658
Platelets (/mm <sup>3</sup> )	294739 (121741)	261000 (153000)	236400 (69603)	244000 (122000)	0.048
Creatinine (mg/dL)	1.2 (0.5)	1.1 (0.4)	1.7 (0.8)	1.5 (0.6)	0.002
D-dimer (ng/mL)	2370 (3006)	1300 (1653)	4073 (9149)	1239 (3826)	0.893
GOT (U/L)	41.1 (22.8)	35.0 (26.0)	59.4 (33.5)	51.1 (35.3)	0.010
GPT (U/L)	48.9 (35.2)	40.3 (20.7)	46.7 (40.6)	35.5 (34.5)	0.313
PCR (mg/dL)	13.3 (8.7)	10.5 (14.2)	14.7 (8.6)	14.0 (10.1)	0.829
IMC (kg/m <sup>2</sup> )	29.1 (6.2)	28.2 (7.5)	29.2 (4.8)	29.0 (7.9)	0.509
AC (cm)	32.0 (5.4)	31.0 (8.0)	32.5 (4.3)	33.0 (7.0)	0.567
CC (cm)	36.3 (4.6)	36.0 (6.0)	36.7 (4.9)	36.0 (5.0)	0.534

**Nota.** SD = standard deviation; IQ = interquartile range; GOT= Oxaloacetic Transaminase; GPT = Pyruvic Transaminase; BMI = body mass index; AC = Arm Circumference;



Of the sample, 39.66% of the patients were discharged, of whom 56.52% were men and 43.48% were women. Also noteworthy was the high mortality, especially among older patients, that is, those aged over 60 years (44.83%) of whom 76.92% were male.

## **Discussion**

The present study sought to correlate the clinical profile, anthropometric data and laboratory tests of Covid-19 patients admitted to the ICU with their clinical outcome, to provide evidence of nutritional screening in predicting outcomes for critically ill patients.

The role of the immune system is to protect the individual against pathogens. Diet is one of several factors that determine the immune response, and adequate nutrition is important to support the immune response (CALDER, 2021). The negative impact of poor diet on the immune system may be one explanation for the higher risk of more severe consequences of SARS-CoV-2 infection seen in older and obese individuals (CALDER, 2021). A balanced diet ensures a strong immune system that can withstand any attack by viruses (AMAN; MASOOD, 2020).

Nutritional status is an often overlooked component of infection severity (THOMAS et al., 2021). It is known that malnutrition severely compromises the immune system, weakens the immune response, and consequently increases the risk of infection and disease severity (SILVERIO et al., 2020). Many vitamins (A, B6, B12, folic acid, C, D, and E) and trace elements (zinc, copper, selenium, iron) play important roles in supporting the human immune system and reducing risk has been shown to fulfill of infection (CALDER, 2020). Balanced nutrition during disease progression and recovery is critical for improving health outcomes (KURTZ et al., 2021).

Anthropometric measurements are important for assessing the nutritional status of individuals, making it possible to obtain the composition of lean body mass and adipose tissue. Measurements of body mass index, arm circumference, body weight and height are commonly used (FONTOURA et al., 2006). Muscle mass plays an important role in modulating the immune response and supporting metabolic stress (LI e WANG, 2020).

Nutritional support is one of the biggest clinical challenges within the intensive care unit when talking about critically ill patients and, for some time now, the association between

malnutrition and the worst clinical evolution of critically ill patients has been admitted (NUNES et al., 2011).

The most recorded chronic diseases were SAH, DM and obesity, as was also observed in a study carried out in New York, based on the analysis of medical records of hospitalized Covid-19 patients (RICHARDSON et al., 2020). Obese patients with COVID-19 or who have been exposed to areas at high risk of COVID-19 infection, especially those who later develop suspected symptoms of COVID-19, should visit a health care facility for viral testing as soon as possible (YU et al., 2021). As obesity increases the risk of severe COVID-19 progression, more attention should be paid to infection surveillance and clinical management of obese COVID-19 patients (YU et al., 2021).

All patients analyzed had SARS-CoV-2 infection as risk factors, most were older adults (38; 65.52%) - the risk of death from coronavirus disease-2019 (COVID-19) increases significantly with age (TANG et al., 2020) - and some already had decreased renal function (increased creatinine) on admission. Impaired renal function in hospitalized Covid-19 patients is associated with increased in-hospital mortality and worse clinical outcomes (PECLY et al., 2021).

As COVID-19 becomes more serious, some patients may have hemophagocytic syndrome, causing a decrease in the number of red blood cells and, consequently, a decrease in hemoglobin, which is a protein found inside red blood cells, due to increased activity of macrophages in the splenic reticuloendothelial system and the liver, which can lead to splenomegaly, hepatomegaly (with increased GOT and GPT) and systemic lymph node enlargement (JUNIOR et al., 2020). The results of the present study corroborate the data in literature.

It was observed that of the patients in the present study, 27.59% had Ddimer levels six times higher than the reference value, while 17.24% had values ten times higher than the established reference value, which was 500 ng/dL. Elevation of the D-dimer is associated with an intense inflammatory reaction from the viral infection, as well as a greater risk of thromboembolic events during infection with the new coronavirus, which worsens the prognosis and increases the death rate (ROCHA et al., 2020).

According to studies on Covid-19, SARS-CoV-2 affects the elderly, obese and chronically ill more severely. In addition, the diagnosis of the disease was associated with factors such as malnutrition, and consequently lower anthropometric indices, leading to an increase in morbidity and mortality in the elderly population (MARTINEZ et al., 2020). Therefore, now more than ever,

widespread access to healthy food is a top priority, and people are adopting healthy eating habits to reduce vulnerability and long-term complications of COVID-19. is needed (BUTLER; BARRIENTOS, 2020).

### Limitations

The main limitation of the present study was its small sample size. This is because the study was carried out during the first wave of infection with the new coronavirus and there is no institutional protocol requiring all patients to have the same laboratory tests requested on admission, as well as to be evaluated by the Nutrition Service, ideally within the first 48 hours of hospitalization.

### Conclusions

In view of the theoretical basis and clinical observation to date, it was found that the older the patient, the lower the anthropometric values, and that older patients with chronic diseases had a worse prognosis for the evolution of Covid- 19. The importance of nutritional and laboratory screening of critically ill patients can therefore be seen and is required for an effective approach that reduces the mortality of these patients.

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Recebido em 28/11/2022 – Aprovado em 10/03/2023