International
Journal of
Health
Science

FACTORS ASSOCIATED WITH THE CLINICAL OUTCOME OF PATIENTS WITH COVID-19 ADMITTED TO AN INTENSIVE CARE UNIT

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Abstract: Introduction: The COVID-19 disease is a viral infection that can be complicated by different risk factors and can lead to death. Objective: To analyze the factors associated with the outcome (discharge or death) of patients with Covid-19 admitted to an intensive care unit. **Methodology** : Retrospective cross-sectional study with data from medical records of patients with Covid-19 admitted to the ICU of a university hospital in Cuiabá-MT, aged ≥ 20 years, of both genders, including pregnant women. Demographic, clinical, nutritional status and patient outcome variables were collected. Bivariate analysis was performed using Fisher's Exact Test and binary logistic regression using SPSS 17.0, with p<0.05 considered significant. **Results**: A total of 125 patients were evaluated, of which 53.6% were Gender Female and 46.3% were pregnant, with a mean age of 48.66 ± 18.33 years, most adults (71.2%) and of race/color brown (72.0%). Regarding comorbidities, 32.8% of the patients had arterial hypertension, 15.2% diabetes, 9.6% cardiovascular diseases, 5.6% other comorbidities, and 31.2% developed acute kidney injury (AKI). In the bivariate analysis, the outcome death was associated with Age of the elderly (p<0.001), hypertensive (p=0.002), presence of AKI (p=0.014) and two or more comorbidities (p=0.007), and Gestation (p=0.037). In the final multiple analysis, the outcome of death remained associated with the age of the elderly (p=0.004) and the presence of AKI (p=0.006). **Conclusion**: The presence of comorbidities, older age and the development of AKI were factors significantly associated with death in patients with Covid-19.

Keywords: COVID-19; Nutritional status; Comorbidities.

INTRODUCTION

COVID-19 is an infectious disease caused by the SARS-Cov-2 virus, which causes respiratory infections, ranging from the common cold to severe acute respiratory syndrome1. Declared a global emergency infection on January 31, 2020 by the World Health Organization (W.H.O.), around 627 million confirmed cases have been registered worldwide, and 6.5 million deaths from Covid-19 as of 30 October 20222;3.

With the increase in cases and the worsening of the disease, there was an increase in the number of admissions to the Intensive Care Unit (ICU) and a greater need for the use of respiratory support through pulmonary respirators4. The high number of people infected by severe cases started to generate high mortality rates for patients, especially those admitted to the ICU, the elderly and those with underlying medical conditions, such as the cardiovascular diseases, diabetes, chronic respiratory diseases or cancer4. Gestation was also considered a risk factor for Covid-195,6.

In view of the high mortality rate in the ICU, the epidemiological profile and clinical characteristics of patients who evolved to the most severe manifestation of Covid-197 were observed. In a study analyzed, it was observed that moderate to severe malnutrition was considered a risk factor for longer hospitalization8, while in several studies that evaluated overweight, and in particular obesity, proved to be an important prognostic factor in the increase of mortality in these patients. patients9,7,10.

It is known that most individuals admitted to the ICU in critical condition have a high nutritional risk, regardless of the clinical diagnosis, and that this risk increases considering several factors, such as length of stay, disease severity, age and length of stay. nutritional status prior to hospitalization. It is estimated that approximately 43 to 88% of critically ill patients admitted to the ICU have moderate to severe malnutrition, mainly

those on mechanical ventilatory support[9].

Given the above, this study aimed to analyze the factors associated with the clinical outcome of patients with Covid-19 admitted to an intensive care unit.

METHODOLOGY

This is a retrospective cross-sectional study with secondary data from the medical records of patients diagnosed with COVID-19 who underwent clinical treatment in the intensive care unit of the Hospital Universitário Júlio Muller, located in the city of Cuiabá, Mato Grosso, between the months of April 2020 to April 2021.

Data from patients of both genders, aged 20 years or older, pregnant or not, who tested positive for coronavirus (RT-PCR with detectable result for SARS-CoV2 or positive result for IgM antibodies and/or IgG, before or during hospitalization in the unit) and who underwent clinical treatment in the ICU during the study period. Medical records of patients with insufficient data were excluded from the survey.

Data were collected by consulting electronic medical records and the Nutrition Service. Demographic variables were investigated, namely: Gender (Male and Female); age, in complete years, subdivided into two age groups: 20-59 years (adults) and ≥60 years (elderly) and race/color (white, black, brown, oriental or indigenous). The clinical variables sought were: length of stay (in days); clinical outcome (discharge or death); and for pregnant patients, gestational age data (in complete weeks) were collected at admission. In addition, the presence or absence of comorbidities (diabetes, cardiovascular disease, chronic kidney disease, systemic arterial hypertension, acute kidney injury and other comorbidities) was investigated.

Anthropometric measurements of weight and height were collected from the medical record and refer to measurements obtained by the health team upon patient admission. From these measurements, the Body Mass Index (BMI) was calculated by dividing weight (in kg) by height squared (in meters). The nutritional status through BMI of non-pregnant men and women was classified according to age: adults[11] or elderly[12]. Pregnant patients had their nutritional status classified according to BMI by Gestational Age (GA)[13]. Based on the classification of nutritional status by BMI and/or BMI/GA, all patients were categorized as underweight, adequate weight or overweight (including cases of overweight and obesity in this category). Additionally, the categorization of the weight condition was performed by classifying them as "not overweight" (underweight and adequate) and "overweight" (overweight and obesity).

Data were stored in an Excel database and then analyzed using the SPSS statistical package, version 17.0 (SPSS Inc. Chicago IL, USA). In the descriptive analysis of the data, measures of central tendency of the data (mean, median, mode) were estimated and the absolute and relative frequencies of the Variables were calculated, to verify the consistency of the data and define the categories of the Variables. Continuous quantitative variables were presented as mean ± standard deviation and categorical variables were described as absolute and relative frequencies (%), with presentation in tables.

Bivariate analysis was performed using Pearson's chi-square test or Fisher's exact test to verify the association between categorical variables. The independent variables that presented p≤0.10 in the bivariate analysis were included in the binary logistic regression model. Were considered statistically significant the results that, in the final model, presented p<0.05.

This study was approved by the Ethics Committee for Research with Human Beings

of the Hospital Universitário Júlio Muller.

RESULTS

A total of 125 patients admitted to the ICU diagnosed with COVID-19 were included in the study. Most patients were Gender Female (53.60%, n=67) and among these, 46.30% (n = 31) were pregnant. The mean age was 48.66 ±18.33 years, with 71.20% (n=89) being adults and 28.80% (n=36) being elderly. Regarding race/color, 21.6% (n=27) were white, 72% (n=90) were brown, 5.6% (n=7) were black and 0.8% (n=1) was indigenous.

Regarding the presence of comorbidities, it was found that 32.8% (n=42) of the patients had systemic arterial hypertension (SAH), 15.2% (n=19) diabetes, 9.6% (n=12) cardiovascular diseases and 5.6% (n=7) had other comorbidities. Upon admission, 31.2% (n=39) of patients developed acute kidney injury. The average length of stay in the ICU was 21.57 (±16.71) days, ranging from 5 to 82 days of hospitalization.

In assessing the nutritional status, it was observed that 7.2% (n=9) were underweight, 29.6% (n=37) were classified as adequate weight and 63.2% (n=79) were overweight. Weight. Table 1 presents the bivariate analysis of initial weight according to demographic and clinical variables. There was no association between nutritional status and the variables Gender and race/color. However, there was a significant association between the initial nutritional status and age, showing that adult individuals had a higher frequency of overweight when compared to the elderly (p=0.024).

As for the outcome, 74.4% (n=93) of the patients were discharged and 25.6% (n=32) died. Table 2 presents the bivariate analysis of the patients' outcome according to demographic, clinical and nutritional status variables.

Among the demographic variables, only age group was significantly associated with the outcome, with a higher frequency of death in the elderly compared to adults (p<0.001). When analyzing the association between pregnancy and outcome, a significant difference was observed (p=0.037), demonstrating that non-pregnant women had a higher frequency of death, and pregnant women had a better outcome.

Of the total number of patients (n=42) who had SAH upon admission, 43.9% (n=18) died, thus associating the occurrence of SAH with a worse outcome (p=0.002). Furthermore, it was also analyzed that patients who developed AKI during hospitalization had a higher frequency of worse outcomes (p=0.014). In addition, the presence of two or more comorbidities was associated with the outcome of death (p=0.007). The outcome was not associated with the patients' initial weight status (p=0.673).

Table 3 presents the results of the crude multiple analysis by binary logistic regression between the outcome and the independent variables that presented p≤0.10 in the bivariate analysis by Pearson's Chi-Square or Fisher's Exact test. The pregnancy variable was not included in the final model because it has an absolute frequency different from the others.

In the multiple analysis, the variables age group (p=0.004) and acute kidney injury (p=0.006) remained associated with the outcome. Regarding age group, elderly people were 3.35 times more likely to die compared to adults. Patients who developed acute kidney injury were 3.71 times more likely to die compared to those patients who did not develop the disease.

DISCUSSION

With the development of this study, it was possible to verify that most of the patients admitted to the ICU with a diagnosis of COVID-19 were adults, female, mostly non-

Variables		Weight condition				Total		p-value#
		Without Overweight		Overweight				
		n	%	n	%	n	%	
Gender	Female	28	41,8	39	58,2	67	100	0,265
	Male	18	31,0	40	69,0	58	100	
Race/color	White and indian	7	25,0	21	75,0	28	100	0,183
	Brown and black	39	40,2	58	59,8	97	100	
Age	Adult	27	30,3	62	69,7	89	100	0,024*
	Elderly	19	52,8	17	47,2	36	100	
Gestation	Yes	14	45,2	17	54,8	31	100	0,628
	No	14	38,9	22	61,1	36	100	

#Fisher's Exact Test; *p ≤ 0.05 with significant differences

Table 1 - Bivariate analysis of initial weight condition, gestation and demographic variables of patients with Covid-19 admitted to the ICU of a university hospital, Cuiabá-MT, 2020-2021.

Variables (n=125)		Conclusion				Total		p-value#
		Discharge		Death				
		n	=%	n	%	n	%	
Gender	Female	52	77,6	15	22,4	67	100	0,416
	Male	41	70,7	17	29,3	58	100	
Age	Adult	75	84,3	14	15,7	89	100	<0,001*
	Elderly	18	50	18	50	36	100	
Race/color	White/indian	20	71,4	8	28,6	28	100	0,806
	Brown/black	73	75,3	24	24,7	97	100	
Gestation (n=67)	Yes	28	90,3	3	9,7	31	100	0,037*
	No	24	66,7	12	33,3	36	100	
Diabetes	Yes	11	57,9	8	42,1	19	100	0,089
	No	82	77,4	24	22,6	106	100	
Systemic Arterial Hypertension	Yes	23	56,1	18	43,9	42	100	0,002*
	No	70	83,3	14	16,7	84	100	
Cardiovascular disease	Yes	8	66,7	4	33,3	12	100	0,502
	No	85	75,2	28	24,8	113	100	
Acute Kidney Injury	Yes	23	59,0	16	41,0	39	100	0,014*
	No	70	81,4	16	18,6	89	100	
Number of comorbidities	0 - 1	61	83,6	12	16,4	73	100	0,007*
	≥ 2	32	61,5	20	38,5	52	100	
Weight Condition	Without overweight	33	71,7	13	28,3	46	100	0,673
	Overweight	60	75,9	19	24,1	79	100	

#Fisher's Exact Test; *p ≤ 0.05 with significant differences.

Table 2 – Bivariate analysis of the outcome according to demographic, clinical and nutritional status variables of patients with Covid-19 admitted to the ICU of a university hospital, Cuiabá-MT, 2020-2021.

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Variables	Raw Analysis		
	OR	(IC95%)	p-value
Age			0,004*
Elderly	4,35		
Adults	1,00	1,61-11,76	
Diabetes			0,223
Yes	2,38	0,60-9,62	
No	1,00		
Systemic Arterial Hypertension			0,152
Yes	2,43	0,72-8,17	
No	1,00		
Acute Kidney Injury			0,006*
Yes	4,71	1,55-14,34	
No	1,00		
Number of comorbidities			0,505
0-1	0,64	0,17-2,39	
2 or over	1,00		

OR: odds ratio; 95% CI: 95% confidence interval; *p<0,05.

Table 3. Binary logistic regression between the outcome and independent variables, of patients with Covid-19 admitted to the ICU of a university hospital, Cuiabá-MT, 2020-2021.

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pregnant, of mixed race/color, and who had at least one comorbidity prior to hospitalization. Of the observed comorbidities, systemic arterial hypertension, diabetes and acute kidney injury were the most prevalent and most patients were overweight on admission.

In other studies carried out with patients admitted to the ICU and with a picture of Covid-19, the age of the patients ranged from 20 to 92 complete years. [14,15]. In relation to race/color, corroborating the present study, a higher frequency of brown and black people was observed [16,17,18]. With regard to sex, a higher frequency of women was observed in this study and it is believed that this data is due to the fact that the ICU of the hospital where the data were collected was a reference for the care of pregnant or postpartum women with Covid-19 in the state of Mato Grosso. In national and international studies, ICU admission due to Covid-19 has been more frequent in males[10,15,19].

Regarding comorbidities, different studies have shown that patients with Covid-19 admitted to the ICU had some previous comorbidity [20,8,21]. A study carried out in Pernambuco at the University Hospital of Alagoas with 97 patients aged between 27 and 95 years, mostly female, found that 66.9% of patients were hypertensive and 41.2% were diabetic[22]. Another study carried out in a reference hospital for COVID-19 in the Federal District with 153 patients, it was observed that 65.3% had a diagnosis of hypertension and 36.6% a diagnosis of type 2 diabetes[20]. Another research carried out with the collection of retrospective data from 5 hospitals in California, in which 4,730 patients were evaluated, observed that 35.2% had hypertension, 33.3% had heart disease, 24% type 2 diabetes, and 17.3% were obese.[23]. In all these cited studies, an association between the presence of comorbidities and higher recurrence of deaths was suggested, as well as in the present study.

As it is a reference ICU for pregnant and puerperal women with Covid-19, it was observed in this study that most of the pregnant women attended had an improvement in their clinical condition and were discharged. Since it is a physiological process that involves several metabolic and nutritional changes to the body, most of the pregnancy tends to evolve without intercurrences.[5]. Regarding Covid-19 during pregnancy, there is still little information about it, but it is known that, with all these physiological changes, there are consequently changes in the immune cells of the lung, which can lead to worse prognoses[6].

In a study carried out in a reference maternity hospital in Salvador (BA), in which 412 pregnant patients who tested positive for COVID 19 were evaluated, the authors observed that 17.7% were hypertensive and 5.1% were diabetic, and of the total of patients, 93.4% were discharged, 5.8% were transferred to another unit, and only 0.7% died[24]. In another study, carried out with retrospective data from 408 pregnant women in Egypt, the authors compared the clinical course of the disease in relation to non-pregnant patients and observed that pregnant patients were more likely to be hospitalized, had a greater need for the use of a mechanical ventilator and had a severe evolution. of the disease, not being related to a significant number of deaths of these patients[25].

In the present study, a higher frequency of overweight was observed among adults compared to the elderly, at the time of admission to the ICU due to Covid-19 (p=0.024). Similar data were found in other studies [10,26-27]. In the USA, a survey with information from 7,424 patients hospitalized with Covid-19 in 88 hospitals in the state, the authors concluded that the highest BMI categories were associated with younger age [26]. Nationally, the Ministry of Health presented

descriptive and retrospective data collected through epidemiological disclosures from February to August 2020, also demonstrating that adults had a higher frequency of overweight [10]. Another study carried out in a hospital in the Federal District in the period 2020/2021, through data collection in electronic medical records, evaluated that 84.6% of adult patients were overweight and obese, while only 58% of the elderly had this same parameter[27].

In the bivariate analysis between the outcome and demographic variables, only the age group variable was significantly associated with the outcome, with older people dying more than adults (p<0.001). Similar data were also found in most of the analyzed studies.[7,22,23], in which they associated the most frequent outcome death among elderly patients. Nascimento et al. (2020) and Silva (2022) relate this prevalence of worse outcome among older patients to the presence of comorbidities and consequent susceptibility to clinical aggravations[28,29].

Among the evaluated comorbidities, SAH was significantly associated with the outcome of death (p=0.002). This result was also observed in several national studies [7,20,22] and international[23,30,31]. Such data were also found by Deng et al. (2021), which relates this to the association of hypertension and death due to the decrease in the activity of the angiotensin-2 converting enzyme (ACE-2), an enzyme that is a receptor for SARS-CoV-2, thus facilitating viral infiltration in the lung cells[32].

In addition, data were found in a study carried out in Bahia where 1768 patients were analyzed, of which 329 (18.6%) developed acute kidney injury, and of these patients with AKI, most were hypertensive (63,52%)[33]. Another study carried out in a private hospital in Rio de Janeiro, where 102 patients admitted to the ICU with Covid-19 were evaluated, and showed that 55.9% of these patients evolved to AKI during hospitalization, and of these patients with AKI, 66.7% had a diagnosis of SAH, pointing to it as an independent predictor for the development of acute kidney injury[21]. Based on these data, there is a significant relationship between SAH and the development of AKI.

The development of AKI in the evaluated patients was associated with the outcome death (p=0.014), similarly to what was observed in other studies [21,34]. So far, there are no studies that clearly clarify whether AKI in Covid 19 is caused by a cytopathic effect or due to the systemic inflammatory response itself. [35], what is suggested in severe AKI is the association with patients who progress to the most severe form of the disease, evolving with respiratory failure, followed by factors such as sepsis, need for nephrotoxic drugs and use of contrast for exams[34].

In the present study, a greater number of comorbidities was significantly associated with the outcome (p=0.007), and patients with 2 or more comorbidities at admission had a worse outcome. Corroborating these data, a survey carried out in China with retrospective information on 1,590 patients hospitalized with Covid-19, related higher numbers of comorbidities to worse clinical outcomes.[30]. Similar results were also found by Nuño et al. (2021), showing that patients with multiple comorbidities were more likely to be admitted to the ICU and/or die [23]. The cumulative effect of several associated comorbidities and the worsening and mortality due to covid-19 is still not known for sure, but it is known that a sum of comorbidities can together act to facilitate the entry of the virus into cells, favoring a more severe inflammatory response [36].

In the final multiple analysis, the variables age group (p=0.004) and acute kidney injury (p=0.006) remained associated with the outcome, with elderly patients having a 3.35 times greater chance of death compared

to adults and patients who developed AKI were 3.71 times more likely to die compared to those patients who did not develop the disease. Similar data from this same method of multiple analysis were also observed in a survey carried out with retrospective data from a university hospital in New York, where it was shown that patients with AKI and those who were older had significantly greater chances of mortality due to Covid-19[37].

The use of retrospectively collected data from medical records may present some limitations already manifested in the literature [38,39], related to incomplete notes, lack of necessary information and the presence of discrepancies in information since it is data filled in by third parties. However, even with these possible biases, the use of this information is feasible, especially in a pandemic period and the risk and difficulty of collecting data directly from patients with COVID-19. In addition, the use of BMI to assess the nutritional status of patients admitted to the ICU may be subject to biases related to the clinical condition of the patient, such as the presence of edema [40]. However, epidemiological studies have shown that, as it is a simple and quick measure, BMI can be used as a generic measure to assess the nutritional status of different populations [41].

CONCLUSION

Through this study, it was found that elderly, hypertensive patients who developed AKI and with two or more comorbidities had a significantly higher frequency of death. In the final multiple analysis, the elderly age group and the presence of AKI remained significantly associated with death. Thus, it was concluded that patients who developed AKI and those who were older had a higher frequency of the worst outcome, emphasizing the importance that this higher-risk population needs more rigorous monitoring. It must be noted that,

with the expansion of vaccination coverage of the population against Covid-19, it is possible that there will be variation in the analyzes carried out so far.

CONFLICTS OF INTEREST

We declare that there is no conflict of interest.

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