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Complications in hospitalized patients with SARS-CoV2 infection.

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ARTIGO ORIGINAL

ABSTRACT

OBJECTIVES: The present study aimed to assess the prevalence of complications during hospitalization in patients diagnosed with COVID-19, as well as the association with mortality and prognosis. **METHODS:** A retrospective cohort study involved 306 patients admitted to a COVID ward and ICU aged 18 years or older with confirmed SARS-CoV2 infection admitted to a Brazilian Tertiary Hospital. Demographic, clinical, biochemical, radiological and outcome data were collected from the patients' charts. **RESULTS:** According to the data analyzed during hospitalization, 230 (75.2%) patients developed complications, 281 (91.8%) patients had comorbidities and 169 (55.2%) patients died. There are no differences regarding the sex of the patients. The most prevalent complication was ventilator-associated pneumonia, present in 130 (42.5%) patients, followed by acute kidney injury or chronic kidney disease requiring hemodialysis, presented by 100 (32.7%) patients. The calculation of the relative risk of death according to the occurrence of complications showed $p<0.0001$ for acute renal failure, $p<0.0001$ for orotracheal intubation and $p=0.0434$ for acute myocardial infarction. **CONCLUSION:** The relative risk of death in COVID-19 is significant, showing an increase in relation to age, length of hospital stay and complications. Prevention, early diagnosis and appropriate treatment are essential to reduce the mortality rate in patients with SARS-CoV-2 infection.

Keywords: complications, covid-19, sars-cov2.

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INTRODUCTION

The resulting complications of SARS-CoV-2 infection account for about 20% of hospital admissions [1]. And among those hospitalized, 25% become critical patients, requiring admission to an intensive care unit [2]. The most common complications are related to the respiratory, neurological and cardiovascular systems, in addition to secondary infections [3-8].

Complications due to COVID-19 are frequently observed in the intensive care environment, and are considered a risk factor for increased mortality [9]. In addition to pulmonary complications, other systems can also be affected, such as the cardiovascular, immunological, hematopoietic, gastrointestinal and neurological systems, which can result in single or multiple organ failure and disseminated intravascular coagulation [10].

Severe SARS-CoV-2 infection is characterized by numerous dependent pathways triggered by hypercytokinemia, especially IL-6 and TNF-alpha, leading to systemic inflammation, hypercoagulability, and multiple organ dysfunction, which results in an unfavorable prognosis [11]. Although the virus mainly affects the respiratory system, extrapulmonary involvement appears to be an important contributor to its lethality and morbidity. Endocrine, metabolic and electrolyte disturbances caused by COVID-19 have been described [12].

Retrospective studies have described variable mortality in relation to pulmonary complications related to SARS-CoV-2 [13]. However, death can occur from numerous conditions, including cardiovascular and neurological complications [14]. Many complications are underdiagnosed in environments with limited resources due to hemodynamic instability of many patients, which makes it impossible to perform imaging tests and the short hospital stay due to death [7].

This study retrospectively analyzed in a cohort of critically ill patients with confirmed COVID-19 infection admitted to a Brazilian University Hospital the prevalence of complications related to this pathology during admission and hospitalization.

PATIENTS AND METHODS

To conduct this study, ethical standards in accordance with the Declaration of Helsinki were followed. It was approved by the Ethics Committee of the Hospital of the Federal University of Mato Grosso do Sul. Also, consent forms were collected from patients or legal representatives.

This is a retrospective cohort study, based on the review of medical records of patients with COVID-19 hospitalized from July 2020 to August 2021 at Hospital Universitário Maria Aparecida Pedrossian, Campo Grande, Brazil. During this period, to meet the public health requirements imposed by the SARS-CoV-2 pandemic, the Hospital's Adult Emergency Room was converted into an Intensive Care Unit (ICU).

The study included 306 patients over 18 years of age with confirmed COVID-19 infection. Figure 1 shows the patient register. The diagnosis of SARS-CoV2 infection was confirmed by nasopharyngeal swab RT-PCR tests, immunological test for nasal swab antigen search, and antigen tests. Patients were considered positive for COVID-19 if at least one of the tests was positive, in combination with clinical signs and symptoms of COVID-19 infection. After initial clinical evaluation, patients underwent laboratory tests and routine management in the ward or ICU. Demographic, clinical, biochemical, radiological and outcome data were collected from the patients' charts.

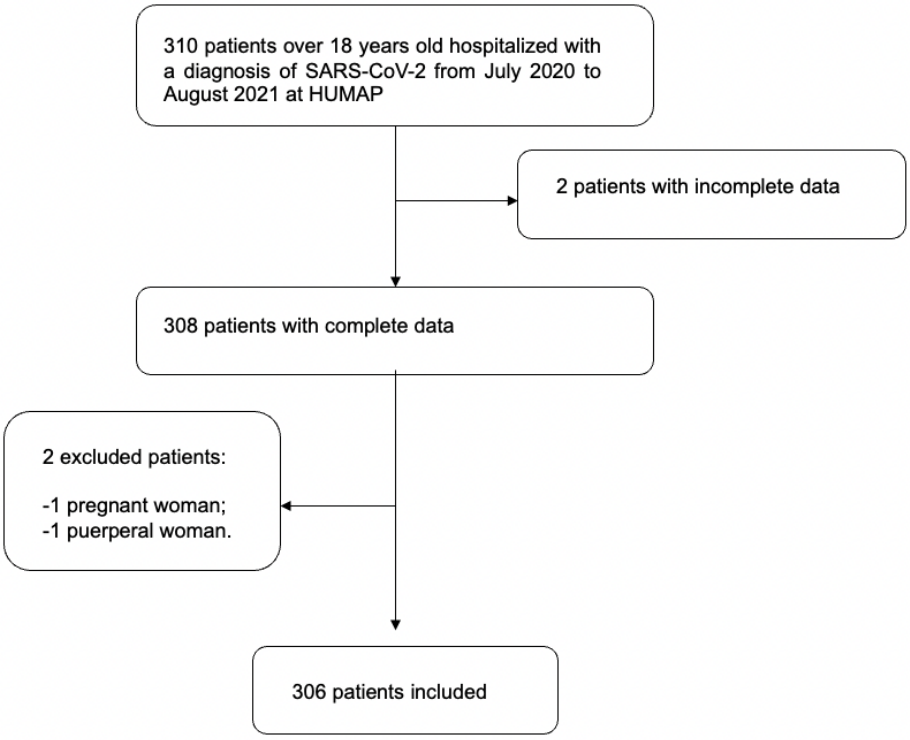

Figure 1. Study flowchart. The flowchart shows patient selection. In total, 310 patients were hospitalized with a positive diagnosis for SARS-CoV-2 and over 18 years of age in the period from July 2020 to August 2021. 2 patients had insufficient data for the study. 308 patients had complete data. 2 patients were excluded due to pregnancy-related body changes. 306 patients were included in the study.

Results are presented as mean ± standard deviation (SD) for normally distributed data and as median and interquartile range for non-normally distributed data. Proportion tests were used for the variables analyzed, as well as relative risk calculation. All tests were performed in Microsoft Excel for Mac, version 16.58.

RESULTS

A total of 306 patients were evaluated, of which 141 (46.1%) were female. The mean age of patients was 59.2□15.0 years, with female patients having a mean age of 58.4□14.5 years, and male patients 60.0□15.4 years, not an age difference between the sexes was observed (p = 0.3575; Student's t test for independent samples). The mean length of hospital stay was 22.6□17.5 days (01 to 100 days).

Table 01: distribution of patients regarding the need for orotracheal intubation, outcome, presence of comorbidity and complications during hospitalization (Campo Grande, 2022, n = 306).

	Absolute frequency	**Relative frequency**
Presence of comorbidities	281	91,8%
Need for orotracheal intubation	256	83,7%
Complications during hospitalization	230	75,2%
Deaths	169	55,2%

Table 02: distribution of patients regarding respiratory system complications (Campo Grande, 2022, n = 306).

	Absolute frequency	**Relative frequency**

Pneumonia associated with mechanical ventilation (with isolated germ)	130	42,5%
Pneumothorax	17	5,6%
Aspergillosis	7	2,3%
Lung disease requiring drainage	5	1,6%
Pneumomediastinum	4	1,3%
Hemothorax	2	0,7%

Table 03: distribution of patients regarding neurological system complications (Campo Grande, 2022, n = 306).

	Absolute frequency	**Relative frequency**
Convulsion	6	2,0%
Cerebral ischemia	6	2,0%
Cerebral hemorrhage	5	1,6%

Table 04: distribution of patients regarding complications of the cardiovascular system (Campo Grande, 2022, n = 306).

	Absolute frequency	**Relative frequency**
Cardiorespiratory arrest with return to spontaneous circulation	30	9,8%
Acute atrial fibrillation + Flutter	20	6,5%
Acute myocardial infarction	15	4,9%
Confirmed pulmonary thromboembolism	14	4,6%
High suspicion of pulmonary thromboembolism	14	4,6%
Monomorphic ventricular tachycardia	2	0,7%

Table 05: distribution of patients regarding other complications observed (Campo Grande, 2022, n = 306).

	Absolute frequency	Relative frequency
Acute kidney injury or chronic kidney disease requiring hemodialysis	100	32,7%
Nosocomial urinary tract infection	43	14,1%
Colitis requiring treatment with antibiotics	40	13,1%
Skin and soft tissue infection	32	10,5%
Bloodstream infection	13	4,2%
High digestive bleeding	7	2,3%
Hearing loss	2	0,7%

After the initial analysis, a comparison was made between the incidence of complications according to the death outcome. To compare the numerical variables, the Mann-Whitney test was used and the analysis of the categorical variables was performed using the Z Proportions Test.

Table 06: Characteristics of patients according to sex and age, length of stay, need for OTI and occurrence of complications according to the outcome (Campo Grande, 2022, n = 306).

	Death		
	Yes	**No**	**p-value**
Gender (F/M)[1]	78/91	63/74	0,6026
Age[2]	63,3±15,1	54,2±13,2	<0,0001
Hospitalization Days[2]	18,8±16,2	27,3±17,9	<0,0001
Orotracheal intubation[1]	166 (98,2%)	90 (70,3%)	<0,0001
Complications[1]	144 (85,2%)	86 (62,8%)	<0,0001

[1]Test of Proportions Z; [2]*Mann-Whitney Test*

Table 07: Test of Proportions for the occurrence of Pneumonia associated with mechanical ventilation (with isolated germ), pneumothorax, pneumomediastinum, hemothorax, lung disease requiring drainage, aspergillosis, cerebral hemorrhage, cerebral ischemia, seizure, acute kidney injury or kidney disease Chronic requiring hemodialysis, nosocomial urinary tract infection and upper gastrointestinal bleeding according to the outcome (Campo Grande, 2022, n = 306).

Complications	Death	N	Proportion	p-value
Pneumonia associated with mechanical ventilation (with isolated germ),	S	78	0,4615	0,1560
	N	52	0,3796	
Pneumothorax	S	11	0,0651	0,4182
	N	6	0,0438	
Pneumomediastinum	S	4	0,0237	0,0434
	N	0	0,0000	
Hemothorax	S	1	0,0059	0,8840
	N	1	0,0073	
Lung disease requiring drainage	S	1	0,0059	0,1470
	N	4	0,0292	
Aspergillosis	S	3	0,0178	0,5286
	N	4	0,0292	
Cerebral hemorrhage	S	4	0,0237	0,2400
	N	1	0,0073	
Cerebral ischemia	S	4	0,0237	0,5658
	N	2	0,0146	
Convulsion	S	3	0,0178	0,8040
	N	3	0,0219	
Acute kidney injury or Chronic Kidney Disease requiring hemodialysis	S	78	0,4615	<0,0001
	N	22	0,1606	
Nosocomial urinary tract infection	S	24	0,1420	0,8870
	N	19	0,1387	

High digestive bleeding	S	7	0,0414	0,0070
	N	0	0,0000	

Table 08: Test of Proportions for the occurrence of confirmed Pulmonary Thromboembolism, suspected pulmonary thromboembolism, deep vein thrombosis, acute atrial fibrillation + Flutter, venous thrombosis, acute myocardial infarction, cardiorespiratory arrest with return to spontaneous circulation, skin and parts infection moles, antibiotic-treated colitis, bloodstream infection, and hearing loss according to outcome (Campo Grande, 2022, n = 306).

Complications	Death	N	Proportion	p-value
Confirmed pulmonary thromboembolism	S	3	0,0178	0,0170
	N	11	0,0803	
Suspected pulmonary thromboembolism	S	7	0,0414	0,6964
	N	7	0,0511	
Deep vein thrombosis	S	2	0,0118	0,3092
	N	4	0,0292	
Acute atrial fibrillation + Flutter	S	15	0,0888	0,0576
	N	5	0,0365	
Venous thrombosis	S	2	0,0118	0,1566
	N	0	0,0000	
Acute myocardial infarction	S	12	0,0710	0,0382
	N	3	0,0219	
Cardiorespiratory arrest with return to spontaneous circulation	S	21	0,1243	0,0814
	N	9	0,0657	
Skin and soft tissue infection	S	19	0,1124	0,6234
	N	13	0,0949	
Colitis treated with antibiotics	S	20	0,1183	0,4890
	N	20	0,1460	

Bloodstream infection	S	6	0,0355	0,5192
	N	7	0,0511	
Hearing loss	S	0	0,0000	0,1702
	N	2	0,0146	

Table 09: Calculation of the relative risk of death according to the occurrence of complications (Campo Grande, 2022, n = 306).

Complication	Relative risk	Confidence interval	p-value
Acute renal failure	2,87	$1,90 \leq \mu \leq 4,36$	<0,0001
Acute myocardial infarction	3,24	$0,93 \leq \mu \leq 11,26$	0,0434
Orotracheal intubation	1,50	$1,32 \leq \mu \leq 1,69$	<0,0001

DISCUSSION

In the present study, 306 Brazilian patients admitted to a tertiary hospital with confirmed SARS-CoV-2 infection were retrospectively evaluated. We observed a relatively high prevalence of complications during their stay in this hospital (75.2%). Similar outcomes and prognosis (age, days of hospitalization, orotracheal intubation, death) were observed between male and female patients. We also observed an increase in the death rate in relation to complications.

The prevalence of comorbidity in our study differs from previously published data, as some studies reported a prevalence of less than 50% of comorbidity in patients with COVID-19 [15-17]. According to our data Docherty et al. also reported a higher prevalence of comorbidity (77.5%) in patients with COVID-19 in a mixed series (ICU and general ward) [18]. Our study, in line with previous work, includes patients in the general ward and critically ill patients with SARS-CoV-2.

Our data suggest a predominance of orotracheal intubation in patients affected by SARS-CoV-2. According to our data, one study observed the need for orotracheal intubation in 98.11% of patients [19]. In fact, the severity of COVID-19 disease has

already been associated with the need for mechanical ventilation [20], and the presence of complications appears to contribute to ICU admission [21].

During hospitalization, we observed that 75.2% of the patients developed complications. When we relate the rate of complications with the need for mechanical ventilation, this percentage increases even more (85.6%). Evaluating patients with COVID-19, Chen et al. observed, according to our data, that approximately 70% of patients develop complications during hospitalization [16, 22-23]. A recent study indicated that orotracheal intubation is significantly associated with complications [24]. In our series, up to 83.7% of patients used invasive mechanical ventilation during hospitalization, which could partially explain the acquired complications. In agreement with this suspicion, pneumonia associated with mechanical ventilation (with germ isolation) was the most frequent complication in relation to the pulmonary system. Previously published data corroborate our study [17, 21].

In our study, the second most prevalent complication was acute renal failure (or chronic kidney disease) requiring hemodialysis, in line with previously published data [11, 23, 25-26]. In addition, our data confirmed the association between acute kidney failure/chronic kidney disease (requiring hemodialysis) and mortality in COVID-19 ($p<0.001$). Studies point to higher mortality and worse prognosis [27-29].

The prevalence of neurological complications in our study differs from previously published data, as some studies reported a prevalence of 62.7% in hospitalized patients [30]. Our study, in contrast to previous publications, evaluated critically ill patients, many of whom were uncooperative or had a lowered level of consciousness at hospital admission and/or remained bedridden during the entire stay (impossible to carry out more complex exams).

As for complications of the cardiovascular system, when we evaluated pulmonary thromboembolism in relation to the outcome, we obtained a significant p ($p=0.0170$). In our study, the prevalence was relatively low (4.6%), however, it is believed that this value is underestimated because the hemodynamic instability of most of our patients made it impossible to travel to carry out confirmatory tests. In contrast to our study, pulmonary thromboembolism has been a much-cited complication [4, 31]. Another complication of the cardiovascular system with a significant p in relation to the outcome was acute myocardial infarction ($p=0.0382$), however, this pathology has a

relatively low frequency (4.9%) and does not present underdiagnosis as the previous one. In line with our study Saad et al. presented considerable risk of death in patients with acute myocardial infarction during COVID-19 infection [32].

Our data confirmed the relative risk of death according to the occurrence of some complications such as orotracheal intubation ($p<0.0001$), acute renal failure ($p<0.0001$) and acute myocardial infarction ($p=0.0434$). Many studies have observed a relationship between complications and mortality [4, 15, 21, 30, 33-35], no studies were found to contradict this statement.

The main strength of this study is the confirmation of SARS-CoV-2 in all included patients, in addition, it covers patients admitted to a sickbed and intensive care unit for COVID-19. This study has limitations, we have limited information about the date of onset of complications and the general condition of patients at hospital admission. Many patients were admitted in poor general condition, which limited the performance of bedside exams due to the lack of transport conditions for more complex and evidentiary exams for some pathologies.

DECLARATION OF INTEREST

The authors report no conflicts of interest in this work.

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