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Original Article

Pharmaceutical interventions in patients with Covid-19 in the Intensive Care Unit: A retrospective cohort

Intervenções farmacêuticas em pacientes com Covid-19 em Unidade de Terapia Intensiva: Uma coorte retrospectiva

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ABSTRACT

Objectives: to describe the role of the clinical pharmacist, patient profile, medications, exams, death rate and length of stay in patients admitted to the intensive care unit (ICU) due to Covid-19. **Methods:** non-compared retrospective cohort study of adult patients admitted to the Covid-19 ICU from six months. Data on dose, frequency and treatment time of the following classes of medications were collected: antimicrobials, corticosteroids, anticoagulants, colchicine, ivermectin and neuromuscular blockers. And, exam results: creatinine, D-dimers, ALT (alanine aminotransferase), AST (aspartate aminotransferase) and bilirubin. As well as the reason, quantity and outcome of the pharmaceutical interventions carried out. Data refer to the first 15 days of hospitalization and were collected from the electronic medical record, Scola® laboratory exam portal and the NoHarm® artificial intelligence system. **Results:** 174 patients were included, the average age was 61.8 ± 14.1 years, length of stay was 17.3 ± 14.4 days, male (58.0%), with previous comorbidities (95, 4%), using mechanical ventilation (75.4%) and a mortality rate of 58.0%. Antimicrobials were the most used followed by corticosteroids and anticoagulants. Age, use of mechanical ventilation, indication of anticoagulants, changes in creatinine and ALT were associated with death. One pharmaceutical intervention was carried out for every 13.1 prescriptions evaluated, with an acceptance rate of 86.8%. **Conclusions:** Pharmaceutical interventions and their outcomes showed the importance of the pharmacist in the care of Covid-19 patients together with the multidisciplinary team.
Keywords: COVID-19; SARS-CoV-2; Intensive Care Units; Pharmacy Service; Hospital, Pharmaceutical Services; Artificial Intelligence.

RESUMO

Objetivos: Descrever a atuação do farmacêutico clínico, perfil dos pacientes, medicamentos, exames, taxa de óbito e tempo de internação de pacientes internados em unidade de terapia intensiva (UTI) por Covid-19. **Métodos:** Estudo de coorte retrospectivo não-comparado de pacientes adultos internados em UTI por Covid-19 no período de seis meses. Foram coletados os dados de dose, frequência e tempo de tratamento de antimicrobianos, corticosteroides, anticoagulantes, colchicina, ivermectina e bloqueadores neuromusculares e resultados dos exames de creatinina, D-dímeros, ALT (alanina aminotransferase), AST (aspartato aminotransferase) e bilirrubina. Bem como, o motivo, quantidade e o desfecho das intervenções farmacêuticas realizadas. Os dados referem-se aos primeiros 15 dias de internação e foram coletados do prontuário eletrônico, portal Scola® de exames laboratoriais e do sistema de inteligência artificial NoHarm®. **Resultados:** Incluiu-se 174 pacientes, a média de idade foi de 61,8 ± 14,1 anos, tempo de internação de 17,3 ± 14,4 dias, sexo masculino (58,0%), com comorbidades prévias (95,4%), em uso de ventilação mecânica (75,4%) e mortalidade de 58,0%. Os antimicrobianos foram mais utilizados, seguido de corticosteroides e anticoagulantes. Idade, uso de ventilação mecânica, indicação para uso de anticoagulante, alteração de creatinina e ALT foram associados com o óbito. Foi realizada uma intervenção farmacêutica a cada 13,1 prescrições avaliadas, com uma taxa de aceitação de 86,8%. **Conclusões**: As intervenções farmacêuticas e seus desfechos mostraram a importância do farmacêutico no cuidado do paciente crítico com Covid-19 em conjunto com a equipe multiprofissional.
Palavras-chave: COVID-19; SARS-CoV-2; Unidades de Terapia Intensiva; Serviço de Farmácia Hospitalar; Assistência Farmacêutica; Inteligência Artificial.

Introduction

COVID-19 caused by the emerging coronavirus SARS-CoV-2 can present in various forms, ranging from asymptomatic infection to severe infection with primarily respiratory symptoms, potentially leading the patient to develop multiple organ failure and progress to death.[1,2] About 17% to 35% of hospitalized patients with COVID-19 require treatment in an Intensive Care Unit (ICU) due to hypoxemic respiratory failure.[3]

In this scenario, the clinical treatment and management of patients hospitalized for COVID-19 have become a significant challenge.[4] For pharmacists working in the ICU, the routine practice that was already considered stimulating, due to the complexity of prescriptions, the risk of multiple organ failure, clinical instability, and multiple critical conditions[5], has become even more complex with the increase in cases of patients infected with SARS-CoV-2.

Until the second half of 2021, no treatment had proven effective against the infection caused by SARS-CoV-2, and the search for effective therapies continues to be a challenge.[6] However, some classes of medications are used in clinical practice as adjunctive therapy, such as antivirals, anti-inflammatory agents, low molecular weight heparins, plasmas, and immunoglobulins. The choice of therapy may vary depending on the patient's profile and the stage of the disease.[7]

Clinical pharmacy is focused on the practice of rational drug use, where pharmacists provide patient care to optimize pharmacotherapy, promote health and well-being, and prevent diseases.[8] Studies show that the presence of a clinical pharmacist in the ICU is associated with fewer adverse drug events and better clinical outcomes, as well as cost reduction.[9,10,11] Pharmaceutical interventions refer to a series of actions in which pharmacists provide individualized and patient-centered care, making and documenting recommendations aimed at preventing or resolving medication-related problems (MRPs).[12]

The role of the hospital pharmacist during the COVID-19 pandemic has proven to be quite extensive, encompassing strategies to ensure the availability, dispensing, and safe use of medications, as well as facilitating effective interaction and communication with the multidisciplinary healthcare team.[13] According to García-Gil (2020), the presence of a pharmacist in the ICU facilitates the questioning of doubts by multiprofessional clinical teams.[14] Thus, it is possible to maximize the effectiveness and minimize the risks associated with medication therapies that are inherent to the current pandemic scenario.[13]

Objectives

To describe the profile of hospitalized patients, the main medications used, present clinical aspects, laboratory tests, mortality rate, and length of stay of patients hospitalized for COVID-19 in an adult ICU. Additionally, it aims to describe the profile of pharmaceutical interventionsa performed, the outcomes regarding acceptance, and to demonstrate the importance of the clinical pharmacist's role in patient monitoring in the ICU.

Methods

A non-comparative retrospective cohort study was conducted in an ICU of a general hospital within a healthcare complex in southern Brazil, originally with twenty beds, which were expanded to twenty-eight specifically for patients with COVID-19 due to the increase in cases of the disease.

Patients hospitalized in the ICU for COVID-19, aged eighteen years or older, who remained in the unit for more than 48 hours between September 1, 2020, and February 28, 2021, were included, totaling a six-month period. Patients with incomplete information in their medical records were excluded. The sample was identified by census based on the hospital occupancy report provided for the sector of interest.

Data were collected regarding the first 15 days of hospitalization using a pre-structured spreadsheet, based on electronic medical records in the Tasy®

system, the Scola® portal for laboratory tests, and the NoHarm® artificial intelligence system.

The collected variables related to the patient included: age, sex, weight, height, body mass index (BMI), pre-existing comorbidities prior to hospitalization (transplant, asthma, chronic obstructive pulmonary disease (COPD), systemic arterial hypertension (SAH), diabetes mellitus (DM), HIV, cancer, hepatitis, chronic kidney disease (CKD), obesity), use of azithromycin, hydroxychloroquine, and ivermectin before hospitalization, duration of mechanical ventilation (MV), length of stay, and outcome (discharge to walking or death). Data on dosage, frequency, daily dose, and days of use of the following classes of medications were collected: antimicrobials, corticosteroids, anticoagulants, colchicine, ivermectin, and neuromuscular blockers (NMB). Regarding laboratory tests, the following exams were monitored: creatinine, D-dimers, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin.

The hospital under study has a team of clinical pharmacists who work extensively across all hospital beds and clinical pharmacists in residency in the intensive care unit. For this study, pharmaceutical interventions carried out by the clinical pharmacist in person with the team were included. The clinical pharmacy service uses the NoHarm® system for recording pharmaceutical interventions, which has its own classification for the types of interventions, including: allergies, scheduling, presentation, medication reconciliation, dilution/infusion rate, dose adjustment based on renal/hepatic function, extra dose, dose omission, overdose, underdose, duplicity, lack of documentation/workflow, pharmaceutical form, frequency, incompatibilities, indication/necessity, drug interactions, drug shortages, monitoring, non-standardized medications, guidance, protocols, route of administration, and others. Interventions related to dosing were grouped as dose adjustments for the presentation of the study results. Data collected included the number of prescriptions evaluated, the number of pharmaceutical progress notes made in the electronic medical record, the number and type of pharmaceutical interventions, outcomes (accepted, not accepted, and not applicable), and the medications involved. For assessing the acceptance of the intervention, pharmaceutical interventions not subject to acceptance by the prescriber were excluded, such as identifying the need for monitoring (of serum levels, laboratory tests, or treatment duration), which is used to signal such follow-up for the pharmacist. For these interventions, the term "not applicable" was applied.

For the calculation of BMI, the classification of the World Health Organization (WHO)[15] was used for patients up to 60 years old, according to the scale of the Pan American Health Organization (PAHO)[16] for patients over 60 years old. The results of qualitative variables were presented through frequency and percentage, and quantitative variables through mean and standard deviation. The association of qualitative variables with outcomes was verified using the Chi-Square test or Fisher's Exact test, when appropriate, and for quantitative variables using the Student's t-test and Mann-Whitney test for symmetric and asymmetric distributions, respectively. The quantity of medications was calculated by summing the amounts of the different medications found. Medications were presented through the average dose, average daily frequency, and total average duration of use, such that for a patient who received different doses of the same medication, the average dose and average frequency were assigned, while the days of use were summed. Results with a p-value <0.05 were considered significant. The analyses were performed using the SPSS statistical software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

The study was submitted and approved by the Ethics and Research Committee, according to opinion number 4.634.952.

Results

A total of 174 patients were included in the study, with an average age over 60 years and pre-existing comorbidities. The mortality rate was 58.0%, as presented in Table 01.

Table 01. Clinical data of adult patients (n=174) with COVID-19 hospitalized in the Intensive Care Unit of a tertiary hospital from September 1, 2020, to February 28, 2021.

Variable	Number of patients (n=174) or mean + standard deviation	Percentage (%)
Sex		
Feminine	73	42,0
Masculine	101	58,0
Age (years)	61,8 ± 14,1	
Need for mechanical ventilation		
Yes	131	75,3
No	43	24,7
Length of hospital stay (days)	17,3 ± 14,4	
BMI(kg/m²)	28,9 ± 7,3	
Outcome		
Discharge	73	42,0
Death	101	58,0
Previous comorbidities		
Yes	166	95,4
No	8	4,6
Transplant	23	13,2
Renal	19	82,6
Hepatic	4	17,4
Asthma	12	6,9
Chronic obstructive pulmonary disease	18	10,3
Systemic arterial hypertension	102	58,6
Diabetes mellitus	53	30,5
HIV	1	0,6
Cancer	26	14,9
Hepatitis C	9	5,2
Chronic kidney disease	14	8,0
Use of medication prior to hospitalization for Covid-19		
Yes	14	8,0
No	160	92,0
Azithromycin	13	7,5
Ivermectin	6	3,4
Others	7	4,0
Presence of changes in exams in the first 15 days		
Creatinine	124	71,3
D-dimer	151	86,8
ALT	64	36,8
AST	116	66,7
Total bilirubin	17	9,8

Source: Prepared by the authors

During the first fifteen days of hospitalization in the ICU, considering the classes of medications included in the study, the average number of medications prescribed per patient was 6.37. Antimicrobials were the most frequently used therapeutic class, followed by corticosteroids and anticoagulants, as presented in Table 02.

Table 02. Average dose, average frequency, average daily dose, and duration of use of antimicrobials, corticosteroids, anticoagulants, colchicine, ivermectin, and neuromuscular blockers used by adult patients with COVID-19 during the first 15 days of hospitalization in the Intensive Care Unit of a tertiary hospital in Porto Alegre/RS, from September 2020 to February 2021.

Therapeutic class	Medicine	N patients (n=174)	%	Average dose	Average frequency	Average daily dose	Duration of use (days)
Antimicrobials	Meropenem, mg	95	54,6	893,3	3,0	2679,9	7,9
	Polymyxin B, UI	74	42,5	1087172,3	2,0	2174344,6	7,5
	Azithromycin, mg	60	34,5	500	1,0	500	4,6
	Vancomycin, mg	57	32,8	1000	1,8	1800	5,5
	Piperacilin + Tazobactam, g	48	27,6	4,4	3,0	13,2	6,0
	Ampicilin + Sulbactam, mg	41	23,6	2902,4	3,7	10738,9	5,6
	Ceftriaxone, mg	50	28,7	1680,0	1,3	2184	6,5
Corticosteroids	Dexamethasone, mg	144	82,8	6,0	1,0	6,0	9,5
	Methylprednisolone, mg	42	24,1	89,7	2,7	242,2	11,2
	Prednisone, mg	7	4,0	22,9	1,0	22,9	3,0
	Hydrocortisone, mg	30	17,2	66,7	3,4	226,78	6,0
Anticoagulants	Subcutaneous Heparin, UI	91	52,3	5000	2,4	12000	*
	Enoxaparin, mg	111	63,8	56,9	1,5	85,35	*
	Heparin	44	25,3	Infusão contínua		-	*
	Fondaparinux, mg	3	1,7	3,5	1,3	4,55	*
	Colchicine, mg	15	8,6	0,5	2,7	6,75	7,1
	Ivermectin, mg	16	9,2	13,9	1,0	13,9	2,1
NMB	-	97	55,7	-	-	-	-

Source: prepared by the authors.
NMB: neuromuscular blocker
*Data were not collected as they varied greatly throughout hospitalization (infusion speed) according to the patients' clinical examinations.

The variables age, use of Mechanical Ventilation, indication of anticoagulant, alteration of creatinine, and ALT were significantly associated with mortality, as shown in Table 03.

Table 03: Bivariate association between clinical variables and discharge or mortality of adult patients with COVID-19 during the first 15 days of hospitalization in the Intensive Care Unit of a tertiary hospital in Porto Alegre/RS, from September 2020 to February 2021.

Variable N		Discharge		Death		p-value
		%	N	%		
Sex	Feminine	32	43,8	41	56,2	0,669
	Masculine	41	40,6	60	59,4	
Age	up to 60 years	37	62,7	22	37,2	**0,000**
	60 years or older	36	31,3	79	68,7	
Body Mass Index	Mean and SD	29,4	8,6	28,6	6,2	0,429
Mechanical ventilation	Yes	34	26,0	97	74,0	**0,000**
	No	39	90,7	4	9,3	
Previous comorbidities	Yes	69	41,6	97	58,4	0,722
	No	4	50,0	4	5,0	
Creatinine*	Changed	33	26,6	91	73,4	0,000
	No change	40	81,6	9	18,4	
D-dimers*	Changed	62	41,1	89	58,9	0,719
	No change	4	50,0	4	50,0	
Indication of anticoagulation	Yes	30	34,1	58	65,9	**0,035**
	No	36	50,7	35	49,3	
Alanine transaminase*	Changed	25	39,1	39	60,9	0,569
	No change	41	43,6	53	56,4	
Aspartate transaminase*	Changed	42	36,2	74	63,8	**0,013**
	No change	24	58,5	17	41,5	
Total bilirubin*	Changed	3	17,6	14	82,4	0,064
	No change	60	43,5	78	56,5	

Source: prepared by the authors
*Exams with changes in the first 15 days of hospitalization in the Intensive Care Unit.

A total of 8,252 prescriptions were generated, of which 8,123 (98.4%) were evaluated by the pharmacist. 369 pharmaceutical evolutions were recorded in the electronic medical record. Additionally, 621 pharmaceutical interventions were documented, resulting in a rate of 1 intervention for every 13.1 evaluated prescriptions. The types of pharmaceutical interventions performed can be seen in Table 04.

Of the total pharmaceutical interventions performed, 212 were acceptable by the prescriber, resulting in an acceptance rate of 86.8%, with the most frequent being for duplication (27.4%). For pharmaceutical interventions where acceptance does not apply, we can highlight the identification of the need for laboratory monitoring (57.2%) of tests or medications, which is carried out by the clinical pharmacy team.

Table 04: Type and number of pharmaceutical interventions performed on prescriptions for adult patients with COVID-19 in the Intensive Care Unit of a tertiary hospital in Porto Alegre/RS, from September 1, 2020, to February 28, 2021.

Type of intervention	Number	%
Monitoring	355	57,17
Dose adjustment	99	15,94
Duplicity	58	9,34
Guidance	28	4,51
Frequency - If necessary	23	3,70
Presentation	16	2,58
Non-standardized	13	2,09
Treatment time	7	1,13
Indication	7	1,13
Appointment	3	0,48
Pharmaceutical form	3	0,48
Route of administration	3	0,48
Replacement of missing medication	2	0,32
Others	2	0,32
Dilution/infusion rate	1	0,16
Protocols	1	0,16
Total	621	100

Source: prepared by the authors.
IN: if necessary.

Regarding the medications involved in the interventions, polymyxin B had the highest number of interventions (n=22), primarily related to the dosage of the antimicrobial (Table 5). Dexamethasone had 13 interventions, most of which pertained to the duration of treatment.

Discussion

In the present study, we found a rate of 1 pharmaceutical intervention for every 13.1 prescriptions evaluated for patients hospitalized in the ICU with COVID-19. The acceptance rate of the interventions was 86.8%. The identification of the need for monitoring medication use by the pharmacist, dose adjustments, and the occurrence of duplications were the three most frequent interventions.

The profile of adult patients with COVID-19 hospitalized in the ICU primarily includes male patients with an average age over 60 years, a high mortality rate, and significant use of antibiotics, corticosteroids, neuromuscular blockers, and the need for anticoagulation.

As this is an emerging disease, the profile of the patients most affected by COVID-19 was unknown. According to reports from the most recent literature, during the period when the research was conducted, the majority of patients hospitalized in the intensive care unit for COVID-19 were male and around 60 years old[17], which aligns with the findings in this study's sample. The high mortality rate of 58%, when compared to other studies, can be justified by the fact that the data was only collected from patients admitted to the ICU, who are clinically more severe and unstable.[18,19] Furthermore, a significant portion of the study's patients required mechanical ventilation, which was associated with the outcome of death, potentially explaining the elevated mortality rate as well.

Regarding the presence of comorbidities, a meta-analysis conducted on the epidemiological characteristics of patients hospitalized in the ICU with COVID-19 indicated that hypertension was the most common pre-existing comorbidity in the population, as demonstrated in this study. Additionally, obesity was frequently observed in patients who developed severe complications.[20]

Tabela 05: Medicamentos envolvidos, motivos, quantidade e percentual das intervenções farmacêuticas em relação ao total das intervenções passíveis de aceite realizadas no período de 6 meses em pacientes adultos com Covid-19 em uma unidade de terapia intensiva de um hospital terciário de Porto Alegre/RS.

Medicamento	Type of intervention	Number	%
Polymyxin B	Dose	20	9,4
	Frequency	2	0,9
Dexamethasone	Treatment time	7	3,4
	Dose	5	2,4
	Duplicity	4	1,9
	Pharmaceutical form	1	0,5
Meropenem	Dose	4	1,9
	Duplicity	3	1,4
	Frequency	3	1,4
	Indication	1	0,5
Vancomycin	Dose	8	3,8
	Frequency	3	1,4
	Duplicity	2	0,9
	Indication	1	0,5
Heparin	Dose	5	2,4
	Duplicity	2	0,9
	Frequency	2	0,9
	Presentation	1	0,5
Anidulafungin	Dose	8	3,8
	Indication	1	0,5

Source: prepared by the authors.

Regarding the medications used in the first fifteen days of hospitalization, the findings were consistent with the literature, considering the period and scientific evidence on the treatment of patients with COVID-19. The Surviving Sepsis Campaign Coronavirus Disease 2019 indicates that potential pharmacotherapy for adult patients with severe or critical COVID-19 requiring ICU admission includes systemic corticosteroids, with dexamethasone recommended over other medications in this class, as well as the use of venous thromboprophylaxis.[21]

The use of antimicrobials was notably present, particularly those with empirical coverage for gram-negative bacilli (GNB), such as Meropenem and Polymyxin B, which is consistent with the retrospective study conducted in Wuhan involving 1,495 patients, where 85% of them had GNB in cultures.[22,23] Azithromycin was used by approximately 34% of the sample and has been proposed as an adjunct therapy for COVID-19 due to its antiviral and immunomodulatory activity, although the evidence regarding its use does not demonstrate any benefit. Despite this, azithromycin has frequently been used in conjunction with hydroxychloroquine, which has also shown no benefits.[24]

In the present study, dexamethasone was used at an average daily dose of 6 mg for an average duration of 9.5 ± 4.5 days by 82.8% of the patients, which justifies why the pharmaceutical intervention regarding treatment duration was the most frequent and accepted for this medication. The randomized clinical trial RECOVERY, which utilized dexamethasone at a dose of 6 mg/day for 10 days or equivalent, demonstrated a reduction in mortality at 28 days among patients who received the medication and were on mechanical ventilation or requiring oxygen.[25]

Regarding the alteration of D-dimers, a biochemical marker related to coagulation used in clinical practice, along with other tests, to determine the need for anticoagulation in the patient[26], 95% of the study population presented changes in this condition. Concerning thromboprophylaxis or anticoagulation in this patient profile, its use is justified by evidence of microvascular thrombosis in the lungs of patients who died from COVID-19 and also because it is common in this population to observe thrombocytopenia, elevated levels of fibrinogen and D-dimers, in addition to other alterations related to blood coagulation.[27] According to the evidence used, anticoagulation is suggested for patients with very high levels of D-dimers ($> 3.0\ \mu g/mL$)[28]; this cutoff value for determining the need for treatment-dose anticoagulants means that not every patient with any alteration in D-dimers will be anticoagulated, which justifies having more patients with altered D-dimers than those requiring anticoagulation.

The low molecular weight heparin (LMWH), enoxaparin, was the most prescribed anticoagulant (65.5%). According to Smith et al. (2020), LMWH was suggested as the anticoagulant of choice compared to unfractionated heparin (UFH) due to its ability to reduce the need for healthcare personnel to have direct contact with infected patients. However, specific characteristics of each patient must be considered to guide therapy, such as laboratory results, renal function, and the presence of bleeding.[29] Considering that 71.3% of the patients had altered creatinine levels, indicating impaired renal function, dose adjustments and frequency or even a change in the type of heparin should be considered for these patients, which justifies the types of pharmaceutical interventions conducted.

Another notable aspect of the studied patients was the significant association between the use of neuromuscular blockers (NMB) (55.7%) and the outcome of death in this population (71.4%). The need for NMB in adult patients on mechanical ventilation is justified in cases of moderate to severe acute respiratory distress syndrome (ARDS) and in those with persistent ventilatory asynchrony or those requiring continuous deep sedation.[21] A multicenter prospective observational study demonstrated that patients with COVID-19 experienced extensive and prolonged use of NMB, and there was no association with a lower extubation rate by the 28th day of the disease course.[30]

Another significant variable related to patient outcomes was the alteration of AST. Changes were observed in both AST and ALT, as well as in total bilirubin. The frequency of these alterations is similar to that reported in the literature and is more commonly found in severe patients.[31] However, although the association between the outcome and this laboratory alteration was significant, we must also consider other factors that could cause these changes, such as medication-induced hepatotoxicity, especially since this study was conducted during a pandemic period when many medications were used at off-label dosages.[31]

Ivermectin and colchicine have been used as alternative strategies for the treatment of COVID-19, with less than 10% of the studied population using these medications during the first 15 days of hospitalization in the unit, and no correlation was observed between the use of these drugs and the clinical outcomes of the patients. A recent randomized clinical trial investigated the use of ivermectin in reducing symptoms in patients with mild disease and found no significant improvement in the time to symptom resolution; furthermore, serious adverse events, such as organ failure, were reported.[32] Colchicine, used in combination with other medications with anti-inflammatory properties, was evaluated in a study aimed at assessing the effect of this drug on cardiac and inflammatory biomarkers and on clinical outcomes in patients hospitalized with COVID-19.[33] The results showed a significant improvement in the time to clinical deterioration among the patients; however, no considerable differences were observed in troponin levels or C-reactive protein.[34]

Regarding the pharmaceutical interventions, the acceptability rate of 87% is consistent with the literature, which can vary from 47% to 100%.[36] This high rate can be justified by the verbal communication conducted by the clinical pharmacist within the intensive care unit directly with the healthcare team. It is noteworthy that the presence of the pharmacist in the ICU is due to the existence of a multiprofessional residency program in Intensive Therapy, which has been in place at this hospital for the past 10 years.

Antimicrobials were the therapeutic class with the most pharmaceutical interventions carried out, followed by corticosteroids. This can be justified by the high consumption of these medications in the Intensive Care Unit and their use for the condition in question. Previous studies indicate that the class of anti-infectives is one of the main contributors to medication-related problems (MRPs).[35,36] Furthermore, among the interventions that were accepted, those related to medication dosing were the most frequent in the ICU, which is extremely important to avoid harm to the patient's clinical condition and to ensure the effectiveness of the treatment.[37]

In light of this panorama, the characterization of pharmaceutical interventions in patients with COVID-19, their acceptance rate, and the outcomes are the main scientific contributions to the literature. Reports of pharmaceutical interventions in the hospital setting have been published with the aim of sharing the advancements and importance of clinical pharmacy services in Brazil.

The present study has some limitations, such as clinical data of patients collected directly from the electronic medical records based on the progress notes of the multiprofessional teams. As this is a retrospective study, there may have been underreporting of medications used prior to hospitalization due to recall bias. Furthermore, data related to medications were collected from electronic prescriptions, which may differ from those actually administered to the patient, particularly in cases of suspensions prepared by the team or when medications were prescribed "as needed" or "at the discretion of the medical team." Continuous infusion medications did not have their infusion rates collected due to constant variation and the lack of reports on the duration of administration at each infusion rate, making it impossible to calculate the dose received by the patient.

Conclusions

The presence of a clinical pharmacy service in a context of extreme severity can prevent prescription errors regarding dosage, frequency, and duration of treatment indicated. Furthermore, in an exceptional scenario such as the COVID-19 pandemic, the interaction among the multiprofessional team in decision-making and discussions adds value and accuracy to the therapeutic choices for patient treatment.

During the first fifteen days of hospitalization in the ICU, antimicrobials, corticosteroids, and anticoagulants were the classes of medications most frequently used, demonstrating a correlation with COVID-19 or complications arising from it or from hospitalization. A pharmaceutical intervention was performed for every 13.1 prescriptions evaluated. The pharmaceutical interventions were aligned with the profile of the medications used and the characteristics of the patients. The high acceptance rate of the interventions highlighted the importance of having a pharmacist present in the unit to monitor and work alongside the multiprofessional team for adult patients with COVID-19 hospitalized in the ICU.

Contributions of the authors:
GL: investigation, methodology, administration, planning, and editing; TDH: writing, editing, and data curation; MCW: responsible for review, editing, and supervision; CRB: responsible for review, editing, supervision, and formal analysis.

Conflicts of Interest:
All authors declare that there are no conflicts of interest.

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