Impact of the COVID-19 Pandemic on Pharmacist Interventions: A Retrospective Study with Inpatients in a University Hospital

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ABSTRACT

Background: Despite growing interest in understanding the challenges faced by multidisciplinary health teams during the COVID-19 pandemic, there is a lack of studies specifically focusing on changes in pharmacist interventions and drug-related problems.

Objectives: To analyze and compare the interventions performed by pharmacists during comprehensive medication management in the adult intensive care unit and general internal medicine ward of the University Hospital of the University of São Paulo, Brazil, for defined periods before the onset of the COVID-19 pandemic and during the pandemic itself.

Methods: All pharmacist interventions performed in relation to inpatient prescriptions from March to December 2019 (before the pandemic) and from March to December 2021 (during the pandemic) were collected and tabulated. These interventions were then classified according to the Pharmaceutical Care Network Europe (PCNE) system, version 9.1, and categorized based on first-level codes of the Anatomical Therapeutic Chemical classification system.

Results: The analysis revealed substantial changes in the patterns of pharmacist interventions and the therapeutic classes of drugs for COVID-19-positive and COVID-19-negative patients during the pandemic relative to patients in the pre-pandemic period. Among COVID-19-positive patients, interventions were predominantly related to enhancing patient safety (PCNE code P2), drug selection (C1), dose selection (C3), prescribing and dispensing processes (C5), the drug-use process (C6), and patient transfers between different levels of care (C8). The drug-related problems addressed by pharmacist interventions primarily involved COVID-19-positive patients in the pandemic period and were related to systemic hormonal preparations (excluding sex hormones and insulins), anti-infective agents for systemic use, nervous system and drugs for the blood and blood-forming organs.

Conclusion: The results of this study highlight the adaptability and competence of pharmacists in responding to critical scenarios such as the COVID-19 pandemic. These scenarios are characterized by new work dynamics, the hiring of additional professionals, an increase in the number of beds, the rapid evolution of evidence-based information, and drug shortages that necessitate the use of alternative medications. Pharmacists play a crucial role in ensuring patient safety during these difficult times.

Key words: clinical pharmacy, pharmacist interventions, pandemic, COVID-19

RÉSUMÉ

Contexte : Malgré un intérêt croissant pour la compréhension des défis auxquels les équipes de santé multidisciplinaires ont été confrontées pendant la pandémie de COVID-19, peu d'études portent sur les changements chez les interventions des pharmaciens et les problèmes liés aux médicaments en particulier.

Objectifs : Analyser et comparer les interventions réalisées par les pharmaciens lors de la gestion globale des médicaments dans l'unité de soins intensifs pour adultes et le service de médecine interne générale de l'hôpital universitaire de l'Université de São Paulo, Brésil, pendant des périodes définies avant le début de la pandémie de COVID-19 et pendant la pandémie elle-même.

Méthodologie : Toutes les interventions des pharmaciens réalisées en lien avec les prescriptions hospitalières de mars à décembre 2019 (avant la pandémie) et de mars à décembre 2021 (pendant la pandémie) ont été collectées et compilées. Ces interventions ont ensuite été classées selon le système du Pharmaceutical Care Network Europe (PCNE), version 9.1, et catégorisées sur la base des codes de premier niveau du système de classification anatomique, thérapeutique et chimique.

Résultats : L'analyse a révélé des changements substantiels dans les types d'intervention des pharmaciens et dans les classes thérapeutiques de médicaments pour les patients positifs pour la COVID-19 et négatifs pour la COVID-19 pendant la pandémie par rapport aux patients d'avant la pandémie. Parmi les patients positifs pour la COVID-19, les interventions étaient principalement liées à l'amélioration de la sécurité des patients (code PCNE P2), au choix des médicaments (C1), à la sélection des doses (C3), au processus de prescription et de délivrance (C5), au processus d'utilisation des médicaments (C6), et aux transferts de patients entre différents niveaux de soins (C8). Les problèmes liés aux médicaments traités par les interventions des pharmaciens concernaient principalement les patients positifs pour la COVID-19 pendant la période de la pandémie et se rapportaient aux préparations hormonales systémiques (à l'exclusion des hormones sexuelles et des insulines), aux agents anti-infectieux à usage systémique, au système nerveux ainsi qu'au sang et aux organes hématopoïétiques.

Conclusion : Les résultats de cette étude mettent en évidence l'adaptabilité et la compétence des pharmaciens pour répondre à des scénarios critiques tels que la pandémie de COVID-19. Ces scénarios se caractérisent par une nouvelle dynamique de travail, l'embauche de professionnels supplémentaires, une augmentation du nombre de lits, l'évolution rapide des informations fondées sur des données probantes et des pénuries de médicaments nécessitant le recours à des médicaments alternatifs. Les pharmaciens jouent un rôle crucial pour assurer la sécurité des patients pendant ces périodes difficiles.

Mots-clés : pharmacie clinique, interventions des pharmaciens, pandémie, COVID-19

INTRODUCTION

The emergence of COVID-19 in December 2019 led to global spread, with severe forms of the disease resulting in severe acute respiratory syndrome.[1] The prevalence of the disease has been linked to obesity, hypertension, diabetes mellitus, and coronary artery disease.[2-5] Among the countries significantly affected by COVID-19, Brazil has faced considerable challenges, with reports of 38 million cases and 712 000 deaths (as of May 2024).[6] Approximately 14% of infected individuals experience severe disease, requiring hospitalization and oxygen therapy, with 5% of this group needing admission to the intensive care unit (ICU). Severe disease may eventually lead to sepsis, septic shock, multiple organ failure, acute kidney injury, and cardiac injury.[7]

Given the limited effectiveness of therapies for hospitalized patients with COVID-19, there has been a global discussion regarding appropriate drug management of the disease.[8] In Brazil, treatment guidelines for hospitalized patients were first published in 2021; these guidelines recommended the use of corticosteroids for patients receiving oxygen therapy, as well as thromboembolism prophylaxis, antimicrobials (according to institutional protocols) in cases involving suspected bacterial infection, and, if available, tocilizumab for patients receiving non-invasive ventilation.[9,10] The guidelines highlight the clinical benefit of remdesivir in the early phase to prevent progression to severe COVID-19, as well as the lack of evidence for the use of high-risk drugs such as azithromycin, casirivimab in combination with imdevimab, chloroquine, colchicine, hydroxychloroquine, and convalescent plasma.[9,10]

Because of its severity, the pandemic has had a significant impact on health care services worldwide, which has led health care professionals to adopt various strategies to mitigate its adverse effects and adapt to new work dynamics.[11,12] In hospitals, clinical pharmacists play a crucial role in comprehensive medication management through pharmacist interventions, which encompass actions aimed at optimizing the care process, disease management, and patient safety, including proposing modifications to drug use and preventing inappropriate medication use or harm.[13,14]

Despite the profound impact of the COVID-19 pandemic, few studies have addressed its effects on clinical pharmacy practice. In this study, we aimed to analyze and compare the interventions performed by clinical and resident pharmacists during comprehensive medication management in the adult ICU and general internal medicine (GIM) departments of the University Hospital of the University of São Paulo in São Paulo, Brazil. Specifically, we compared the pandemic period (March to December 2021) and the pre-pandemic period (March to December 2019) in terms of pharmacist interventions performed.

METHODS

This study received approval from the research ethics committees of the University Hospital (ID 3422497; approval no. 5.377.704; April 29, 2022) and the School of Pharmaceutical Sciences (ID 3358233; approval no. 5.341.552; April 9, 2022) of the University of São Paulo. These committees waived the requirement for informed consent from patients.

Study Design and Setting

In this retrospective, observational, cross-sectional study, we analyzed pharmacist interventions performed before and during the COVID-19 pandemic. The study used data from patients admitted to the GIM and ICU departments of the University Hospital of the University of São Paulo. The hospital is classified as a medium complexity facility, characterized by a bed complexity ranging between 51 and 150, with secondary level care services. These services include basic emergency services, general medical and surgical specialties, diagnostic and imaging capabilities, inpatient care, and a broad range of medical specialties, such as pediatrics, orthopedics, cardiology, neurology, psychiatry, gynecology, and ophthalmology, as well as surgical services excluding transplantation, neurosurgery, and cardiac surgery.

Traditionally, the hospital had 147 beds available for referrals from the local community and the university's academic community. During the pandemic, there was a moderate increase (by 26%) in the number of beds in the GIM division and a significant increase (by 66%) in the ICU (Table 1). However, there was a lower increase in the number of staff members, especially nurses and licensed practical nurses, and no increase in the number of pharmacists and pharmacy residents (Table 1). Due to the changing situation, patients were frequently transferred between different levels of care, such as from the GIM to the ICU and vice versa.

Inclusion Criteria

In this study, we analyzed data and information for patients admitted to hospital between March 1 and December 31, 2019, and between March 1 and December 31, 2021. The inclusion criteria encompassed age over 18 years and hospitalization for longer than 24 hours (to allow for the possibility of pharmacist interventions). During the pandemic period, all patients admitted to the hospital underwent real-time polymerase chain reaction testing for SARS-CoV-2, regardless of their clinical condition. Patients with a positive test result were admitted to isolation beds in the GIM division or the ICU.

Pharmacist Interventions

Pharmacists documented their interventions daily in a noncomputerized database maintained by the Clinical Pharmacy Service. The activities performed by pharmacists

TABLE 1. Hospital Resources and Patient Data before and during the COVID-19 Pandemic

Variable	GIM			Adult ICU		
	Before Pandemic	During Pandemic		Before Pandemic	During Pandemic	
Hospital resources						
No. of hospital beds	30	38		12	20	
No. of health care professionals						
Nurses	13	17		14	15	
Physicians	6	8		12	16	
Licensed practical nurses	27	37		26	28	
Clinical pharmacists	1	1		1	1	
Pharmacy residents	2	2		2	2	
Patient data	**No COVID testing**	**COVID positive**	**COVID Negative**	**No COVID Testing**	**COVID Positive**	**COVID Negative**
No. of patients	488	288	302	109	96	88
No. of deaths	34	60	22	19	68	28
Mortality (%)	7.0	20.8	7.3	17.4	70.8	31.8

GIM = general internal medicine, ICU = intensive care unit.

included medication reconciliation, assessment of patient needs, evaluation of drug therapy efficacy and safety, review of medical prescriptions, identification of drug interactions and compatibility, determination of appropriate dosage forms, monitoring of serum drug levels, participation in medical rounds, pharmacovigilance, patient counselling, and assistance to the multidisciplinary team. Interventions were performed directly with the patient or were suggested to the patient's primary practitioner or during medical rounds.[15]

To ensure consistent classification for our study, the pharmacist interventions were reclassified using the Pharmaceutical Care Network Europe (PCNE) system. A resident pharmacist (G.C.A.) and the head of the Clinical Pharmacy Service (K.D.P.) conducted the reclassification independently, with consensus achieved through discussion. Version 9.1 of the PCNE system was chosen because it is the most up-to-date version and covers the required aspects described in a classification system. The PCNE version 9.1 provides codes for 3 primary domains for different types of problems (designated P1–P3), 9 primary domains for causes (C1–C9), 5 primary domains for interventions (I0–I4), and 3 primary domains for acceptance of interventions (A1–A3).[16] Medications were categorized according to the Anatomical Therapeutic Chemical (ATC) first-level codes. Each pharmacist intervention aimed to address and optimize one or more drug-related outcomes.[17]

Statistical Analysis

The results were analyzed using Prisma software (version 9.1.2; GraphPad) and SPSS (version 20; IBM). The significance level was set at 5%. After classifying the interventions, we calculated crude odds ratios (ORs) and 95% confidence intervals (CIs) for the pandemic period relative to the pre-pandemic period (reference).

RESULTS

The interventions or treatments provided to patients were recorded according to the department where each patient was located at the time of the intervention (GIM or ICU; Table 2). The percentages of patients with pharmacist interventions were similar between the pre-pandemic and pandemic periods, regardless of whether the patient had COVID-19. Among the 1371 hospitalized patients included in the study, a total of 1146 patients received one or more interventions over the course of both study periods. The percentage of patients in the GIM division or the ICU who received interventions ranged from 78.7% to 88.5% across the 2 study periods (Table 2).

The acceptance rate for these interventions was reported to be 90.6% for patients in the GIM division and 98.7% for those in the ICU. The number of patients receiving interventions was similar between the GIM and ICU (Table 2). However, in the GIM division, there was an increase in the number of patients with an intervention for COVID-19-positive patients relative to COVID-19-negative patients in the same period, specifically 261 COVID-19-positive patients with an intervention and 255 COVID-19-negative patients with an intervention.

In the GIM division, regardless of whether patients were COVID-19-positive or COVID-19-negative, certain types of pharmacist interventions decreased during the pandemic, including drug selection, drug form, dose selection,

intervention at the prescriber level, and intervention acceptance (Figure 1). However, there were increases in interventions related to dispensing, the drug-use process, patient transfer (referred to as "patient related" in the figure), and interventions at the patient level. Specifically, for COVID-19-positive patients in the GIM division, there was a clear decrease in treatment effectiveness and an increase in treatment safety (Figure 1).

In the ICU, similar trends were observed regardless of patients' COVID-19 status. There were decreases in interventions related to dispensing, interventions at the prescriber level, and intervention acceptance. Conversely, there were increases in interventions related to drug form, patient transfer ("patient related"), and interventions at the patient level. For COVID-19-positive patients in the ICU, there were increases in interventions related to treatment safety, drug selection, dose selection, and the drug-use process (Figure 1).

According to the analysis of pharmacist interventions in relation to therapeutic classes in the ATC classification system, several notable findings were observed in both the GIM and the ICU (Figure 2). In the GIM division, regardless of COVID-19 status, there was an increase in interventions related to the cardiovascular system therapeutic class. However, for COVID-19-positive patients, there was a decrease in interventions in the category for "various" therapeutic classes and increases in interventions related to the classes for anti-infectives for systemic use and systemic

TABLE 2. Interventions by Pharmacists before and during the COVID-19 Pandemic

	GIM			Adult ICU		
	Before Pandemic (No COVID Testing)	During Pandemic		Before Pandemic (No COVID Testing)	During Pandemic	
Variable		COVID Positive	COVID Negative		COVID Positive	COVID Negative
No. of pharmacist interventions	1287	462	1850	1570	521	1486
No. of patients with a pharmacist intervention	384	261	255	91	72	83
% of patients with a pharmacist intervention	78.7%	86.4%	88.5%	83.5%	81.8%	86.5%
Mean no. of pharmacist interventions per patient	3.3	1.8	7.2	17.2	7.2	17.9

GIM = general internal medicine, ICU = intensive care unit.

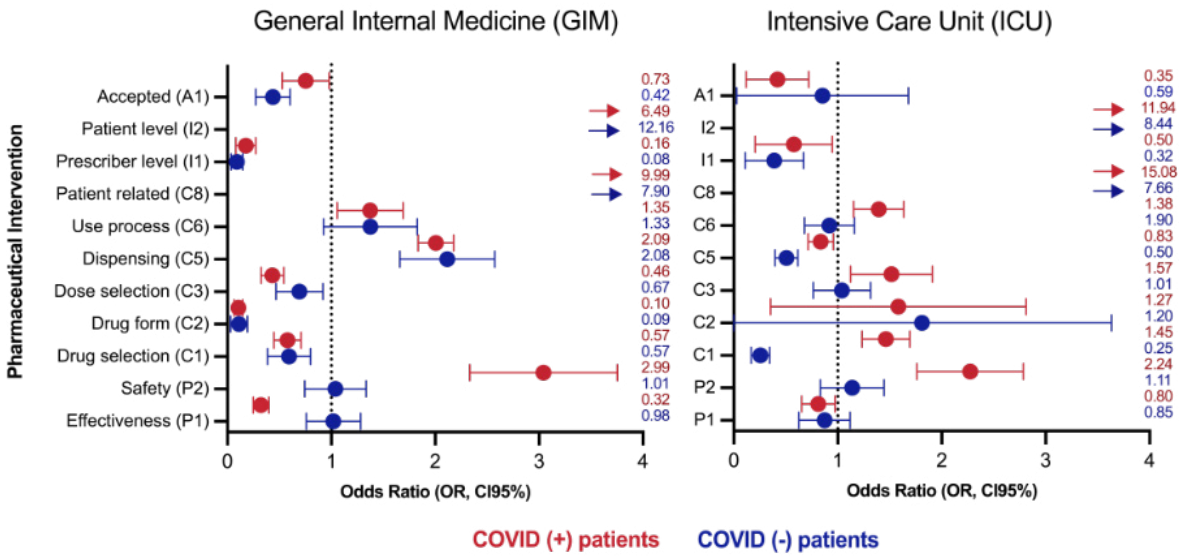

FIGURE 1. Odds ratios (ORs) and 95% confidence intervals (CIs) for number of pharmacist interventions in COVID-19-positive (+) and COVID-19-negative (-) patients during the pandemic period (March to December 2021) compared with patients in the pre-pandemic period (March to December 2019), categorized by type of intervention. The interventions were performed in the general internal medicine (GIM) division and intensive care unit (ICU) of a university hospital in São Paulo, Brazil, in accordance with the Pharmaceutical Care Network Europe system (version 9.1).[16] The figure shows only the interventions that changed relative to the pre-pandemic period. The OR values for each intervention type are provided on the right. Right-facing arrows indicate OR values beyond the highest value on the horizontal scale (> 4.0). More detailed information is available by request to the corresponding author.

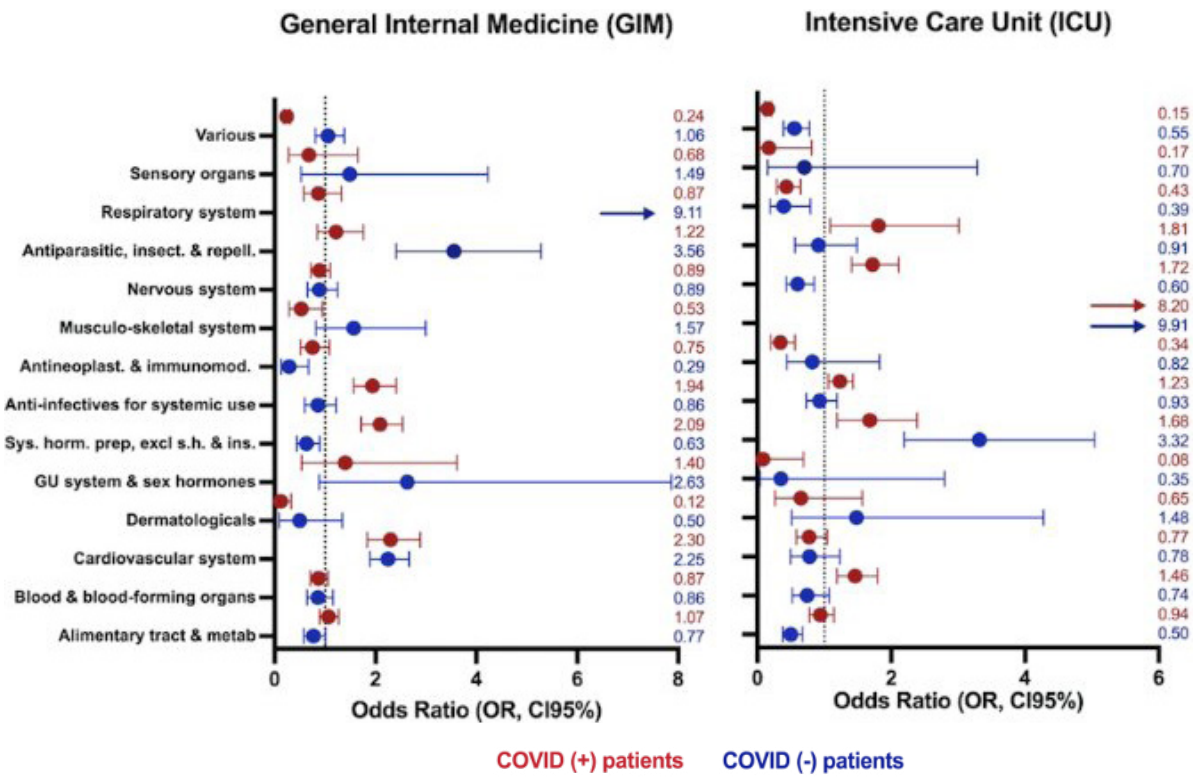

FIGURE 2. Odds ratios (ORs) and 95% confidence intervals (CIs) for number of pharmacist interventions in COVID-19-positive (+) and COVID-19-negative (-) patients during the pandemic period (March to December 2021) compared with patients in the pre-pandemic period (March to December 2019), according to therapeutic classes of medication, as set out in the Anatomical Therapeutic Chemical classification system.[17] The interventions were performed in the general internal medicine (GIM) division and the intensive care unit (ICU) of a university hospital in São Paulo, Brazil. The OR values for each therapeutic class are provided on the right. Right-facing arrows indicate OR values beyond the highest value on the horizontal scale (> 8.0 for GIM division; > 6.0 for ICU). More detailed information is available by request to the corresponding author. GU = genitourinary; "insect. & repell." = insecticides and repellants; "sys. horm. prep, excl. s.h. & ins." = systemic hormonal preparations, excluding sex hormones and insulin.

hormonal preparations (excluding sex hormones and insulins). These trends reflect the increased focus on treating and preventing infections in patients with COVID-19 and managing hormonal imbalances caused by the disease. For COVID-19-negative patients in the GIM division, there were increases in interventions related to the therapeutic classes for the respiratory system and for antiparasitic products, insecticides, and repellents (Figure 2).

In the ICU, regardless of COVID-19 status, there were decreases in interventions related to medications in the respiratory system and "various" therapeutic classes. Conversely, there were increases in interventions related to systemic hormonal preparations (excluding sex hormones and insulins) and the musculoskeletal system therapeutic class. Also in the ICU, there was a decrease in interventions for managing hormonal imbalances. For COVID-19-positive patients specifically, there were increases in interventions related to anti-infectives for systemic use; the nervous system therapeutic class; the blood and blood-forming organs therapeutic class; and antiparasitic products, insecticides, and repellents. However, there was a decrease in interventions related to antineoplastic and immunomodulating agents, which might indicate a shift in focus away from cancer treatment and immune modulation in the ICU during the pandemic (Figure 2).

DISCUSSION

This study has shown that the COVID-19 pandemic brought important changes in the numbers and types of pharmaceutical interventions at our institution relative to the pre-pandemic period. These differences were not limited to COVID-19-positive patients but also affected COVID-19-negative patients. Several factors contributed to these changes. One key factor seemed to be the increased severity of inpatient conditions, as evidenced by the elevated mortality rates among both COVID-19-positive and COVID-19-negative patients as compared with mortality in the pre-pandemic period (Table 1). Other contributing factors include alterations in work dynamics, the hiring of new professionals, an increase in the number of beds, challenges in implementing evidence-based protocols for COVID-19 management, and excessive prescription of certain drugs, which led to drug shortages and the need for drug substitutions.

In the GIM, the percentage of patients with pharmaceutical interventions increased from 78.7% in the pre-pandemic period to 86.4% for COVID-19-positive patients during the pandemic. However, in the ICU, the frequency of interventions remained relatively stable, with 83.5% of patients having interventions before the pandemic and 81.8% of COVID-19 positive patients having interventions during the pandemic. The increase in interventions in the GIM division may be attributed to the expansion of dispensing and drug-use processes, as well as transitions between different levels of care, likely because of changes in work routines. Other contributing factors were uncertainties surrounding drug use and discharge instructions due to the substitution of drugs that were not the prescriber's first choice. In the ICU, although the frequency of pharmacist interventions for COVID-19-positive patients remained unchanged, the types of interventions changed substantially, particularly concerning drug and dose selection and drug-use processes. This discrepancy can be attributed to changes in the literature, patient-specific factors, managerial decisions, drug substitutions, and the hiring of new professionals.[18]

Few studies have explored the impact of the COVID-19 pandemic on pharmacist interventions, and only 1 study has compared COVID-19-positive and COVID-19-negative patients. That study, conducted in a French secondary-level university hospital similar to ours, found no difference in the number of pharmacist interventions between COVID-19-positive and COVID-19-negative patients in the ICU.[18] However, the study did not analyze data from the pre-pandemic period, nor did it include patients receiving care in the GIM department.[18]

In addition to interventions related to the drug-use process and dispensing, our study highlights the role of pharmacists in selecting appropriate drugs for COVID-19 treatment, demonstrating their ability to correlate the severity of SARS-CoV-2 infection with the need for early therapeutic management. Pharmacists at our institution recommended evidence-based therapies, such as the use of corticosteroids (dexamethasone) for patients receiving oxygen therapy,[9,19] prophylactic or therapeutic anticoagulation for critically ill patients,[20] and the use of anti-infectives only for confirmed infectious cases. The pharmacist collaborated with the health care team to promote the use of high-quality evidence-based medications.[8]

Pharmacist interventions related to dose selection were also prevalent, representing 10.8% (n = 200) and 23.3% (n = 347) of interventions for COVID-19-negative patients in the GIM division and the ICU, respectively, which aligns with findings from other studies.[19-21] The production of consensus guidelines for the clinical management of COVID-19 patients during the pandemic contributed to these interventions.[19-21] Common dose adjustment issues were related to use of antithrombotic agents (enoxaparin/heparin) without consideration for renal function, underdosing or overdosing of steroids and antibiotics, inappropriate dosing of neuromuscular blockers, and inadequate analgesia. Pharmacists play a crucial role in optimizing therapy and ensuring medication safety in both the ICU and GIM settings.

In accordance with previous research, our study found that pharmacist interventions increased during the COVID-19 pandemic due to the stressful and disrupted nature of the health care environment.[22-24] These interventions were linked to challenges in identifying patients or prescribers; difficulties in prescribing drugs that were unfamiliar to the prescriber; and use of unconventional concentrations, dilutions, doses, and timing of medications. These factors were particularly relevant given that treatment recommendations for COVID-19 fluctuated over time, as new information became available; the presence of newly hired professionals with limited experience added to the complexity of care. The implementation of pharmacist interventions played a crucial role in ensuring patient safety, preventing harm, and mitigating errors in the medication-use process.

Regarding COVID-19-negative patients, we believe that the observed changes in pharmacist interventions reflect the global reality of reduced services offered to these patients during the pandemic.[25,26] In the GIM department, the number of pharmacist interventions declined, likely because of the dynamics of the pandemic. In the ICU, although disease severity increased, as evidenced by higher mortality rates, there was a reduction in the number of pharmacist interventions. This observation may be attributed to the diversion of resources and attention toward the pandemic, including the opening of new beds[27-31] and a relative neglect of diseases other than COVID-19. Consequently, COVID-19-negative patients sought health care only in emergent situations, and they had reduced access to specialized care for acute and chronic conditions unrelated to COVID-19. The discouragement of self-presentation to the emergency department and the fear of becoming infected likely contributed to the decline in emergency department visits. During lockdown periods, admissions for specialties such as traumatology, dermatology, gastroenterology/hepatology, and cardiology declined, while admissions for respiratory diseases and severe cases of other diseases increased, highlighting the severity of illnesses during the pandemic.[32]

Limitations

This was a retrospective study conducted in a noncomputerized hospital setting. Pharmacist interventions may have been under-reported due to the manual recording process. However, if present, this limitation likely affected COVID-19-positive and COVID-19-negative patients equally. The lack of computerized systems also limited the availability of more detailed information that might have been valuable for

our analysis, such as patient demographic details (e.g., sex, age), comorbidities, reasons for hospitalization unrelated to COVID-19, and length of hospital stay. The absence of such data may have influenced the depth and generalizability of our findings.

CONCLUSION

The COVID-19 pandemic has significantly affected pharmacist interventions in both COVID-19-positive and COVID-19-negative patients. Pharmacists have played a crucial role in optimizing therapy, addressing drug selection and dosage issues, and ensuring patient safety. Their adaptability and expertise have been instrumental in navigating the challenges posed by the pandemic. These findings highlight the importance of integrating pharmacists as essential members of the health care team for managing complex health care scenarios.

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