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Cross-sectional analysis of drug-related problems in an intensive care unit

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Abstract

Objective: To analyze the evolution of the profile of drug-related problems (DRPs) identified by clinical pharmacists in an Intensive Care Unit (ICU), considering the implementation of pharmaceutical care services in the hospital. **Methods:** Cross-sectional study focusing on the analysis of DRP records that required pharmaceutical interventions in a clinical/surgical adult ICU of a tertiary teaching hospital in Southern Brazil, within two distinct periods: from July 2019 to April 2020 (Period A), and from April to October 2024 (Period B). The analysis included a description of DRP characteristics, the pharmacological categories involved and the acceptance of pharmaceutical interventions. **Results:** During Period A, 239.5 DRPs/1,000 patient-days were identified, whereas 425.6 DRPs/1,000 patient-days were recorded in Period B, indicating an increasing trend in the identification of potential problems. In Period A, the primary DRPs were related to effectiveness (61.8%), whereas Period B showed greater diversification, with an increased representation of problems classified as "others" (38.5%), including unnecessary treatment. The most frequent causes of DRPs included drug selection and dosing, with a possible increase in problems related to treatment duration in Period B. Regarding pharmaceutical interventions, most were conducted at the drug level (94.0% in Period B compared to 53.6% in Period A) and had a good acceptance rate by the multidisciplinary team (92.2% in Period A and 97.0% in Period B). **Conclusion:** These findings reflected the consolidation of pharmaceutical care as an essential tool for the safety and effectiveness of drug therapies, highlighting the positive impact of pharmaceutical practice in the ICU over the years.

Keywords: medication review; clinical pharmacy service; pharmaceutical care; intensive care units; pharmacotherapy.

Análise transversal dos problemas relacionados a medicamentos em uma unidade de terapia intensiva

Resumo

Objetivo: analisar a evolução do perfil de problemas relacionados a medicamentos (PRMs) identificados por farmacêuticos clínicos em uma Unidade de Terapia Intensiva (UTI), a partir da implementação de serviços clínicos providos por farmacêuticos na unidade. **Métodos:** Estudo transversal, focado na análise dos registros de PRMs que necessitaram de intervenções farmacêuticas em uma UTI adulto de um hospital terciário de ensino da região Sul do Brasil, em dois períodos distintos: de julho de 2019 a abril de 2020 (período A), e de abril a outubro de 2024 (período B). A análise incluiu a descrição das características dos PRMs, categorias farmacológicas envolvidas e aceitação das intervenções farmacêuticas. **Resultados:** durante o período A, foram identificados 239,5 PRM/1000 pacientes-dia, enquanto no período B, foram registrados 425,6 PRM/1000 pacientes-dia, com uma tendência de aumento na identificação de problemas potenciais. Os principais PRMs no período A estavam relacionados à efetividade (61,8%), enquanto no período B houve uma diversificação, com maior representação de problemas classificados como "outros" (38,5%), incluindo tratamento desnecessário. As causas de PRMs mais frequentes incluíram seleção de medicamentos e dose, com possível aumento de problemas relacionados à duração do tratamento no período B. Quanto às intervenções farmacêuticas, a maioria ocorreu em nível do medicamento (94,0% no período B, em comparação com 53,6% no período A) e apresentou boa taxa de aceitação pela equipe multidisciplinar (92,2% no período A e 97,0% no período B). **Conclusão:** esses resultados refletiram a consolidação do cuidado farmacêutico como ferramenta essencial para a segurança e efetividade das terapias medicamentosas, evidenciando o papel positivo da atuação farmacêutica na UTI ao longo dos anos.

Palavras-chave: revisão de medicamentos; serviço de farmácia clínica; cuidados farmacêuticos; unidade de terapia intensiva; farmacoterapia.

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Introduction

Pharmaceutical care is a practice model focused on providing direct clinical services to patients, aiming to promote the rational use of medicines and optimize pharmacotherapy, with the purpose of achieving outcomes that improve patients' quality of life.[1] In the context of an intensive care unit (ICU), where patients frequently undergo complex and invasive treatments, the clinical role of the pharmacist can be crucial in achieving better clinical outcomes and preventing drug-related problems, given the complexity of critically ill patients, the number of prescribed medicines, and the pharmacokinetic and pharmacodynamic variability in this population.[2]

As defined by the Pharmaceutical Care Network Europe (PCNE), a drug-related problem (DRP) is "any event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes." [3]

A systematic review with meta-analysis concluded that pharmacist participation in multidisciplinary teams can improve patient health outcomes by reducing mortality rates, length of ICU stay, and preventing adverse effects. [4] Drug therapy is one of the essential treatments in this setting, and the incidence of drug-related problems is twice as high as in general wards, in addition to being more serious and predictable. [2,5]

Previous studies have already demonstrated the importance of the clinical pharmacist in identifying DRPs. A study conducted in a Brazilian ICU identified that the most prevalent DRPs were related to treatment safety, with the most frequently involved pharmacological classes being drugs acting on the nervous system and antimicrobials.[6] The economic impact of pharmaceutical interventions in ICUs, assessed in a multicenter study conducted between 2018 and 2019, revealed cost avoidance both in terms of direct drug costs and in preventing problems by initiating non-prescribed therapy. These amounted to approximately 23 million US dollars, resulting in a cost-saving ratio in relation to the clinical pharmacist's salary of up to US$ 9.6:1. [7]

Despite the potential positive impact of implementing pharmaceutical care in intensive care, there is still a scarcity of studies investigating the implementation of clinical pharmacy services in Brazilian hospitals, where most of the published works have focused on evaluating the performance of pharmaceutical practice. [8]

Within the scope of implementation science, the aim is to test the effectiveness and adherence of implementing clinical innovations in real-world practice, generating new knowledge through understanding the processes, barriers, and facilitators that influence the success of the implementation strategy.[9] In this sense, analyzing adherence indicators to interventions may serve as a valuable approach to identify areas for improvement in order to achieve greater effectiveness and sustainability of pharmaceutical care implementation, especially in intensive care.

To understand the evolution of pharmaceutical care implementation in an ICU after five years of service—based on its ability to identify, prevent, and resolve drug-related problems—the general objective of this study was to analyze the evolution of the profile of pharmaceutical interventions and DRPs recorded in two distinct periods: at the beginning of the implementation of clinical services provided by pharmacists in the unit and five years later.

Methods

Study design

A cross-sectional study was conducted based on the retrospective analysis of DRP records by clinical pharmacists in an adult ICU, across two distinct periods: from July 2019 to April 2020 (Period A), totaling ten months, and from April to October 2024 (Period B), totaling seven months. The selected periods represent the beginning and five years after the implementation of clinical services provided by pharmacists in the unit, in addition to involving the same pharmacist throughout and having systematized DRP records in a database. The choice of a cross-sectional design across two different periods aimed to analyze the effect of the duration of pharmaceutical care implementation in the unit on the profile of identified DRPs and the interventions performed. [10]

It is important to highlight that DRP recording in Period A was interrupted before the onset of care for patients infected with SARS-CoV-2; therefore, the COVID-19 pandemic period did not affect the analyses performed.

Setting and workflow

The study site was the ICU of a medium-sized teaching hospital, with medium- and high-complexity care, currently comprising approximately 226 active beds and around 1,000 monthly admissions. The institution provides care in internal medicine, surgery, obstetrics and gynecology, and pediatrics, offering specialized inpatient and outpatient assistance, diagnostic, and therapeutic services. [11] The ICU is a general unit dedicated to the care of adult and elderly medical and surgical patients. Between 2019 and 2020, the unit had 12 beds; from April to September 9, 2024, this number increased to 14 beds, and was later expanded to 16 beds.

The unit includes a multidisciplinary team, comprising permanent staff and residents. The professional categories involved include nursing, medicine, physical therapy, occupational therapy, nutrition, pharmacy, psychology, speech therapy, and social work.

Clinical services were provided by one permanent clinical pharmacist, experienced in critical care, and two pharmacy residents during both periods, working directly in the adult ICU from Monday to Friday, between 7:00 a.m. and 5:00 p.m. On weekends, patients were assisted by on-call pharmacists between 7:00 a.m. and 7:00 p.m., performing only prescription analysis for medicine dispensing, without systematic recording of interventions.

All patients admitted to the unit received pharmaceutical care, and services provided included medication reconciliation, pharmacotherapeutic follow-up, and prescription analysis. Reconciliation was performed in patients admitted to the ICU without prior evaluation by another clinical pharmacist in the hospital. Pharmacotherapeutic follow-up covered all patients, using a Microsoft Excel spreadsheet built based on the FASTHUG-MAIDENS mnemonic, which assesses aspects such as nutrition, sedation, prophylaxis for thromboembolism and stress ulcer, antimicrobials, drug interactions, and other relevant aspects. [12] Finally, all prescriptions were reviewed before dispensing by the pharmacy.

During the provision of clinical services, upon identifying a DRP, pharmacists intervened with the care team to resolve potential underlying causes. Databases consulted to support clinical decision-making included: UpToDate, Micromedex Solutions, Sanford Guide, as well as Clinical Protocols and Therapeutic Guidelines from the Brazilian Government and other national and international health societies. Interventions were recorded as clinical notes in the patient's medical record following the SOAP method and in the service's form for recording DRP indicators and pharmaceutical interventions.

Participants

To enable this retrospective study, it was not possible to obtain patient consent due to the impossibility of contacting those involved in the interventions and exposed to DRPs during the study periods, as well as the absence of such information in the data source used. Therefore, individual patient characteristics could not be retrieved. No sampling of records was performed; all records available in the database were analyzed in their entirety.

Data source

The form used to record the DRP identification indicator in this study is an integral part of the service indicators and was developed on the Microsoft® Forms platform. It was built based on the classification system proposed by the PCNE in the document *Classification for Drug-Related Problems*, version 9.0 (used in the 2019–2020 period), and updated according to version 9.1 (used in 2024), with both versions being compatible. [3] The Portuguese translation and adaptation of versions 9.0 and 9.1 of the classification instrument can be found in the Supplementary Material, in Tables 1 and 2, respectively. Once completed, all records were automatically compiled, generating the database in an Excel spreadsheet. It is noteworthy that the study exclusively used the databases generated from these records and no data exclusion was required.

Variables

Variables collected were related to the classification of identified DRPs, including: primary cause of the DRP (effectiveness, safety, and other undefined causes), pharmacological category of the drug involved, problem class (drug selection, dosage form, dose, treatment duration, dispensing, medication use process, patient-related, patient transfer-related, and others), and acceptance of the intervention by the healthcare team. DRPs were classified as manifest problem when they had already caused an impact on the patient at the time of identification, requiring corrective intervention by the pharmacist. *Potential* DRPs were those identified and intervened upon in advance, before the problem resulted in harm to the patient, thus characterizing a preventive action. The total number of interventions carried out in each analyzed period was also obtained. All these variables were present in the extracted database. Additionally, the number of patient-days was collected as an indicator of unit occupancy, used as the denominator for estimating DRP prevalence and pharmacist workload.

Bias

This study presents limitations inherent to its retrospective design and the use of secondary data. The absence of demographic information on participants prevented analysis of potential variations in the population profile, such as sex, age, and clinical outcome, as well as the assessment of their impact on the evolution of pharmaceutical care. Data collection in different months of each year may have introduced bias related to seasonality, especially considering that the reason for hospitalization was not recorded, making it impossible to identify changes in patients' clinical profiles. Finally, the classification of DRPs and their causes may have been influenced by subjectivity in the pharmacist's interpretation. However, this bias was minimized through group discussions aimed at standardization and resolution of divergences.

Statistical methods and measures used

Data were extracted from the database generated by form completion into a Microsoft Excel spreadsheet. Comparison between the periods was obtained using mean calculations for the patient-day denominator and prevalence rate, according to Formula 1, for the different types of DRPs identified.

Prevalence= ((Total number of DRPs) / (Total patient-days)) ×1000((1)

Drugs involved in the problems were classified according to the first and fifth levels of the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization. [12]

Ethical considerations

This research was conducted in accordance with the ethical principles contained in Resolution No. 466 of December 12, 2012, and was approved by the Research Ethics Committee of the Federal University of Santa Catarina, under opinion CAEE No. 79423224.8.0000.0121. As it used anonymous secondary data, without any form of patient identification and without diagnostic or therapeutic interventions, the requirement for an Informed Consent Form was waived. All researchers signed a commitment to ensure the anonymous use of the data, safeguarding the integrity of the information.

Results

There were 471 ICU admissions during the 2019–2020 period (Period A), corresponding to an average occupancy of 9.9 patient-days. From April to October 2024 (Period B), with the expansion of the number of beds, there was a total of 2,916 patient-days, with an average occupancy of 13.6 patient-days.

In Period A, 723 problems were identified by clinical pharmacists, with a mean of 2.4 DRPs/patient-day and a prevalence rate of 239.5 DRPs/1,000 patient-days. Of these, 576 DRPs were identified as potential, corresponding to 79.6% possible harm and 20.4% actual harm. In Period B, 1,241 DRPs were identified, with a mean of 5.8 DRPs/patient-day and a prevalence rate of 425.6 DRPs/1,000 patient-days. Among these problems, 135 were identified as manifest (10.8%) and 1,106 as potential (89.2%) (Table 1).

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Table 1. Comparison between periods of parameters related to the number of DRPs identified, occupancy rate, prevalence, and classification of DRPs as actual or potential.

	Period A	Period B
Total DRPs recorded	723	1241
Total patient-days	3019	2916
DRPs/patient-day	2.4	5.8
DRP prevalence rate per 1000 patient-days	239.5	425.6
Manifest problem	147	135
Potential problem	576	1106

Legend: DRP – drug-related problem.

As shown in Table 2, the main problem identified in the first period, according to the primary domain, was effectiveness (61.8%), followed by "others" (20.2%) and, lastly, safety (18.0%). In 2024, 47.5% of the problems recorded were related to effectiveness, 38.5% were classified as "others," and 14% as safety. The problem "drug treatment effect not optimal" was the most prevalent in Period A, followed by "adverse drug event (possibly) occurring" and "no drug treatment despite indication." In Period B, DRPs related to "unnecessary drug treatment," "untreated symptoms or indications," and "drug treatment effect not optimal" were the most prevalent, respectively.

Regarding the causes of DRPs, in the first period, most occurred at the level of drug selection (36.4%), followed by dose (28.7%) and dispensing (11.1%). In the second period, they were primarily related to drug selection (42.5%), treatment duration (27.8%), and dose (20.5%) (Table 3).

At the level of interventions, the most frequent were drug-level interventions (53.6% in Period A, and more prominently in Period B with 94%), followed by prescriber-level interventions (39.4% in Period A and 3% in Period B). Drug-level interventions included suggestions to switch one drug for another, adjust the dose, formulation, or dosage regimen, and/or initiate or discontinue a drug. Prescriber-level interventions included requests for vancomycin serum level monitoring in the system and discussions regarding the therapeutic plan of an antimicrobial, for example.

More than 90% of interventions were accepted in both periods (92.2% in Period A and 97.0% in Period B). In both periods, the main reason for non-acceptance of an intervention was disagreement between the pharmacist and the prescriber (3.4% in Period A and 2.3% in Period B) (Table 4). In Period A, disagreements were fairly distributed among effectiveness problems (40.0%), safety (20.0%), cost-effectiveness (16.0%), and unnecessary drug therapy (16.0%), with the main causes being drug selection, dose, and dosage form. The drugs most frequently involved were piperacillin+tazobactam (n=5), meropenem (n=3), and ranitidine (n=3). In Period B, most disagreements occurred regarding unnecessary drug therapy interventions (41.3%) and effectiveness (37.9%), mainly involving omeprazole (n=13), meropenem (n=5), and heparin (n=2).

Regarding outcomes, in Period A, 83.2% of problems were fully resolved, while only 10.1% were unresolved, mostly because there was no need or possibility to resolve them—for example, in cases where the suggested intervention was not feasible, such as a change in the administration route that was not available. In the second period, 93.5% of problems were fully resolved, with unresolved problems mainly due to lack of prescriber cooperation (5.3%).

Table 2. Distribution of drug-related problems according to the PCNE classification in periods A and B.

	Período A		Período B	
	DRP n (%)	P	DRP n (%)	P
Effectiveness	**447 (61.8)**	**148.1**	**589 (47.5)**	**202.0**
P1.1 No effect of pharmacotherapy despite correct use	115 (15.9)	38.1	22 (1.8)	7.5
P1.2 Pharmacotherapy effect is not optimal	248 (34.3)	82.1	266 (21.4)	91.2
P1.3 Untreated symptoms or indications	84 (11.6)	27.8	301 (24.3)	103.2
Safety	**130 (18.0)**	**43.1**	**174 (14.0)**	**59.7**
Adverse drug reaction (possibly occurring)	130 (18.0)	43.1	174 (14.0)	59.7
Others[1]	**146 (20.2)**	**48.4**	**478 (38.5)**	**163.9**
Cost-effectiveness problems	54 (7.5)	17.9	31 (2.5)	10.6
Unnecessary pharmacotherapy	88 (12.2)	29.1	429 (34.6)	147.1
Antimicrobial stewardship[2]	-	-	18 (1.5)	6.2
Unspecified problem/complaint	4 (0.55)	1.3	-	-

Legend: P – prevalence of DRPs per 1,000 patient-days in the period for each primary domain.[1]In version 9.0, the cause "cost-effectiveness problems" was coded as P3.1 and was later removed in version 9.1. Records of this cause in period B were registered under code P3.2 (unspecified problem/complaint). Due to this change between versions, the cause "unnecessary pharmacotherapy" is represented by code P3.2 (version 9.0), whereas in version 9.1 it is coded as P3.1.[2]The cause "antimicrobial stewardship" is not coded in the PCNE instrument and was recorded under "unspecified problem/complaint" (P3.2, v. 9.1).

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Table 3. Distribution of primary and secondary causes involved in the DRPs recorded in periods A (version 9.0) and B (version 9.1).

	Period A			Period B		
Primary domain	Nt (%)	Cause code	DRP n	Nt (%)	Cause code	DRP n
Drug selection	263 (36.4)	C1.6	89	528 (42.5)	C1.5	298
		C1.4	59		C1.1	117
		C1.3	42		C1.2	67
		C1.2	27		C1.3	29
		C1.1	26		C1.4	11
		C1.5	15		C1.6	6
		C1.7	5			
Dosage form	72 (9.9)	C2.1	72	24 (1.9)	C2.1	24
Dose	208 (28.7)	C3.2	69	254 (20.5)	C3.2	85
		C3.1	53		C3.1	66
		C3.4	39		C3.4	65
		C3.5	27		C3.3	35
		C3.3	20		C3.5	3
Treatment duration	31 (4.3)	C4.2	30	345 (27.8)	C4.2	345
		C4.1	1			
Dispensing	80 (11.1)	C5.2	42	8 (0.6)	C5.1	6
		C5.1	37		C5.4	1
		C5.3	1		C5.2	1
Medication use process	30 (4.1)	C6.4	10	18 (1.5)	C6.1	13
		C6.6	8		C6.4	3
		C6.1	8		C6.2	1
		C6.5	2		C6.3	1
		C6.2	2			
Patient-related	23 (3.2)	C7.9	14	1 (0.1)	C7.9	1
		C7.7	5			
		C7.3	2			
		C7.8	1			
		C7.5	1			
Patient transfer-related	5 (0.7)	C8.3	2	21 (1.7)	C8.1	1
		C8.4	1			
		C8.1	1			
		C8.2	1			
Others	11 (1.5)	C9.1	11	42 (3.4)	C9.1	35
					C9.2	7

Legend: Nt – total number of primary domain occurrences; DRP – drug-related problem; C1.1 – drug not in accordance with protocol/therapeutic guideline; C1.2 (Period A, version 9.0) – contraindicated drug; C1.3 (Period A, version 9.0) and C1.2 (Period B, version 9.1) – no indication for the drug; C1.3 (Period B, version 9.1) – inappropriate combination of drugs, or between drugs and herbal products, or between drugs and food; C1.4 (Period A, version 9.0) – drug interaction, or between drug and herbal product, or between drug and food; C1.5 (Period A, version 9.0) and C1.4 (Period B, version 9.1) – inappropriate duplication of drug or therapeutic group; C1.6 (Period A, version 9.0) and C1.5 (Period B, version 9.1) – incomplete or absent treatment for an existing indication; C1.7 (Period A, version 9.0) and C1.6 (Period B, version 9.1) – excessive drugs prescribed for the same indication; C2.1 – inappropriate dosage form (for this patient); C3.1 – insufficient drug dose; C3.2 – excessive drug dose; C3.3 – insufficient dosing schedule; C3.4 – excessive dosing schedule; C3.5 – incorrect, unclear, or missing dosing instructions; C4.1 – treatment duration too short; C4.2 – treatment duration too long; C5.1 – prescribed drug not available; C5.2 – mandatory information or form not provided; C5.4 (Period A, version 9.0) and C5.3 (Period B, version 9.1) – dispensed drug, quantity, concentration, or presentation incorrect; C6.1 – inappropriate timing, administration time, or dose interval; C6.2 – drug administered below dose; C6.3 – drug administered in excessive dose; C6.4 – drug not administered; C6.5 – wrong drug administered; C6.6 – drug administered via wrong route; C7.3 – patient misuses drug (unregulated excessive use); C7.5 – patient consumes interacting food; C7.7 – inappropriate dosing time or interval; C7.8 – patient uses/administers drug incorrectly; C7.9 – patient unable to use the drug or dosage form as prescribed; C8.1 – medication reconciliation not performed during patient transfer; C8.2 – absence of an updated medicine list; C8.3 – incomplete or missing discharge/transfer medicine information; C8.4 – insufficient clinical information about the patient; C9.1 – inadequate or absent therapeutic monitoring; C9.2 – other cause, specify.

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Table 4. Distribution of intervention acceptance across the periods.

	Period A	Period B
	DRP n (%)	DRP n (%)
Accepted intervention	667 (92.3)	1204 (97.0)
Fully implemented	633 (94.9)	1170 (97.2)
Partially implemented	18 (2.7)	4 (0.3)
Not implemented	16 (2.4)	29 (2.4)
Implementation unknown	-	1 (0.1)
Non-accepted intervention	30 (4.1)	33 (2.7)
Not feasible	4 (13.3)	2 (6.1)
Disagreement	25 (83.3)	29 (87.9)
Other reason	1 (3.3)	2 (6.1)
Proposed intervention, acceptance unknown	9 (1.2)	-
Intervention not performed	17 (2.4)	4 (0.3)
Total	723	1241

Legend: DRP – drug-related problem; n – number of DRPs recorded.

A total of 155 drugs were involved in 825 DRPs during Period A and 122 drugs in 1,452 DRPs in Period B. During Period A, the drug classes most frequently involved according to the ATC classification were group J (anti-infectives for systemic use), group A (alimentary tract and metabolism), and group N (nervous system). The five most involved drugs were meropenem, piperacillin+tazobactam, omeprazole, ranitidine, and sulfamethoxazole+trimethoprim. In Period B, the drug classes most frequently involved in DRPs were group J, group A, and group B. The most involved drugs were omeprazole, meropenem, vancomycin, piperacillin+tazobactam, heparin, and hypromellose+dextran (Table 5). The complete list of ATC classification, drugs involved, and number of DRPs recorded can be found in Table 3 of the supplementary material.

Discussion

The comparison between periods A and B showed a possible trend toward an increase in the prevalence of DRPs identified per patient-day. This growth may be related both to the expansion of ICU beds and to the evolution of the capability of clinical services provided by pharmacists, reflecting the maturity, greater sensitivity, and systematization of the service in identifying DRPs.

Quantitatively, in both periods the number of DRPs found was higher compared to several similar studies in ICUs. The prevalence of DRPs per 1,000 patient-days was 89.22 in the study conducted by Albayrak et al.[13] 112.94 by Martins et al.[14] and 124.7 by Zhao et al.[15] Considering the mean DRPs/patient, the values found (2.4 and 5.8) are higher than those reported in another study carried out in southern Brazil (1.5 DRPs/patient).[16] This difference can be attributed to the profile of the hospital and the unit analyzed: a tertiary hospital with highly complex patients; a teaching hospital, characterized by high staff turnover in all areas, including trainees; and a general ICU of a high-complexity hospital, without a defined specialty, receiving both clinical and surgical patients.

As important as the identification of a DRP is the timeliness with which it is identified. In period A, 147 (20.4%) actual DRPs and 576 (79.6%) potential DRPs were identified, whereas in period B there was a relative reduction to 135 (10.8%) actual DRPs, with a greater proportion of potential DRPs, totaling 1,106 (89.2%). Actual problems reflect situations in which the DRP had already caused an impact and the intervention occurred afterwards, while potential ones represent cases in which pharmaceutical intervention prevented future harm. The trend toward an increase in the number of DRPs could be related to a worsening of patient safety; however, the analysis shows that most DRPs were prevented, demonstrating a greater capacity for early identification, which, in turn, contributes directly to safer treatment. Although the professional involved was already a specialist in intensive care since period A, the experience accumulated over five years of practice in the unit, combined with the strengthening of ties with the multidisciplinary team, may have contributed to expanding the capacity for early DRP identification.

Table 5. ATC Classification and the drugs most involved in the DRPs.

	Period A			Period B		
ATC group	n (%)	Drug	DRP n (%)	n (%)	Drug	DRP n (%)
J	324 (39.3)	Meropenem	54 (6.5)	806 (55.5)	Meropenem	131 (9.0)
		Piperacillin+tazobactam	38 (4.6)		Vancomycin	102 (7.0)
		Sulfamethoxazole+ trimethoprim	21 (2.5)		Piperacillin+tazobactam	97 (6.7)
A	159 (19.3)	Omeprazole	31 (3.8)	183 (12.6)	Omeprazole	168 (11.6)
		Ranitidine	30 (3.6)		Thiamine	4 (0.3)
B	113 (13.7)	Phytomenadione	18 (2.2)	175 (12.1)	Heparin	91 (6.3)
		Heparin	15 (1.8)		Enoxaparin	72 (5.0)
S	8 (1)	Hypromellose+dextran	6 (0.7)	141 (9.7)	Hypromellose+dextran	83 (5.7)
					Retinol+amino acids	56 (3.9)
N	102 (12.4)	Phenytoin	18 (2.2)	75 (5.2)	Midazolam	15 (1.0)
		Risperidone	9 (1.1)		Propofol	9 (0.6)
Total			825			1452

Legenda: J – antiinfectives for systemic use; A – alimentary tract and metabolism; B – blood and blood forming organs; S – sensory organs; N – nervous system; n – total number of DRPs registered.

In this sense, this observation is consistent with the findings of Richter et al. (2016), who demonstrated a higher rate of pharmaceutical interventions when the professional is specialized in intensive care, suggesting that specialization, combined with practical experience and team integration, are key determinants of the effectiveness of clinical pharmacy practice.[17]

The most frequent primary domain was effectiveness in both periods, although its percentage varied over the years, as shown in Table 4. This change may be attributed to the growing impact of clinical pharmacist interventions, especially in identifying the need for prophylaxis in critically ill patients, such as for stress ulcers, ocular injury, and venous thromboembolism. In 2024, the implementation of an internal clinical protocol for stress ulcer prophylaxis translated into a greater number of DRP records related to omeprazole, resulting in a significant contribution to deprescribing of the drug, accounting for 24.9% of the records in the "unnecessary pharmacotherapy" subdomain.

Regarding the primary causes of DRPs, in both analyzed periods drug selection was the most frequently recorded cause. However, the distribution of other causes varied between periods. In period A, dose-related problems were the second most prevalent cause, followed by dispensing issues and treatment duration. In period B, the predominant causes after drug selection were related to treatment duration, followed by dose-related problems and categories classified as "others."

The significant number of dose-related DRPs can be attributed to the clinical complexity of ICU patients, who often present with organ dysfunction such as renal or hepatic impairment.[18] These conditions require precise adjustments to prevent either systemic drug accumulation, which can cause serious adverse effects, or subtherapeutic doses, which compromise effectiveness, particularly in patients undergoing clinical recovery. The daily analysis of individual patient characteristics during pharmacotherapy follow-up, considering clinical and biochemical parameters and using evidence-based criteria, optimized drug use and played a key role in promoting better clinical outcomes.

The probable reduction in the number of dispensing-related problems can be attributed mainly to the evolution of processes involving the dispensing of restricted-use drugs, such as broad-spectrum antimicrobials and high-cost medications. In the first period, the subdomain "required information or form not provided" accounted for most records, due to the requirement at the time for a physical form filled out and manually signed by the attending physician and infectious disease specialist to authorize the use of these medicines. In the second period, with the implementation of an electronic health record system, this process was adapted, improving communication between clinical pharmacists, infectious disease specialists, and hospital pharmacists. This modernization of workflow not only reduced the bureaucracy involved but also contributed to improving the quality and efficiency of the service provided, reducing dispensing-related problems, in line with what was reported by Lindén-Lhati et al.[19]

The increasing record of DRP causes in the "others" category is mainly related to the subdomain of inadequate or absent therapeutic monitoring (code 9.1). Critically ill patients often require broad-spectrum antimicrobials, and in the case of vancomycin, use is associated with the possibility of MRSA infection, considering risk factors such as clinical severity, prolonged hospitalization, invasive device use, and prior antimicrobial exposure.[20-22] The implementation of vancomycin serum level monitoring between the analyzed periods was essential to prevent serious adverse effects such as ototoxicity and nephrotoxicity, as well as to ensure its effectiveness at appropriate therapeutic concentrations. The clinical pharmacist played a fundamental role in ensuring timely sample collection, proper interpretation of vancomycin levels, and necessary adjustments, as already evidenced in the literature.[23,24]

A greater number of problems related to treatment duration were identified in the second period, involving the subdomain "treatment duration too long." This record reflects the clinical pharmacist's role in deprescription and the rational use of medicines, emphasizing their attention to the need for the drug and to Stop dates . Among the medications involved in this subdomain, prophylactic drugs previously mentioned and antimicrobials stand out.

In line with this finding, the antimicrobial class was the most prevalent in both periods, consistent with studies conducted in Brazil[25], Taiwan[2], and China[15]. The global threat of antimicrobial resistance and its association with the extensive use of these drugs highlight the importance of rational use. As shown in the systematic review conducted by Dighiriri et al.[26], the clinical pharmacist's participation in antimicrobial stewardship programs led to improvements in prescribing practices, reduction of unnecessary use, optimization of therapies, and better clinical outcomes.[26] The hospital in this study has an institutionalized stewardship service, in which the clinical pharmacist works closely with the infectious disease specialist, jointly reviewing cases, discussing therapeutic plans with the care team, and determining the need for discontinuation once treatment is completed. As reported by Martinez et al.[27], this practice reflects the growing commitment to responsible antimicrobial use, aiming to reduce bacterial resistance and minimize the risks associated with prolonged and unnecessary drug exposure.[27]

Acceptance of pharmacist interventions by the multidisciplinary team exceeded 92% in both periods. Although the literature does not define an optimal acceptance rate, the results are comparable to those found in other studies[13,14,25,28,29] and higher than in others[15,30,31]. A probable improvement in acceptance was observed between the two periods, which may be correlated with the pharmacist's longer practice time and the establishment of trust through interdisciplinary collaboration, promoted by rounds and discussions, shared responsibility for pharmacotherapy, and patient-centered care. There was also a probable reduction in non-acceptance rates, from 4.1% in period A to 2.7% in period B, with disagreement between prescribers and pharmacists accounting for more than 80% of the reasons for non-acceptance. These situations mainly occurred in antimicrobial de-escalation and the discontinuation of omeprazole prophylaxis.

Despite the contributions of this study, it is acknowledged that due to its retrospective cross-sectional nature, it does not allow for establishing causality between pharmaceutical interventions and clinical outcomes. The use of secondary data may introduce bias due to the quality of the records, which still rely on manual entry, possibly leading to underreporting. Limitations of the available database prevented the use of more robust comparative statistical techniques to infer the differences observed between the two analyzed periods.

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In addition, the absence of patient characterization data—such as reason for admission, devices used, and age group—as well as the lack of information on clinical outcomes prevented the analysis of potential relationships between the increase in number and changes in the profile of DRPs and service improvement. To overcome these limitations, future studies could broaden the scope by including direct clinical outcomes and adopting more suitable methodological designs, such as prospective studies, clinical trials, and implementation studies.

Conclusion

This study analyzed DRPs identified in an ICU over two distinct periods, aiming to assess the evolution of clinical pharmacy practice years after the service was implemented. A possible increase in DRP identification was observed, particularly those classified as potential, suggesting a more proactive approach and greater capacity for harm prevention. The change in the intervention profile, with a potential reduction in DRPs related to dispensing and a relative increase in records involving pharmacotherapy adjustments, suggests a shift in pharmaceutical care toward patient-centered practice, integrated with the multidisciplinary team, and focused on solving care process issues. Therefore, this study reinforces the importance of the clinical pharmacist's active presence in the ICU and the need for further development of their role to consolidate practices that ensure patient safety and treatment effectiveness.

Although methodological limitations prevent robust conclusions about the direct impact of clinical pharmacy services on care quality and primary clinical outcomes, the findings emphasize the importance of systematic intervention recording and highlight opportunities for improvement. Among these, the implementation of clinical protocols—such as vancomycin monitoring and stress ulcer prophylaxis—stands out for contributing to evidence-based standardization of practices and reducing variability in clinical care. The analysis of the changes in the DRP profile also underscores the need for deeper investigation into the techniques and work processes of clinical pharmacists in this setting, using more controlled methodological designs that allow for more precise assessment of the clinical impact of pharmaceutical practice on ICU patient outcomes.

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Contributors

Project conception (AIOP, VC). Data collection, analysis, and interpretation (AIOP, ACA, VC). Manuscript drafting (VC). Critical manuscript review (AIOP, FCM). All authors approved the final version to be published and take responsibility for all information contained in the work.

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Conflict of interest statement

The authors declare no conflicts of interest related to this article.

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