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Clinical pharmacist interventions in an intensive care unit reduces ICU mortality at a tertiary hospital in Dubai, United Arab Emirates

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ABSTRACT

Background: Drug-related problems (DRPs) are prevalent in critical care settings and can be life-threatening. Involving clinical pharmacists (CP) within the critical care team is recommended to optimize therapy and improve patient survival.
Objective: To classify DRPs identified by a CP in the Intensive Care Unit (ICU) and to assess the impact of CP interventions accepted by physicians on the length of ICU stay and in-hospital survival.
Methods: This study was conducted prospectively at the Medical ICU of Rashid Hospital, a tertiary hospital in Dubai, over a 16-month period from September 2021 to December 2022. The study included patients admitted to ICU during the study period. CP interventions were documented, and DRPs were classified using the modified Pharmaceutical Care Network Europe V.9.1.
Results: During the study period, 1004 interventions were recommended for 200 patients. The majority of these interventions, 92% ($n = 922$), received physician acceptance, and 82% ($n = 820$) were fully implemented by the physician. In total, 1033 drug-related problems (DRPs) were identified, with a median of 3 DRPs per patient. The most common DRPs was drug selection (61%), followed by dose selection (22%). There were 337 DRPs related to antimicrobial agents. Interestingly, we noted that when we adjusted for patients' demographic data and the Glasgow Coma Scale severity score, patients who received >4 implemented interventions exhibited lower cumulative hazard of death within 90 days of their ICU stay in comparison to their counterparts (adjusted Hazard Ratio: 0.10, 95% CI of 0.02–0.41; $P = 0.027$).
Conclusion: The study emphasizes the critical role of CP in the ICU, addressing DRPs, and enhancing overall patient care. Furthermore, it highlights the potential impact of pharmacist interventions in improving patient survival outcomes. This underscores the importance of implementing CP services in ICUs across the UAE.

1. Introduction

Drug-related problems (DRPs) are defined as an "incidence or event involving drug therapy that actually or potentially interferes with optimal health outcomes".[1] Polypharmacy and multiorgan failure increase the incidence of DRPs, which are prevalent in critical care and pose potentially life-threatening risks.[2] DRPs can lead to serious clinical complications, including increased length of hospital stay, unnecessary costs, and a higher risk of death.[3,4] The rate of DRPs is twofold higher in intensive care unit (ICU) patients compared to non-ICU patients. Fortunately, many of these incidents are potentially preventable, and their frequency can be reduced through appropriate drug use.[5] One effective approach to optimizing therapeutic efficacy, safety and preventing DRPs is to include a clinical pharmacist (CP) as a vital member of the critical care team. Detecting and resolving DRPs stands as one of the CP's most crucial responsibilities, as it can help prevent adverse drug events.[6–9] Previous studies have demonstrated that CP involvement in ICU settings can lead to reduced lengths of stay and mortality rates.[10,11]

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Moreover, the economic evaluation of CP activities in the ICU has revealed significant cost savings and a reduction in the workload for ICU staff.[7,12]

A position paper in 2020 from SCCM (Society of Critical Care Medicine), ACCP (American College of Clinical Pharmacy), and ASHP (American Society of Health-System Pharmacists) defined pharmacy services as having both essential and desirable roles, with one of the essential roles being the prevention of potentially inappropriate drug therapies.[13] Practice guidelines with detailed recommendations are required for therapeutic management to guide pharmacists in their daily ICU practice. Studies have shown that barriers in healthcare team interactions hinder the implementation of pharmacy services, emphasizing the need for improved cooperation and understanding among healthcare professionals regarding CP activities.[14] A regional challenge lies in the fact that CP services in the ICU in the United Arab Emirates (UAE) face complexities due to the relatively late introduction of this concept. The perception of clinical pharmacy was first established in the United States in the 1950s, while the first pharmacy college in the UAE was established in 1992.[15]

Several studies have been conducted in the UAE to identify DRPs and assess pharmacist interventions in general wards and outpatient settings.[16,17] However, to the best of our knowledge, no study has recorded the identified DRPs in patients admitted to ICU and evaluated the impact of CP interventions on patient outcomes in the UAE. Therefore, the main aim of this study was the identification and classification of DRPs by CP among patients who were admitted to the ICU during the study period. The second aim was to assess the impact of CP interventions on the patient clinical outcomes such as length of ICU stay and in-hospital survival.

2. Methods

2.1. Ethics approval

Ethical approval was obtained from the Dubai Scientific Research Ethics Committee (DSREC) and the Dubai Health Authority at Rashid Hospital (DSREC-09/2022_05). The DSREC did not require written consent from the participants due to the observational nature of the study; however, in case further information was required regarding the identification or assessment of each DRP, verbal informed consent was taken from the respective patient or family member.

2.2. Study design and population

This prospective observational study included patients who were admitted to the Medical ICU at Rashid Hospital from September 2021 to December 2022. The inclusion criteria involved patients admitted to the ICU during the study period, while those who were referred to the ICU only for plasmapheresis or dialysis were excluded from the study. The principal researcher, H.A.H.A., an experienced licensed CP and board-certified in critical care, provided CP interventions. The CP worked full-time in the ICU for 8 h a day, 5 days a week. Notably, no clinical pharmacists had worked in this unit prior to the study.

2.3. Data collection

During the study, to identify DRPs, the CP reviewed the following information: patients' demographic data such as age and gender, past medical and medication histories, diagnosis on ICU admission, and daily laboratory parameters, cultures, lines, clinical images, and medication lists. The identified DRPs were documented in the CP documentation sheet. Clinical decision-making tools used by the CP included UpToDate, Micromedex, Lexicomp, and the Sanford Guide to Antimicrobial Therapy mobile applications. PCNE version 9.1 was used for the classification of DRPs. The dose adjustment for on/off Continuous Renal Replacement Therapy (CRRT) was further considered in the "dose selection" group. CP-related recommendations were discussed face-to-face during medical ICU rounds with the ICU team, which consisted of one consultant, one senior specialist registrar, a clinical pharmacist, a nurse, and a respiratory therapist.

2.4. Study objectives

The primary objective of this study was the identification and classification of DRPs by CP among patients admitted to the ICU during the study period (from September 2021 to December 2022). The second objective was to assess the impact of CP interventions on the patient clinical outcomes, such as the length of ICU stay and in-hospital survival.

2.5. Statistical analysis

In this study, Spearman's correlation coefficient was used to assess the correlation between the number of clinical pharmacist interventions (CPIs) per patient and the length of ICU stay. Moreover, a linear regression model, adjusted for patient age, sex, and severity level based on the Glasgow Coma Scale (GCS), was used to compare the length of stay between those with >4 CPIs and those with <4 CPIs. To evaluate in-hospital mortality as an outcome, COX proportional analysis was conducted, adjusting for patient age, sex, and GCS. A sample size of 70 cases and 70 controls was determined to provide 90% power to detect a significant difference ($\alpha = 0.05$) between subgroups of patients with CPIs $\geq$4 and those with CPIs <4 using G*power software.[18] The statistical analysis was performed using R (packages; ggplot2, foreign, survival, survminer, and tidyverse) and SPSS (version 27.0). All tests were two-tailed, and a *P*-value of <0.05 was considered statistically significant.

3. Results

3.1. Patient demographic

During the study period, a total of 200 patients were reviewed by the CP. Demographic characteristics of patients are deposited in Table 1. The median age of patients was 65 years (range: 19–99), and approximately two-thirds were male (66%, $n = 132$). One-fourth (25%, $n = 50$) required CRRT during their ICU stay due to renal injury.

3.2. Interventions classification and acceptance rate outcome

During the study period, a total of 1004 interventions were carried out by the clinical pharmacist (H.A.H.A.). The majority of these interventions, 92% ($n = 922$), received physician acceptance, and 82% ($n = 820$) were fully implemented by the physician. Moreover, most of these physician-implemented interventions were medication-related (88%, $n = 721$). A smaller proportion (12%, $n = 99$) consisted of non-medication-related interventions, such as daily assessments of indwelling catheters (e.g., central line, Foley's catheter, and arterial line), feeding, and requesting culture.

Table 1
Baseline clinical characteristics of the study population.

	Standard care ($n = 200$)
Age, years, median (IQR), yr	65 (19–99)
Male gender, n (%)	132 (66)
Laboratory findings (normal range)	
White cell count (3.9–11.10 × 10^9 per L)	13 (8.3–19.3)
C-reactive protein (1.0–3.0 mg/L)	105.2 (40.8–168.3)
Procalcitonin	1.3 (0.26–5.68)
Glasgow Coma Scale (GCS)	5.5 (3–11)
CCRT, n (%)	50 (25)

Data are n (%) or median (IQR).
Abbreviation. CRRT, Continuous Renal Replacement Therapy.

3.3. Prevalence of identified DRPs

A total of 1033 DRPs were identified out of the 1004 interventions among 200 patients admitted to the ICU (One intervention could address few DRPs, with median of 3 DRPs per patient and interquartile of 1 to 6). During the 90 days of patients' stay in the ICU, drug selection (61%, $n = 503$) was the most common DRP, with "no indication for drug" being the most frequent subcategory within this group. This was followed by dose selection (22%, $n = 225$). Within the effectiveness and safety group, 'adverse drug events (ADE)' were reported in 29 cases (Fig. 1 and Table 2). We noticed that around one-third of identified DRPs (n=337) were related to antimicrobial agents (Table 2). Details of some of the identified DRPs are provided in the Supplementary Table 1.

3.4. The impact of clinical pharmacist interventions

To evaluate the impact of CP interventions on patients' outcomes in the ICU, we categorized patients into two groups: those with fewer than 4 implemented clinical pharmacist interventions (CPIs <4, 56%, $n = 91$) and those with equal or >4 implemented CPIs (CPIs ≥4, 44%, $n = 71$). We observed a positive correlation between the number of implemented CPIs per patient and the length of ICU stay (Fig. 2A; median of 3 CPIs per patient and median of 18 days ICU stay, $r = 0.235$; $P = 0.001$). Additionally, patients with CPIs ≥4 had longer hospital stays compared to their counterparts, although the difference was not significant after adjustment with patients' demographic and GCS severity score (Fig. 2B; median of 14 days ICU stay in CPIs <4 vs. 23 days ICU stay in CPIs <4 groups; $p = 0.069$).

Next, we found that patients with CPIs ≥4 exhibited lower cumulative hazard of death within 90 days of ICU stay compared to their counterparts when adjusting with patients' demographic and GCS severity score (Fig. 3B, adjusted Hazard Ratio: 0.10, 95% CI of 0.02–0.41; $P = 0.027$).

4. Discussion

The present study demonstrated the most common subgroups of DRPs identified by CP in the ICU setting and assessed the impact of CP interventions on patient outcomes.

The majority of DRPs fell under the subgroup of 'drug selection' and 'dose selection', consistent with a previous study in the ICU setting.[19]

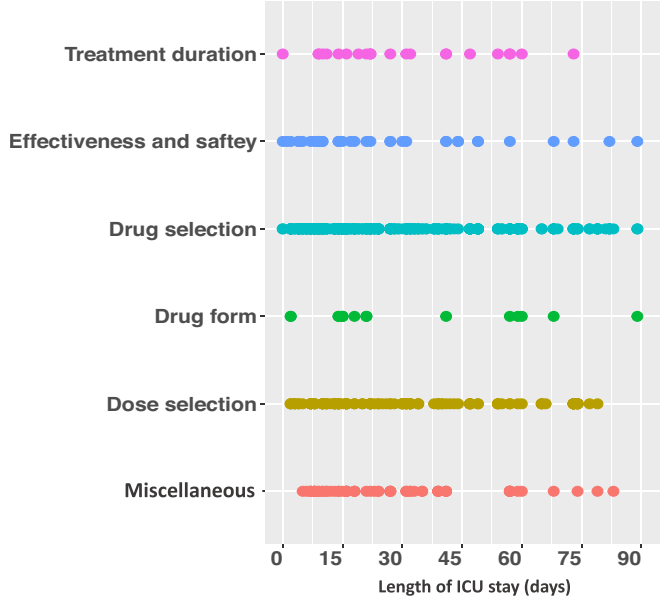

Fig. 1. Distribution of detected DRPs by CP during patients' 90-day ICU stay.

Table 2
Classification of detected DRPs according to PCNE.

		Overall	Antimicrobial
Drug-related problems (DRPs) detected	**Description**	***n* = 1033 (%)**	***n* = 337 (%)**
Drug selection	**Total**	**630** (61)	**126** (42)
	Inappropriate drug according to guidelines/formulary	11 (1)	8 (3)
	No indication for drug/ stop drug	440 (43)	97 (33)
	Inappropriate combination of drugs, or drugs dietary supplements	4 (0.4)	2 (0.7)
	Inappropriate duplication of therapeutic group	27 (3)	10 (3)
	No or incomplete drug treatment in spite of existing indication	111 (11)	4 (1)
	Alternate - change in drug therapy	37 (4)	18 (6)
Drug form	Inappropriate drug form/ formulation	**33** (3)	**2 (0.7)**
Dose selection	**Total**	**225** (22)	**114 (38)**
	On/Off CRRT Dose	53 (5)	52 (17)
	Drug dose too low	39 (4)	24 (8)
	Drug dose too high	48 (5)	19 (6)
	Dosage regimen not frequent enough	20 (2)	8 (3)
	Dosage regimen too frequent	63 (6)	22 (7)
	Dose timing instructions wrong, unclear, or missing	2 (0.2)	2 (0.7)
Treatment duration	**Total**	**56** (5)	**53 (18)**
	Duration of treatment too short	2 (0.2)	2 (0.7)
	Duration of treatment too long	54 (5)	51 (17)
Effectiveness and Safety	**Total**	**57** (5)	**9 (3)**
	TDM	8 (1)	6 (2)
	ADE	29 (3)	3 (1)
	Contraindication /hold	20 (2)	0
Miscellaneous	**Total**	**32** (3)	**7 (2.3)**
	Consultation, provide information for nurse	21 (2)	6 (2)
	Other	11 (1)	1 (0.3)

Abbreviation. CRRT, Continuous Renal Replacement Therapy; TDM, Therapeutic Drug Monitoring; ADE, Adverse Drug Event.

Furthermore, we found that within the subgroup of drug selection, 'no indication for drug' and 'no or incomplete drug treatment in spite of existing indication' were the most prevalent DRPs. A Similar pattern within the drug selection subgroup of DRPs was reported by a regional study conducted in an ICU in Taif City, Saudi Arabia.[20] Accordingly, we noticed that 'No indication for drug' as well as 'duration of treatment too long' were more frequent with antimicrobial therapy. This observation may indicate the necessity of implementing antibiotic stewardship programs in the ICU setting. In support of this, a large randomized controlled trial that assessed the effect of procalcitonin-guided antimicrobial therapy demonstrated a reduction in the treatment duration and daily defined doses in critically ill patients. The study concluded that these interventions were beneficial for patients and led to a significant decrease in mortality.[21]

Moreover, the second most frequent subgroup of DRPs identified was related to dose selection, which is expected given the prevalence of renal failure and the utilization of CRRT among ICU patients (approximately 25% in our study; Table 1). Close monitoring of renal function and daily dosing adjustments are imperative for critically ill patients[22,23] and have been reported to be linked to lower mortality in hospitalized patients with renal impairment.[24]

Notably in our study, the rates of accepted and fully implemented CP

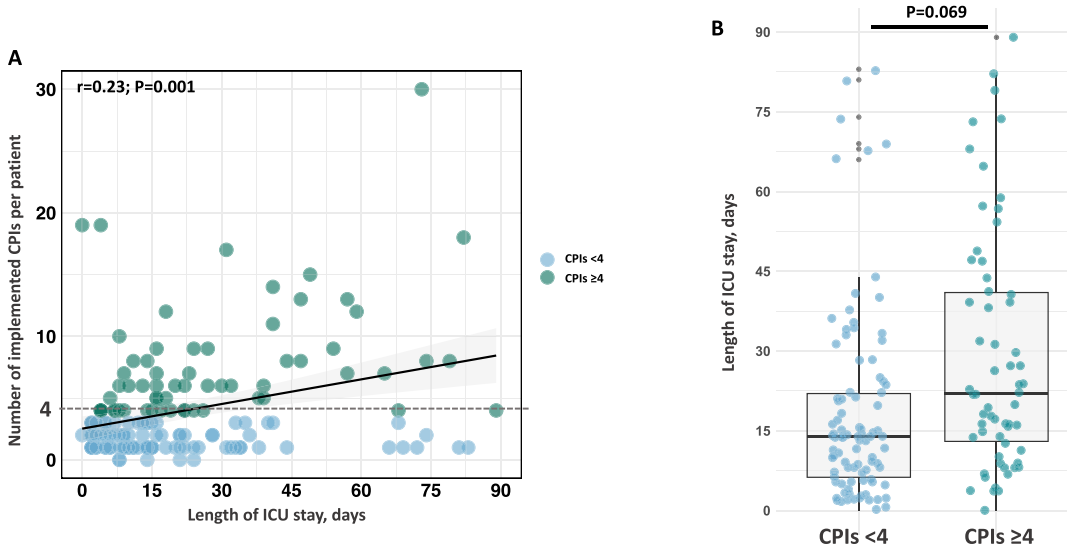

Fig. 2. The relation between implemented CPIs and length of ICU stay. (A) The correlation between the number of implemented CPIs per patient and the length of ICU stay. (B) Comparison of ICU stay length between groups with fewer than 4 CIs and those with equal to or >4 CPIs. Statistical tests: Statistical tests: Spearman's correlation coefficient and linear regression analysis adjusted for patients' demographics and Glasgow Coma Scale severity score. Abbreviation: CPI - Clinical Pharmacist Intervention.

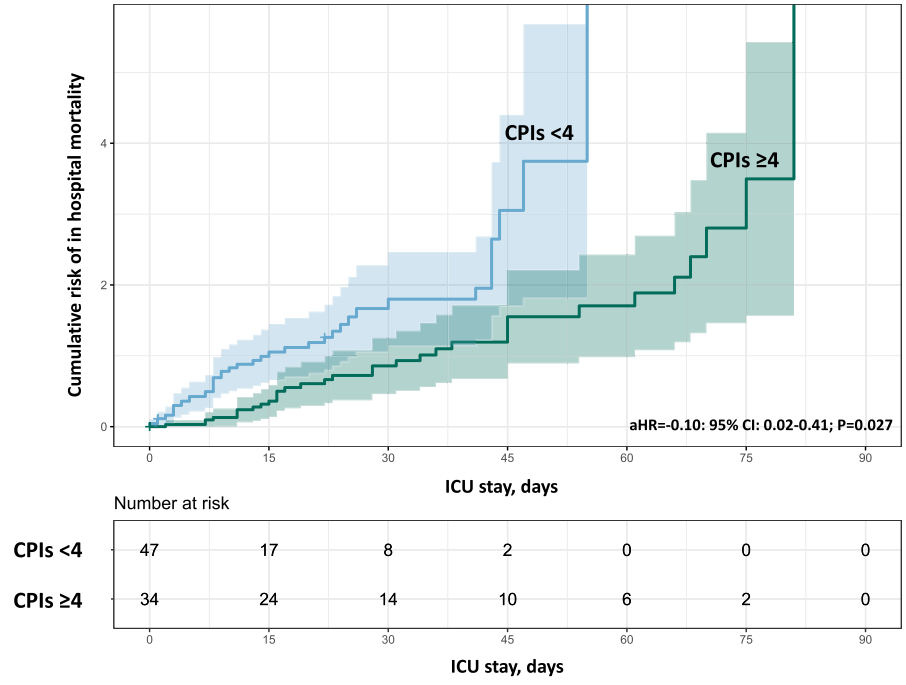

Fig. 3. The Impact of implemented CPIs on 90-day patient survival outcome. Comparison of the hazard of death between groups with fewer than 4 CPIs and those with equal to or >4 CPIs. Statistical tests: Kaplan-Meier curve analysis for these two groups, and COX proportional analysis adjusted for patients' demographics and Glasgow Coma Scale severity score. Abbreviation: CPI - Clinical Pharmacist Intervention.

interventions by physicians were comparable to those reported in previous studies (ranging from 62%–99%). This is important as we have shown that implemented PC interventions have been associated with lower in-hospital mortality. Similar findings were observed in a meta-analysis that evaluated the inclusion of pharmacists in critical care teams and its impact on patient mortality.[10] This is especially valuable in the ICU setting with high mortality rates, where CP interventions can have a significant impact. However, given that the majority of studies were observational, there is a need for larger studies with two pre and post-intervention arms to further validate these findings.

4.1. Study limitations

This investigation has a few limitations that need to be addressed. To account for the severity of critically ill patients, the survival model was adjusted with GCS severity scores. However, there might be other factors related to patient severity that need to be controlled for. Moreover, this study focused on a medical-type ICU, limiting the generalizability of these findings to other types of ICUs, such as surgical and neurosurgical ICUs. Further research is needed to cover all types of ICU. Additionally, this study was conducted at a single center, even though it was carried

out in one of the main governmental hospitals in Dubai, which limits its generalizability to the entire UAE. Lastly, our results do not fully represent the extent of DRPs and pharmacist interventions as some were discussed verbally with the team and not formally documented.

In summary, our study revealed that the most frequent DRPs occurring in ICU patients were related to drug selection, followed by dose selection. A high percentage of CP interventions were accepted by physicians, underscoring the importance of CP involvement in identifying DRPs and ultimately enhancing patient outcomes, as reflected in better 90-day survival outcomes. The implementation of CP services in ICU settings is crucial and should be expanded across the UAE.

CRediT authorship contribution statement

Hawra Ali Hussain Alsayed: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Fatemeh Saheb Sharif-Askari:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Narjes Saheb Sharif-Askari:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Rabih Halwani:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2024.100431.

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