

Assessment of Drug–Drug Interactions in Intensive Care Unit Patients: A Prospective Observational Study in a Tertiary Care Hospital

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Abstract

Drug-drug interactions (DDIs) are a key source of medication-related problems in patients in critical illness admitted to intensive care unit. Complex treatment regimens and polypharmacy raise the probability of clinically significant interactions. Using a prospective observational design, the study examined the frequency, pattern, severity, and mechanisms of drug-drug interactions in patients receiving treatment in the ICU of the study hospital. Over the course of a six-month trial, 103 adult ICU patients who were on two or more drugs were enrolled. Data were collected using a structured case record form. Micromedex, Lexicomp, and Medscape Drug Interaction Checker were used to identify drug-drug interactions. The Kruskal-Wallis test and descriptive measures were employed to summarize the study data. Drug-drug interactions were identified among most of the ICU patients, with moderate-severity interactions being the common category. Pharmacokinetic interactions were relatively more frequent than pharmacodynamic interactions, and cardiovascular drugs, diuretics, anticoagulants, gastrointestinal agents, anti-infective agents, and bronchodilators were the therapeutic classes most commonly involved in interacting drug combinations. In order to enhance drug safety and maximize therapeutic outcomes in patients in critical condition, the results emphasize the significance of routine medication review, rigorous interaction screening, and the active involvement of pharmacists in multidisciplinary ICU care.

Keywords: Drug-Drug Interactions, Polypharmacy, Medication Safety, Clinical Pharmacist, Critical Care

1. Introduction

Drug–drug interactions (DDIs) refer to alterations in the therapeutic effect of a medication resulting from the simultaneous administration of another drug, as well as interactions with dietary components or environmental factors. Interactions involving two or more medications are particularly significant in clinical practice, as they may diminish therapeutic efficacy or increase the likelihood of toxic effects. DDIs occur through either pharmacokinetic mechanisms, impacting a drug's distribution, metabolism, excretion, or absorption, or pharmacodynamic mechanisms, which modify their pharmacological effects at the target site. These drug interactions may result in negative side effects and lengthen hospital stays, extend duration of therapy, and increase healthcare costs.

Drug interactions remain a significant concern in healthcare, particularly in intensive care units (ICUs), where patients in critical condition are frequently exposed to multiple medications concurrently. These interactions may negatively influence therapeutic outcomes by raising the possibility of complications,

prolonging hospital stays, escalating healthcare costs, and, in severe cases, contributing to mortality. Therefore, evaluating the prevalence and characteristics of drug interactions in ICU patients is crucial for improving patient safety and optimizing pharmacotherapeutic management. Patients in critical condition are particularly susceptible to drug–drug interactions due to the complexity of their ailment and the frequent requirement for several therapeutic interventions. These interactions may adversely affect treatment outcomes and patient safety, making their identification and prevention an important aspect of intensive care management.

2. Aim and Objectives

To evaluate drug-drug interactions, frequency, pattern, severity, and contributing factors among patients hospitalized in a tertiary care teaching hospital's intensive care unit.

- To identify the pattern of drug–drug interactions, including the therapeutic classes involved and mechanisms of interactions.
- To assess the prevalence of drug interactions among ICU patients.
- To classify the severity of identified drug–drug interactions using Micromedex, Lexicomp, and Medscape Drug Interaction Checker.
- To evaluate the association between polypharmacy and the incidence of interactions between drugs.

3. Methodology

A prospective observational study was conducted among patients admitted to the Intensive Care Unit of Shadan Institute of Medical Sciences Teaching Hospital and Research Centre, Hyderabad, over a six-month period. Eligible participants were adults aged 18 years or older who received two or more medications concurrently during their ICU stay. Patients with incomplete prescription charts or medical records and those transferred to another healthcare facility before completion of data collection were excluded. A total of 103 participants were included based on sample-size estimation using Cochran's formula. Demographic and clinical information, diagnoses, comorbidities, ICU type, duration of ICU stay, prescribed medications and relevant laboratory information were collected from patient case records, medication charts, laboratory reports, ICU treatment records and progress notes using a structured data collection form. Medication profiles were reviewed throughout ICU admission. Drug-drug interactions were screened using Micromedex Drug Interactions, Lexicomp Drug Interactions and Medscape Drug Interaction Checker. Identified interactions were recorded for severity, mechanism, onset and documentation level; where severity differed between databases, the highest reported severity was adopted. Severity was classified as major, moderate or minor, and mechanisms as pharmacokinetic, pharmacodynamic or unknown. Data were processed using Microsoft Excel and IBM SPSS Statistics version 25.0. Descriptive statistics were used for demographic and clinical characteristics, while the Kruskal-Wallis test was used to assess differences in DDI frequency across minor, moderate and major polypharmacy categories. Statistical significance was set at 0.05. Institutional permission was obtained before study initiation, and participant identity and information were kept confidential.

4. Results

Baseline Demographic Characteristics

The study comprised 103 individuals who were admitted to the intensive care unit during the study period.

Demographic Variable	Value / Distribution
Age (Years) – Mean $\pm$ SD	56 $\pm$ 14
Age Range	23–74
Male	57 (55.3%)
Female	46 (44.7%)

Of the 103 participants in the study, 45% were women and 55% were men. With an age range of 23–74 years, the average age was 56 $\pm$ 14 years, suggesting that most patients were older adults and frequently hospitalized to the intensive care unit. The observed age distribution reflects the patient profile typically encountered in intensive care units, where advancing age is frequently associated with chronic illnesses requiring complex critical care management. The relatively balanced gender distribution indicates that both male and female patients were adequately represented within the study cohort.

ICU Admission Category and Length of Stay

Data regarding the specific intensive care unit (ICU) and the length of ICU stay were documented for all 103 participants. The institution’s critical care departments comprised the Medical ICU (inclusive of cardiology and pulmonology admissions) and the Surgical/Obstetrics ICU. The length of stay (LOS) was analyzed using both continuous descriptive statistics and categorical stratification to assess the period of patient exposure to critical care interventions and complex pharmacological regimens.

Clinical Variable	Overall Cohort (n=103)	Medical ICU (n=66)	Surgical/Obstetrics ICU (n=37)
Admission Distribution	103 (100%)	66 (64.1%)	37 (35.9%)
Mean ICU Stay $\pm$ SD (days)	8.4 $\pm$ 4.2	9.6 $\pm$ 4.5	6.2 $\pm$ 2.8
Median (days)	7.0	8.0	5.0
IQR (days)	4.0–11.0	6.0–13.0	3.0–8.0
Minimum–Maximum (days)	2.0–24.0	3.0–24.0	2.0–14.0
Short Stay (≤ 3 days)	16 (15.5%)	6 (9.1%)	10 (27.0%)
Intermediate Stay (4–7 days)	39 (37.9%)	22 (33.3%)	17 (45.9%)
Extended Stay (8–14 days)	33 (32.0%)	25 (37.9%)	8 (21.6%)
Long Stay (>14 days)	15 (14.6%)	13 (19.7%)	2 (5.4%)

Most patients were admitted to the Medical intensive care unit, indicating that medical illnesses constituted the principal burden of critical care admissions during the study period. Patients managed in the Medical ICU generally required a longer duration of intensive care than those admitted to the surgical/obstetrics ICU, suggesting greater disease complexity and prolonged therapeutic management. Although ICU stay differed widely among study population, most required short- to intermediate-term intensive care, while only a smaller proportion experienced prolonged hospitalization, reflecting the heterogeneous nature of critical illness within the study population.

Distribution of Primary Admission Diagnoses

Diagnostic Category	Specific Clinical Condition	Number of Patients (n)	Percentage (%)
Cardiovascular Emergencies	Overall	35	33.9%
	Acute Coronary Syndrome (e.g., Evolved Anterior Wall Myocardial Infarction, Single Vessel Disease)	22	21.3%
	Heart Failure / Right Heart Failure	13	12.6%
Obstetrics and Surgical Complications	Overall	36	34.9%
	Imminent Eclampsia / Hypertensive Emergencies of Pregnancy	20	19.4%
	High-Risk Post-Operative Monitoring (e.g., Post-Cesarean Section with Severe Anemia)	16	15.5%
Respiratory Emergencies	Overall	32	31.1%
	Acute Exacerbation of Bronchial Asthma	20	19.4%
	Pulmonary Arterial Hypertension (PAH) with Cor Pulmonale	12	11.7%
Total Cohort		103	100.0%

Cardiovascular disorders and obstetric or surgical complications represented the predominant indications for ICU admission in the present study, while respiratory illnesses also contributed substantially to the overall disease burden. Acute coronary syndrome, imminent eclampsia, and acute exacerbation of bronchial asthma emerged as the most frequently encountered individual clinical conditions. The observed diagnostic profile reflects the diverse spectrum of patients in critical condition managed in the study setting and explains the frequent use of multiple therapeutic drug classes during ICU admission.

Clinical Characteristics and Comorbidities

Comorbid Condition	Number of Patients (n)	Percentage (%)
Hypertension	52	50.5%
Cardiovascular Diseases (e.g., ACS, PAH, RHF)	34	33.0%
Diabetes Mellitus	30	29.1%
Respiratory Disorders (e.g., Bronchial Asthma)	18	17.5%
Obstetrics / Pregnancy Complications (e.g., Eclampsia)	12	11.7%

Note: Several patients presented with more than one comorbid condition; therefore, the total percentage exceeds 100%.

Hypertension was the most frequently identified comorbid condition among the study participants, followed by cardiovascular disease and diabetes mellitus. The presence of multiple coexisting illnesses

illustrates the clinical complexity of the ICU population and highlights the need for multidrug therapy to achieve optimal disease management. Such therapeutic complexity explains why the study found an increased risk of drug-drug interactions.

Prevalence of Polypharmacy

Polypharmacy Category	Definition (Concurrent Drugs)	Number of Patients (n)	Percentage (%)
Minor Polypharmacy	2–5 Medications	15	14.6%
Moderate Polypharmacy	6–9 Medications	45	43.7%
Major Polypharmacy	≥10 Medications	43	41.7%

A high proportion of the study population experienced polypharmacy, with the majority of individuals receiving six or more concurrent medications during ICU admission. This finding reflects the complexity of intensive care pharmacotherapy, where management commonly requires the simultaneous administration of multiple therapeutic agents for the treatment of primary illness, associated comorbidities, and supportive care. The predominance of moderate and major polypharmacy suggests that the enrolled patients were inherently more likely to experience clinically significant drug-drug interactions.

Overall Prevalence of Drug-Drug Interactions

Number of Identified DDIs	Number of Patients (n)	Percentage (%)
0 DDIs	10	9.7%
1 to 2 DDIs	36	35.0%
3 to 5 DDIs	37	35.9%
>5 DDIs	20	19.4%

Drug-drug interactions were identified in 90.3% among the enrolled patients, while 9.7% of patients had no identified drug-drug interactions. The majority of participants experienced either 1–2 DDIs (35.0%) or 3–5 DDIs (35.9%), whereas 19.4% experienced more than five documented drug-drug interactions. These findings suggest that drug-drug interactions were frequently observed in the ICU cohort, with a substantial number of patients experiencing multiple concurrent interactions.

Severity Classification of Identified DDIs

Severity Classification	Number of Interactions (n)	Proportion of Total DDIs (%)
Major Interactions	70	21.9%
Moderate Interactions	200	62.5%
Minor Interactions	50	15.6%
Total DDIs Identified	320	100%

Severity assessment was performed for the 320 identified drug-drug interactions detected among the enrolled ICU patients. Moderate-severity interactions emerged as the most common category, comprising 62.5% (n=200) of all identified interactions, followed by major interactions (21.9%, n=70) and minor

interactions (15.6%, n=50). The higher proportion of moderate interactions indicates that most identified DDIs required clinical monitoring, evaluation, or possible modification of therapy. However, the identification of major interactions emphasizes the clinical relevance of regular medication evaluation and monitoring for ICU patients using several drugs.

Mechanisms of Identified DDIs

Mechanism Type	Number of Interactions (n)	Proportion of Total DDIs (%)
Pharmacokinetic	165	51.6%
Pharmacodynamic	140	43.8%
Unknown / Mixed	15	4.6%

Pharmacokinetic mechanisms were the most frequently identified, representing 51.6% of the documented interactions. Pharmacodynamic mechanisms accounted for 43.8% of the total identified DDIs. The 'Mixed' category refers to interactions that demonstrated characteristics of both pharmacokinetic and pharmacodynamic mechanisms or for which clinical databases provided insufficient data to classify into a single mechanism.

Most Frequently Involved Therapeutic Drug Class Combinations

Primary Drug Class	Interacting Drug Class	Frequency of Occurrence (n)	Predominant Severity
Cardiovascular	Diuretics	85	Moderate
Anticoagulants / Antiplatelets	Gastrointestinal Agents	62	Moderate
Anti-infectives	Diuretics	48	Major
Cardiovascular	Bronchodilators	36	Major

Note: Table 9 presents the four most frequently observed therapeutic class combinations. The remaining identified interactions (n=89) involved less frequently occurring drug pairs not individually tabulated.

Comparison of Frequency of Drug-Drug Interactions Across Polypharmacy Categories

Polypharmacy Category	Number of Patients (n)	Mean Number of DDIs per Patient (Mean ± SD)
Minor polypharmacy (2–5 drugs)	15	0.6 ± 0.3
Moderate polypharmacy (6–9 drugs)	45	2.5 ± 1.2
Major polypharmacy (≥10 drugs)	43	4.8 ± 1.6

Statistical analysis: Kruskal-Wallis test. DDI frequency differed significantly among the polypharmacy categories ($p < 0.001$). Patients receiving a greater number of medications demonstrated a higher frequency of identified DDIs than patients receiving a lower number of medications.

5. Discussion

This study was undertaken to evaluate the frequency, pattern, severity, causes, and determinants of drug-drug interactions (DDIs) among patients hospitalized in the intensive care unit (ICU) of a tertiary care setting. The current prospective observational study was carried out because drug-drug interactions are one of the primary medication-related issues that patients in critical condition face because of extensive polypharmacy, multiple comorbidities, altered physiological functions, and frequent modifications of drug therapy during ICU admission. The findings showed that possible DDIs are very common in patients in critical condition and that their incidence is greatly increased by an increasing medication burden.

The study population primarily consisted of middle-aged and elderly adults, with a slight predominance of male patients. This pattern mirrors what is typically seen in ICU populations generally, where older age tends to accompany a greater burden of chronic disease, declining organ function, and more intensive treatment needs. Comparable demographic findings were described by Lima and Cassiani (2009), Wagh et al. (2019), and Kamble et al. (2025). Although male patients constituted a substantial number of patients, gender may not be a major determinant of DDI occurrence. Rather, the complexity of illness and the number of prescribed medications are considered more important contributors to interaction risk.

Most patients were admitted to the Medical ICU, while the remainder received care in the Surgical/Obstetrics ICU. Patients treated in the Medical ICU also experienced longer hospital stays than those admitted to the Surgical/Obstetrics ICU. This finding probably reflects the greater complexity of medical illnesses such as respiratory disorders and metabolic diseases, which often require prolonged pharmacological management and continuous monitoring. Prolonged hospitalization exposes patients to repeated medication changes, supportive therapies, and the addition of new drugs, thereby increasing opportunities for potential drug interactions. This lengthening of ICU stay as a risk factor for DDIs has also been noted by Xu et al. (2025) and Baghaei et al. (2024).

Cardiovascular emergencies represented a frequent indication for intensive care admission, followed closely by obstetric and surgical complications, while respiratory emergencies also accounted for a substantial proportion of admissions. These findings reflect the clinical profile of the study hospital and explain the extensive use of cardiovascular drugs, anticoagulants, bronchodilators, antimicrobials, corticosteroids, and supportive medications. Such therapeutic complexity inevitably increases the possibility of clinically significant DDIs. Indian ICU-based research by Gupta et al. (2016), Singh and Swetha (2018), and Kamble et al. (2025) has also brought attention to cardiovascular and respiratory conditions as contributors to medication-related interaction risk.

Hypertension emerged as the most frequently observed comorbidity, followed by cardiovascular and respiratory conditions together with diabetes mellitus and pregnancy-related complications. The coexistence of multiple comorbid conditions necessitates the concurrent administration of drugs belonging to different pharmacological classes, thereby increasing therapeutic complexity. Previous investigations by Obeid and Karara (2022) and Baghaei et al. (2024) similarly reported that patients with chronic conditions were more prone to receive complex medication regimens and therefore had a greater likelihood of experiencing potential DDIs.

A high degree of polypharmacy was observed among the study population, with most patients receiving six or more medications during ICU admission. Polypharmacy is an inevitable consequence of intensive care management, where treatment frequently includes antimicrobials, cardiovascular drugs, anticoagulants, analgesics, sedatives, bronchodilators, gastrointestinal protective agents, electrolyte replacement therapy, and other supportive medications. Numerous investigators, including Lima and

Cassiani (2009), Askari et al. (2013), Wagh et al. (2019), and Kamble et al. (2025), have consistently identified polypharmacy as the strongest predictor of potential DDIs in patients in critical condition. Most ICU patients had drug–drug interactions, confirming that medication-related interaction risk remains a significant challenge in critical care practice. The observed prevalence is consistent with reports from previous ICU-based studies, which have demonstrated that potential DDIs occur frequently among patients in critical condition despite advances in medication safety practices. Variations in reported prevalence between studies are expected because of differences in prescribing practices, patient characteristics, interaction screening databases, ICU case mix, and study methodology. In the present study, the use of three independent interaction databases may have contributed to more comprehensive identification of clinically relevant interactions.

Moderate-severity interactions constituted the largest proportion of identified DDIs, while major interactions accounted for a smaller but clinically important proportion. The results are supported by previous observations of Lima and Cassiani (2009), Wagh et al. (2019), Baghaei et al. (2024), and Kamble et al. (2025), all of whom reported moderate interactions as the predominant category in ICU patients. Although moderate interactions may not always result in immediate adverse outcomes, they frequently require closer monitoring, laboratory evaluation, dose modification, or adjustment of therapy. The presence of major interactions emphasizes that patients in critical condition remain vulnerable to serious medication-related complications because of altered pharmacokinetics, impaired organ function, and limited physiological reserve.

Evaluation of the mechanisms of DDIs demonstrated that pharmacokinetic interactions occurred more frequently than pharmacodynamic interactions. This predominance may be attributed to altered absorption, metabolism, distribution, and elimination of drugs resulting from hepatic dysfunction, renal impairment, systemic inflammation, and haemodynamic instability commonly observed in patients in critical condition. Pharmacodynamic interactions were also frequently encountered because ICU patients often receive medications with additive or opposing effects on blood pressure, coagulation, electrolyte balance, cardiac rhythm, and central nervous system function. Similar observations were reported by Lima and Cassiani (2009), who also identified pharmacokinetic mechanisms as the predominant type of interaction in ICU patients.

Cardiovascular drugs, diuretics, anticoagulants, gastrointestinal agents, anti-infective agents, and bronchodilators were the drug classes most frequently identified in DDIs. These medications constitute the cornerstone of ICU pharmacotherapy and are frequently prescribed together for the management of cardiovascular instability, respiratory disorders, infections, and supportive care. Consequently, the likelihood of clinically significant interactions involving these therapeutic classes is high.

The statistically substantial correlation between polypharmacy and DDI frequency was one of the study's most notable findings. Patients receiving larger numbers of medications experienced substantially more interactions than those prescribed fewer drugs. This observation strongly supports existing evidence that medication burden is one of the principal determinants of potential DDIs in patients in critical condition. Similar findings have been reported by Lima and Cassiani (2009), and Kamble et al. (2025). The finding highlights the importance of regular medication review, rational prescribing, and deprescribing whenever clinically appropriate to reduce unnecessary interaction risk.

The findings support the significance of rigorous medication surveillance in intensive care units. Routine screening of prescriptions using validated drug interaction databases, combined with multidisciplinary review involving physicians and clinical pharmacists, may facilitate early identification and appropriate

management of clinically significant DDIs. Such interventions have the potential to improve medication safety, optimize pharmacotherapy, minimize preventable adverse drug events, and enhance clinical outcomes among patients in critical condition.

6. Conclusion

The occurrence, pattern, severity, and causes of drug-drug interactions among patients hospitalized to the ICU of tertiary care setting were evaluated in the present observational study. The findings demonstrated that drug-drug interactions were highly prevalent among patients in critical condition, reflecting the complexity of pharmacotherapy and the frequent use of multiple medications in the ICU. Moderate-severity interactions constituted the largest proportion of identified drug-drug interactions, while pharmacokinetic interactions were observed slightly more frequently than pharmacodynamic interactions. Cardiovascular drugs, diuretics, anticoagulants, gastrointestinal agents, anti-infective agents, and bronchodilators were the drug classes most commonly involved in interacting drug combinations. The findings of the study emphasize the significance of thorough prescription screening utilizing validated drug interaction databases, routine medication reviews, and ongoing monitoring of patients in critical condition on several drugs. Clinical pharmacists can improve medication safety and optimize therapeutic outcomes for patients in critical condition by actively participating in the multidisciplinary healthcare team to help identify and manage clinically significant drug-drug interactions early on. Furthermore, the implementation of rational prescribing practices, regular medication review, and multidisciplinary collaboration may improve the standard of patient care in critical care environments and lessen the incidence of avoidable drug-drug interactions.

7. References

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