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A STUDY OF DRUG-DRUG INTERACTIONS AMONG PATIENTS RECEIVING MULTIDRUG THERAPY IN THE INTERNAL MEDICINE UNIT

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ABSTRACT

Background: Drug-drug interactions (DDIs) are a significant but often under-recognized cause of adverse drug events, particularly in hospitalized patients receiving multidrug therapy.
Objective: To evaluate the prevalence, severity, and patterns of drug-drug interactions among hospitalized patients receiving multidrug therapy and to identify factors associated with increased DDI risk.
Methods: This descriptive, cross-sectional study was conducted at Tertiary Care Hospital ,Karachi from 1st December 2024 to 10 May 2025. A total of 235 patients were included in the study. Data were collected using a structured proforma designed to capture demographic information, clinical diagnosis, prescribed medications, and duration of hospital stay. Prescriptions were manually reviewed to identify all concurrent medications, and drug interaction screening was carried out using trusted, evidence-based drug interaction checkers.
Results: Out of 235 patients, 184 (78.3%) had at least one potential DDI, with a total of 527 interactions identified. Moderate interactions accounted for 40.2%, minor for 30.9%, and major for 28.9%. A statistically significant association was found between the number of prescribed drugs and the presence of DDIs ($p < 0.001$). Older age (≥65 years) and multiple comorbidities were also significantly associated with a higher frequency and severity of interactions.
Conclusion: It is concluded that DDIs are highly prevalent among patients on multidrug therapy, especially in older adults and those with polypharmacy.

Introduction

Nowadays, the tendency to more frequent occurrence of chronic diseases and senescence of the population has contributed to the exponential growth of polypharmacy the fact of simultaneous use of several medications by one patient [1]. Although such practice is usually required to ensure an effective management of the disease, there is a high probability of drug-drug interactions (DDIs) as well [2]. In drug-drug interaction, there is a change in pharmacologic or clinical effect of one drug by the presence of another, and may result in loss of therapeutic activity, enhanced toxicity or even unanticipated adverse effect [3]. Such Pour senses might be pharmacokinetic, that is, that interaction with drug taking, distribution, witting, or excretion, or pharmacodynamic, under which the aggregate impact of the drugs either adds up or cancels. Patients under multidrug therapy especially in intensive care units, oncology clinics, patients with comorbid conditions, e.g., diabetes, cardiovascular diseases, renal impairment and infectious diseases, are also at high risks of clinically significant DDIs [4]. Many studies have also indicated that unrecognized DDIs are among the factors which trigger adverse drug reactions (ADRs), hospitalization, longer-term stays, high costs of healthcare, and ultimately, a life-long disability or death. However, even with drug interaction databases, clinical decision support systems, awareness, and monitoring of DDIs are less than ideal in most healthcare establishments and especially in countries with low and middle-income (LMICs) as the electronic infrastructure and pharmacovigilance systems may be incomplete or lacking [5]. DDIs are not always properly taken into consideration in terms of their clinical relevance when an everyday prescription is being made, and in most situations, any healthcare practitioner might not be qualified enough or available in time and resources to assess the possible interactions properly. In addition to this, excessive use of electric medical records without situational discretion in the prescription process may also cause the inappropriate presence or absence of warnings [6][7]. Thus, the education of clinicians and their practical assessment of the DDI schemes are of high importance to guarantee the practice of medication safety [8]. Some articles indicate that most of the DDIs could be avoided through proper screening, documentation, and communication between the prescribers, pharmacists, and patients [9][10]. Polypharmacy not only becomes frequent in groups like elderly and multi-morbid populations, but is usually a requirement in case of overlapping syndromes. As an example, an ischemic heart disease patient, with hypertension and type 2 diabetes will be given antiplatelet modifiers, anti-hypertensive agents, cholesterol-lowering medication, antidiabetic drugs and anticoagulants with potential to interact in a dangerous manner [11]. Any slight change in dosage or new drug may shift the fine balance of pharmacology in these circumstances resulting in a severe outcome in terms of hypoglycemia, arrhythmias, or even bleeding incidents [12]. Moreover, the risk of DDIs can worsen in the hospital environments because of high-alert medications (antibiotics, antiepileptics, antipsychotics, sedatives, and chemotherapeutic substances) that are frequently used in hospital settings [13].

Objective

To evaluate the prevalence, severity, and patterns of drug-drug interactions among hospitalized patients receiving multidrug therapy and to identify factors associated with increased DDI risk.

Methodology

This descriptive, cross-sectional study was conducted at Tertiary Care Hospital ,Karachi from 1st December 2024 to 10 May 2025. A total of 235 patients were included in the study. The sample size was calculated using a prevalence-based formula assuming an expected DDI prevalence of 50% to maximize sample size, with a 95% confidence interval and 5% margin of error. The study included adult patients (≥18 years) who were prescribed two or more

medications during their hospital stay. Both male and female patients were eligible for inclusion.

Inclusion Criteria:

- Patients aged 18 years or older
- Hospitalized for more than 24 hours
- Prescribed at least two systemic medications (oral or parenteral)

Exclusion Criteria:

- Patients with incomplete medical records
- Patients on herbal or over-the-counter medications only
- Day-care or outpatient prescriptions

Data Collection

Data were collected using a structured proforma designed to capture demographic information, clinical diagnosis, prescribed medications, and duration of hospital stay. Prescriptions were manually reviewed to identify all concurrent medications, and drug interaction screening was carried out using trusted, evidence-based drug interaction checkers such as Lexicomp®, Micromedex®, and Medscape®. Each identified DDI was further analyzed and recorded along with its mechanism and clinical significance. The identified drug-drug interactions were categorized into three levels of severity based on their potential clinical outcomes. Minor interactions were those unlikely to cause harm or require intervention. Moderate interactions had the potential to worsen clinical status or require adjustment in dosage or monitoring. Major interactions were those that could be life-threatening or result in significant adverse effects, warranting immediate medical action or alteration in therapy.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 26. Descriptive statistics such as frequencies, percentages, and means were calculated to describe the study population and characteristics of DDIs. Chi-square test was used to examine associations between the number of drugs prescribed and the incidence of DDIs. A p-value of <0.05 was considered statistically significant in all analyses.

Results

The study evaluated 235 hospitalized patients who were receiving multidrug therapy. The mean age of the participants was 57.4 ± 16.2 years, with a slight male predominance (54.5%). Most patients (62.1%) had more than one comorbidity, including hypertension (45.1%), type 2 diabetes mellitus (38.7%), chronic kidney disease (15.7%), and ischemic heart disease (24.3%). The average length of hospital stay was 7.2 ± 3.5 days. The number of drugs prescribed per patient ranged from 2 to 13, with a mean of 6.4 ± 2.1 medications.

Table 1: Patient Demographics and Clinical Characteristics

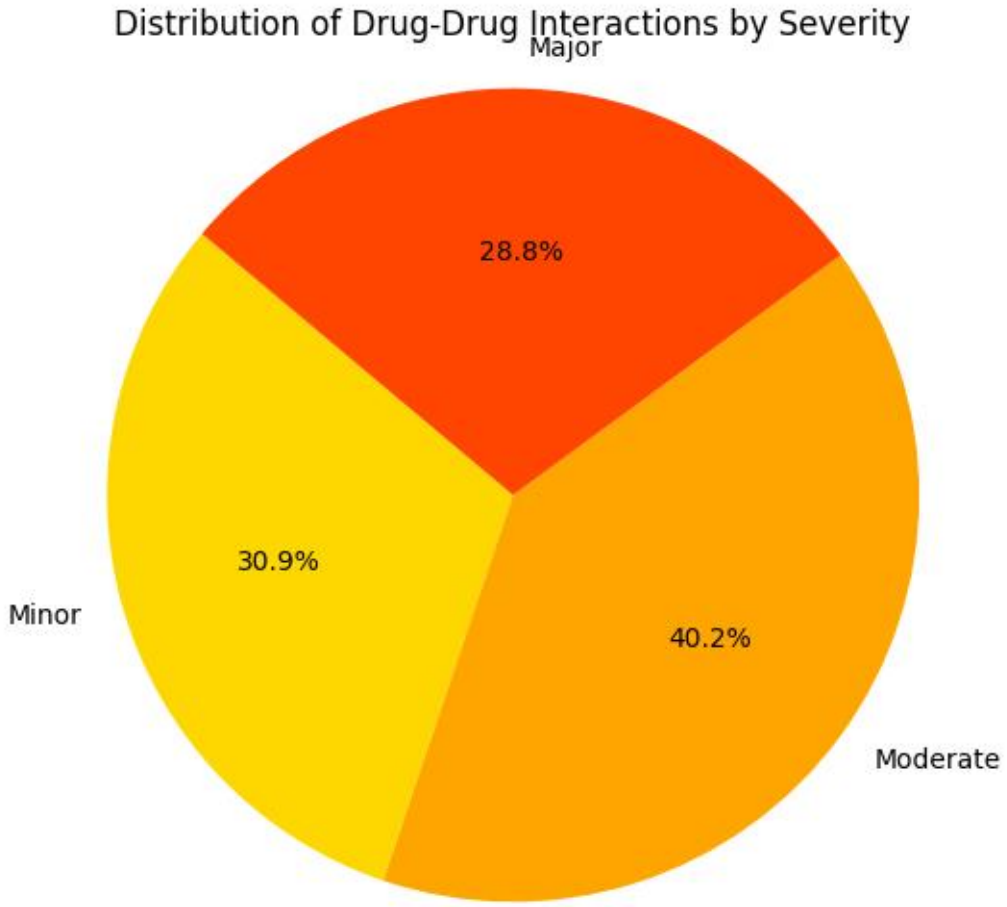
Variable	Value
Mean Age (years)	57.4 ± 16.2
Male (%)	54.5%
≥1 Comorbidity (%)	62.1%
Mean Hospital Stay (days)	7.2 ± 3.5
Mean No. of Drugs Prescribed	6.4 ± 2.1

Out of a total of 527 identified drug-drug interactions, the majority were of moderate severity (212 interactions, 40.2%), followed by minor interactions (163, 30.9%) and major interactions (152, 28.9%). This indicates that nearly 70% of all interactions had the potential to require medical intervention or close monitoring.

Table 2: Distribution of Drug-Drug Interactions by Severity

Severity of Interaction	No. of DDIs (n)	Percentage (%)

Minor	163	30.9%
Moderate	212	40.2%
Major	152	28.9%
Total	**527**	**100.0%**



Among patients receiving five or fewer drugs, 57.1% experienced at least one DDI. This proportion rose sharply to 83.3% in those prescribed 6–8 drugs and reached 98.2% in patients on more than eight medications.

Table 3: Association Between Number of Drugs and DDI Incidence

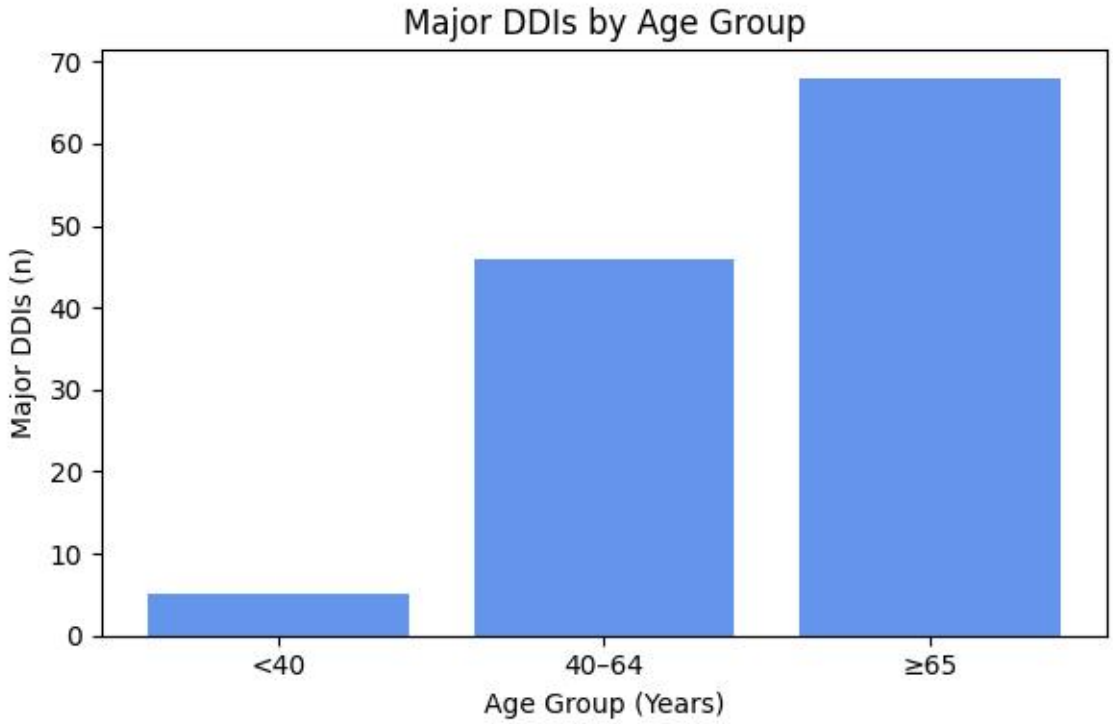
No. of Drugs Prescribed	Patients (n)	Patients with ≥1 DDI (n, %)
≤5	84	48 (57.1%)
6–8	96	80 (83.3%)
>8	55	56 (98.2%)

Cardiovascular agents were the most frequently involved in drug-drug interactions, accounting for 168 cases (31.9%), followed by antibiotics (121, 22.9%) and anticoagulants/antiplatelets (96, 18.2%). Diuretics and proton pump inhibitors also contributed notably, with 11.8% and 8.4% of interactions respectively.

Table 4: Distribution of DDIs by Drug Class Involved

Drug Class Involved	No. of DDIs (n)	Percentage (%)
Cardiovascular Agents	168	31.9%
Antibiotics	121	22.9%
Anticoagulants/Antiplatelets	96	18.2%
Diuretics	62	11.8%

Proton Pump Inhibitors (PPIs)	44	8.4%
Others	36	6.8%
Total	**527**	**100.0%**



Among patients under 40, only 50.0% had at least one DDI and just 13.2% experienced a major interaction. In contrast, 80.8% of those aged 40–64 had DDIs, with 44.2% involving major interactions. The highest risk group was patients aged ≥65, where 87.1% had at least one DDI and 73.1% encountered major interactions, underscoring the heightened vulnerability of elderly patients to serious pharmacological complications.

Table 5: Severity of DDIs by Age Group

Age Group (Years)	No. of Patients (n)	Patients with ≥1 DDI (n, %)	Major DDIs Identified (n, %)
<40	38	19 (50.0%)	5 (13.2%)
40–64	104	84 (80.8%)	46 (44.2%)
≥65	93	81 (87.1%)	68 (73.1%)

Discussion

This experimental study demonstrated that the proportion of drug-drug interactions (DDIs) was very high amongst the hospital patients who were undergoing multidrug therapy whereby it was found that, 78.3 percent of prescriptions had at least one interaction and of the patients in this sample (N= 235), 527 DDIs were discovered. Such results are consistent to those reported previously which have documented the DDI rates between 60-80% in inpatients, especially in a scenario of polypharmacy combined with comorbidity [14]. The median of drugs prescription in our study was 6.4 +/- 2.1 and the risk of DDI as it was evident with an increased number of drugs was significant hypothesizing the already well established correlation between polypharmacy and high DDI risk. Moderate interactions were the highest in the detected DDIs (40.2%), minor interactions were second (30.9%) and major interaction ranked third (28.9%). Remarkably, almost window-third of the interactions were ranked major, which testifies to the clinical significance and a risk of severe adverse effects [15]. Our data also indicate that the distribution of such burden of clinically important DDIs is uneven among elderly patients (87.1 and 73.1 percent, respectively), as only elderly patients

(BA elderly patients (65 years) were overweight in terms of number of patients who had at least one interaction and number of patients who had one or more major DDIs. This affirms the susceptibility of elderly people to drug damages because of changed pharmacokinetics diminished organ roles and raised sensation to medications. Notably, a huge portion of high-risk combinations include aspirin + clopidogrel, and warfarin + ciprofloxacin. These are the classes of drugs frequently utilized in the context of chronic illness treatment, like ischemic heart disease, atrial fibrillation and infection, particularly in the cases of multimorbidity [16]. Their frequent use, combined with narrow therapeutic indices and potential to modulate enzymes, is probably a reason why they are involved in clinically important interactions. The significant statistical links between the rising rate of prescribed medications and the probability of DDIs ($p < 0.001$) justifies the sounding alarm on complications prescribing, especially in hospitals. In spite of digital drug interaction checking, in our group, 1 out of every 20 patients suffered adverse clinical consequences related to DDIs illustrating the inability of digital screening to assess DDIs as well as the necessity of clinical judgment and multidisciplinary review [17]. One of the significant results of the present study included the recording of simultaneous DDI severities of the same patient in more than 36 percent of the presentations. This stratification of risk management makes clinical management complicated and necessitates the reversion of the proactive management that encompasses the prescription and review of medications by a pharmacist regularly, the determination of risk-benefit ratio on an individual case-by-case basis, and the deprescription of the medications where applicable. The study is also insightful into the system-wide monitoring/management system disparities in keeping track of drug interactions, especially in low-resource areas not enjoying uniform distributed electronic health record systems combined with computer-generated warnings. The results encourage the institutional policies to the improvement of DDI surveillance, including the development of Highly DDI Surveillance Staff Education and Clinical review of medication with the help of clinical pharmacist. The weak points of this research are also broadly related to the research design as a cross-section study could only depict prevalence of DDI in a certain time and could not ascertain causality and long-term consequence. It was also a study based in one hospital of the tertiary care setting, which can restrict generalization. Moreover, there was no assessment of possible interactions with herbal or over-the-counter medications, because of the incomplete disclosure or records of the patient.

Conclusion

It is concluded that drug-drug interactions are highly prevalent among hospitalized patients receiving multidrug therapy, with a significant proportion involving moderate to major clinical significance. The risk of interactions increases with the number of medications prescribed, the presence of multiple comorbidities, and advancing age, particularly in patients aged 65 years and above. Cardiovascular agents, antibiotics, anticoagulants, and diuretics were the most commonly implicated drug classes, often involved in high-risk combinations such as aspirin with clopidogrel and warfarin with ciprofloxacin.

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