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Drug-Drug Interactions in Polypharmacy: A Retrospective Hospital Study

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ABSTRACT

Background: Polypharmacy is increasingly common in clinical practice and is associated with a higher risk of drug–drug interactions (DDIs), which can lead to adverse drug events, reduced therapeutic efficacy, and increased healthcare burden. **Objective:** To determine the prevalence, patterns, and predictors of drug–drug interactions among patients with polypharmacy. **Methods:** This retrospective observational study was conducted at Shalamar Hospital, Lahore from September 2025 to January, 2026 , and included 180 adult patients receiving five or more medications. Data were collected from medical records, prescription charts, and electronic databases. Drug–drug interactions were identified using standard interaction databases and classified based on severity and mechanism. **Results:** The mean age of patients was 54.6 ± 15.2 years, with 56.7% males. The average number of medications per patient was 7.8 ± 2.1. Drug–drug interactions were identified in 78.9% of patients, with a mean of 2.9 ± 1.6 interactions per patient. Moderate interactions were most common (42.2%), followed by major (21.1%) and minor (15.6%) interactions. Pharmacokinetic interactions accounted for 60.6% of cases. A significant association was observed between DDIs and number of medications ($p < 0.001$), age ≥60 years ($p = 0.02$), and presence of ≥3 comorbidities ($p = 0.01$). **Conclusion:** Drug–drug interactions are highly prevalent among patients with polypharmacy, with medication burden and comorbidities being the strongest predictors..

INTRODUCTION

Drug-drug interactions (DDIs) are a major and increasing clinical issue in current clinical practice, especially with polypharmacy [1]. Polypharmacy, which is typically defined as the combination of five or more medications, has become more common with age, the increased incidence of chronic diseases and the increased number of therapeutic agents. Although the combination of drugs is frequently required to optimally treat the disease, it also significantly increases the chances of adverse drug events, and DDIs are among the most significant factors [2]. DDIs are caused when the presence of a second drug interferes with the pharmacological activity of the first drug, which results in a decrease in therapeutic activity or an increase in toxicity. These interactions can be pharmacokinetic, in which drugs alter their absorption, distribution, metabolism, or excretion, or pharmacodynamic, in which drugs have additive, synergistic, or antagonistic effects at their sites of action [3]. Clinically significant DDIs can result in serious consequences such as treatment failure, organ toxicity, prolonged hospitalisation, and increased healthcare costs [4]. Physiological alterations, such as diminished hepatic and renal clearance, also increase the risk, as do age-related changes in drug metabolism and clearance [5]. Also, inadequate prescribing, absence of medication examination, and utilisation of non-prescription or herbal drugs are other elements that add to the heightened risk of adverse interactions. In addition to the elderly, polypharmacy is also becoming widespread among younger patients with chronic illnesses like diabetes mellitus, cardiovascular diseases, psychiatric illnesses, and autoimmune diseases [6]. The fact that several diseases may have to be treated with several drugs that can be prescribed at various times, and by various specialists, may lead to the occurrence of unrecognised DDIs [7]. The fragmentation of the healthcare system, the lack of communication between healthcare providers, and the insufficiency of medication history documentation also

contribute to this risk. Another significant aspect of DDIs in polypharmacy is the presence of cytochrome P450 enzymes and drug transporters, which are essential to drug metabolism [8]. Numerous widely prescribed drugs are enzyme inhibitors or inducers, which can significantly affect plasma drug levels [9]. For example, drugs that inhibit CYP3A4 can raise the concentration of other drugs metabolised by the same route, leading to toxicity, and enzyme inducers may lower drug concentrations, leading to poor therapeutic effect [10]. These mechanisms are relevant to the prediction and prevention of clinically relevant interactions, which is why they need to be understood [11]. Regardless of the exact definition of the term, accidental adverse effects of the usage of various medications are a significant reason to be worried [12]. The risk of undesirable reactions is increasing exponentially with twice the number of medications taken; the likelihood of an adverse drug reaction (ADR) is 13% with two drugs, 58% with 5 and 82% with 7 or higher drugs [13].

Objective

To determine the prevalence, patterns, and predictors of drug–drug interactions among patients with polypharmacy.

METHODOLOGY

This was a retrospective observational study conducted at Shalamar Hospital, Lahore, from----------. A total of 180 patients with polypharmacy were included in the study. A non-probability consecutive sampling technique was employed. The study included adult patients (18 years and older) who received five or more medications and had complete medical records, including prescription details. Patients who had incomplete or missing medical records, less than 24-hour admissions, those who were under 18 years of age, and where there were documented medication errors not associated with a drug-drug interaction were excluded.

Data Collection Procedure

The retrospective method was used to collect data from medical records, prescription charts, and patient electronic databases, with approval from the Institutional Review Board (IRB). Age and gender, clinical information (primary diagnosis, comorbidities, the number and type of medications prescribed, and duration of hospital stay) and demographic information were documented through a structured proforma. A standard drug interaction database (Micromedex, Lexicomp, or Drugs.com) was used to determine drug-drug interactions. The identified interactions were classified according to the severity (major, moderate, minor) and mechanism (pharmacokinetic or pharmacodynamic). Clinically significant interactions were identified as those that needed dose adjustment, monitoring or therapy change. The severity types of the interactions, average number of interactions per patient, and identification of risk factors associated with the severity like age, number of medications, and comorbid conditions were also used as secondary outcomes.

Data Analysis

Data were analyzed using SPSS version 26.0. Descriptive statistics were used to summarize the data, with categorical variables presented as frequencies and percentages, and continuous variables expressed as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 180 patients, mean age of participants wasn54.6 ± 15.2 years, with the largest proportion of patients in the 40–59 years age group (41.1%), followed by those aged ≥60 years (38.9%), while 20.0% were younger than 40 years. Males were slightly more represented (56.7%) compared to females (43.3%). Among comorbidities, hypertension was the most common (62.2%), followed by diabetes mellitus (48.9%) and ischemic heart disease (31.1%).

Table 1

Baseline Demographic and Clinical Characteristics (n = 180)

Variable	Category	n (%) / Mean ± SD
Age (years)	—	54.6 ± 15.2
Age Group	<40 years	36 (20.0%)
	40–59 years	74 (41.1%)
	≥60 years	70 (38.9%)
Gender	Male	102 (56.7%)
	Female	78 (43.3%)
Hypertension	Yes	112 (62.2%)
	No	68 (37.8%)
Diabetes Mellitus	Yes	88 (48.9%)
	No	92 (51.1%)
Ischemic Heart Disease	Yes	56 (31.1%)
	No	124 (68.9%)
Number of Medications	—	7.8 ± 2.1

Drug–drug interactions were present in 78.9% of patients, whereas 21.1% had no interactions. The mean number of interactions per patient was 2.9 ± 1.6. In terms of severity, moderate interactions were the most frequent (42.2%), followed by major interactions (21.1%) and minor interactions (15.6%).

Table 2

Prevalence and Severity of Drug–Drug Interactions (n = 180)

Variable	Category	n (%)
Presence of DDIs	Yes	142 (78.9%)
	No	38 (21.1%)
Number of DDIs per Patient	—	2.9 ± 1.6
Severity of DDIs	Major	38 (21.1%)
	Moderate	76 (42.2%)
	Minor	28 (15.6%)

Among patients with drug–drug interactions, pharmacokinetic interactions were more common (60.6%) compared to pharmacodynamic interactions (39.4%). The most frequently involved drug classes included antihypertensives (54.4%), antidiabetics (46.7%), antiplatelets (39.4%), and NSAIDs (33.9%).

Table 3

Type and Drug Class Involvement in DDIs (n = 142)

Variable	Category	n (%)
Type of Interaction	Pharmacokinetic	86 (60.6%)
	Pharmacodynamic	56 (39.4%)
Drug Classes Involved	Antihypertensives	78 (54.4%)
	Antidiabetics	67 (46.7%)
	Antiplatelets	56 (39.4%)
	NSAIDs	48 (33.9%)

Patients aged ≥60 years had a higher prevalence of interactions (91.4%) compared to those younger than 60 years (68.4%), with a p-value of 0.02. Similarly, patients taking ≥8 medications had a markedly higher frequency of interactions (97.8%) compared to those taking fewer than 8 drugs (60.0%), with a highly significant p-value of <0.001. Additionally, patients with three or more comorbidities demonstrated a higher prevalence of interactions (89.9%) compared to those with fewer comorbidities (68.1%), with a p-value of 0.01.

Table 4

Factors Associated with Drug–Drug Interactions (n = 180)

Variable	Category	DDIs Present n (%)	DDIs Absent n (%)	p-value
Age Group	<60 years	78 (68.4%)	36 (31.6%)	0.02
	≥60 years	64 (91.4%)	6 (8.6%)	
Number of Medications	<8 drugs	54 (60.0%)	36 (40.0%)	<0.001
	≥8 drugs	88 (97.8%)	2 (2.2%)	
Comorbidities	<3 conditions	62 (68.1%)	29 (31.9%)	0.01
	≥3 conditions	80 (89.9%)	9 (10.1%)	

DISCUSSION

This study evaluated the prevalence, patterns, and predictors of drug–drug interactions (DDIs) among patients with polypharmacy and demonstrated a high overall burden of interactions. Compared to the clinical importance of polypharmacy as a risk factor of adverse drug events, a significant percentage (78.9) of patients had at least one possible DDI. These results are in line with other studies that have documented a high rate of DDIs among patients on a combination of drugs, especially in hospital settings where the complexity of diseases and the burden of drugs are higher. The median interactions that were most common (42.2) and other major interactions that followed (21.1) suggests that although large percentages of the DDIs are not life threatening per se, a large percentage still have serious clinical effects that should be observed or treated. It has also been found in the past that moderate interactions are most frequently experienced, but the major interactions are clinically significant since they can cause major negative outcomes such as bleeding, arrhythmias or organ toxicity [14,15]. This underlines the significance of a close observation of the medication and clinical care even in cases where the interactions cannot be considered as severe. In this study, 60.6 were prevalent, which was less than the prevalence of the pharmacodynamic interactions. This finding is in line with the previous literature that has also emphasized the role of metabolic pathways especially the cytochrome P450 enzyme systems in order to mediate clinically relevant DDIs [16]. Drugs can be enzyme inhibitor or inducer drugs that can drastically change drug levels and result in toxicity or reduced efficacy. The fact that the percentage of pharmacokinetic interaction was high in this study justifies the significance of the drug metabolism knowledge and the necessity to modify the dose in patients taking more than one drug [17]. Antihypertensives, antidiabetics and antiplatelets were most engaged due to the high percentage of the cardiovascular and metabolic diseases in the study population. Past studies have also found these classes of drugs to be frequent causes of DDIs since they are widely used and have the possibility of interacting. Through the wide use of NSAIDs, particularly with antiplatelets or antihypertensives, there is a further increase in risk because this may lead to complications such as gastrointestinal bleeding or reduction in antihypertensive action [18]. The number of medications and DDI were strongly correlated and patients taking eight or more medications were significantly more at risk [19]. This finding has been corroborated by previous studies that revealed that polypharmacy is always the most significant predictor of DDIs [20]. Each new drug, treatment becomes even more complicated and interactive, and it is important to pay attention to minimizing the number of unnecessary prescriptions and introducing rational approaches to prescribing medications. It was also established that age does play a major role and those patients who are aged 60 years and above are more prevalent with DDIs. This is in line with previous reports that have attributed the increased risk in older patients to be a combination of comorbidities, alterations in the pharmacokinetic profiles and age-related physiological changes, such as reduced renal and hepatic clearance. Similarly, comorbidity (three or more conditions) had a strong influence on the incidence of DDIs because a cumulative effect of disease burden on medication use was found. Although it has strengths, this study has some limitations. Being a retrospective research, it depended on existing medical records, which can be incomplete, or biased in documentation. Potential DDIs were also assessed in the study rather than validating clinical outcomes which exaggerates clinical impacts. However, the findings can be discussed as a worthy addition to the current body of knowledge about prescribing patterns and provide a possibility to enhance medication safety.

CONCLUSION

It is concluded that drug–drug interactions are highly prevalent among patients with polypharmacy, with a significant proportion experiencing moderate to major interactions that may adversely affect clinical outcomes. Pharmacokinetic interactions were more common than pharmacodynamic interactions, and commonly prescribed drug classes such as antihypertensives, antidiabetics, antiplatelets, and NSAIDs were frequently involved.

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