RESEARCH ARTICLE OPEN ACCESS

A Cross-Sectional Study on Prescription Drug Interactions in Private Pharmacies

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ARTICLE HISTORY

Received: July 4, 2025
Revised: October 8, 2025
Accepted: October 14, 2025

Citation: Khan SP, Noor F, Ahmed S, Kazim F, Intekhab S, Navaid S, Waqar A. A cross-sectional study on prescription drug interactions in private pharmacies. Acad Res. 2025; 2(2): 62-69.

DOI: https://doi.org/10.70349/ar.v2i1.32

Abstract

***Background*:** Prescription drug–drug interactions (DDIs) represent a significant threat to patient safety, leading to adverse drug reactions, therapeutic failure, and higher healthcare costs. This study aimed to determine the frequency, severity, and mechanisms of potential DDIs identified in prescriptions collected from private pharmacies in Karachi, Pakistan.

***Methods*:** A cross-sectional study was conducted from September 2023 to September 2024 using prescriptions obtained through convenience sampling from community pharmacies across Karachi. One hundred prescriptions containing two or more drugs were analyzed using the Medscape Drug Interaction Checker to identify potential interactions, their severity (minor, moderate, severe), and mechanisms (pharmacokinetic or pharmacodynamic). Data were analyzed using SPSS version 26. Associations between potential DDIs and patient characteristics were evaluated using chi-square and logistic regression analyses. A p-value < 0.05 was considered statistically significant.

***Results*:** Of the 100 prescriptions analyzed, 43% contained at least one potential DDI. Among these, 20% were minor, 30% moderate, and 5% severe in intensity. Regarding mechanisms, 52% were pharmacodynamic, 38% pharmacokinetic, and 8% unknown. Logistic regression showed significant associations between potential DDIs and increasing age, female gender, and number of prescribed drugs, with polypharmacy (>5 drugs) being the strongest predictor.

***Conclusion*:** Potential drug–drug interactions were identified in nearly half of the prescriptions reviewed, with moderate and pharmacodynamic interactions being most common. Polypharmacy and increasing age were key determinants. Incorporating electronic drug-interaction screening tools and promoting rational prescribing practices can help reduce preventable adverse drug events.

Keywords: Potential drug-drug interactions, pharmacokinetic drug interactions, pharmacodynamic, Medscape Drug Interaction Checker Online.

1. INTRODUCTION

Drug-drug interactions (DDIs) associated with prescription medications represent a major threat to patient safety, potentially leading to adverse drug reactions (ADRs), therapeutic failure, and increased healthcare costs [1]. This risk is particularly pronounced in private pharmacy settings, where patients frequently obtain prescriptions from multiple healthcare providers. The lack of coordination and communication among these providers contributes to the heightened likelihood of DDIs [2].

Research has shown that 40-50% of patients taking multiple medications are at risk of potential DDIs, with a significant proportion resulting in clinically meaningful harm [3]. In low- and middle-income countries, where private pharmacies often serve as the primary point of medication access, the absence of robust electronic prescribing systems and limited pharmacist involvement

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further amplifies the risk [4]. Polypharmacy commonly defined as the use of five or more medications is prevalent, particularly among older adults and patients with chronic diseases. Moreover, self-medication and the widespread availability of over-the-counter (OTC) drugs can compound the risk of interactions [5].

Prescribing medications responsibly, while minimizing the risk of DDIs, is a core duty of medical practitioners and a critical component of rational drug use. The concurrent use of multiple medications, including self-medication, can be life-threatening and may result in serious clinical outcomes [6]. Unfortunately, healthcare provider negligence may also contribute to DDIs. One possible explanation is excessive patient load and overworked staff, though this does not justify lapses in prescribing safety [7].

Studies have reported a higher incidence of DDIs in hospital settings (45%) compared with community pharmacy prescriptions (29.25%), with elderly patients being particularly vulnerable [8]. While improvements in healthcare have increased life expectancy, age-related functional decline remains a major factor predisposing elderly individuals to DDIs. This vulnerability underscores the importance of early detection and prevention strategies in high-risk populations [6].

Despite the clinical significance of DDIs, information remains limited regarding prescribing patterns for specific drug classes, including antidepressants, benzodiazepines, and analgesics [7, 8]. For example, valproic acid remains one of the most commonly prescribed anti-epileptic drugs during pregnancy and in children, despite being blacklisted for these groups [7, 8]. Data related to analgesics are particularly concerning, with reports indicating that 90% of patients experienced at least one DDI, and 60% of these interactions were classified as severe [7]. Polypharmacy was also highly prevalent in analgesic prescriptions, with 51% of cases involving 11-15 drugs and 35.6% involving 6-10 drugs [7, 8].

Technological solutions have also been explored. One study investigated the implementation of a distributed ledger-based electronic prescribing program, "Prescription Abuse Greatly Reduced (PAGR) Prescriptions," to assess the impact of blockchain technology on prescribing efficiency in family medicine clinics [9]. Another study focused on developing and validating a novel teaching module to enhance dental students' prescription-writing skills, particularly for patients with coexisting medical conditions [10].

The significance of the present study lies in identifying critical gaps in prescription monitoring within private pharmacy settings, where interaction screening is often overlooked. This research seeks to generate evidence that may guide the development of pharmacist training programs focused on DDI detection and management. Furthermore, it aims to advocate for the integration of digital alert systems into private pharmacy software to improve medication safety.

This study was conducted to assess the incidence, prevalence, and severity of DDIs in prescriptions collected from different private pharmacies in various localities of Karachi, Pakistan. By providing context-specific data, the findings are expected to support broader efforts to enhance safe medication practices and reduce preventable drug-related harm in outpatient care environments.

2. METHODOLOGY

A cross-sectional study based on prescription analysis was conducted over one year, from September 2023 to September 2024. Prescriptions containing two or more drugs, where potential drug interactions were suspected, were evaluated using the Medscape Drug Interaction Checker. Each prescription was screened by entering all listed drugs into the software, which identified the presence, severity (minor, moderate, or severe), and mechanism (pharmacokinetic or pharmacodynamic) of interactions.

The study was approved by the Ethical Review Committee of Jinnah Medical & Dental College, Karachi, Pakistan (Protocol #000338/23). Prescriptions with fewer than two drugs, a history of drug misuse, or those belonging to surgical patients were excluded. Verbal consent was obtained from all participants, and the identities of both patients and prescribers were anonymized. Data were collected using a structured proforma designed to record demographic details and prescription information according to predefined criteria. A total of 100 prescriptions were collected from private pharmacies in various localities of Karachi, including STH, MCGH, Korangi, Karsaz, and Shahrah-e-Faisal, using a convenience sampling technique. The sample size was determined using a statistical calculator based on a previous study [11], assuming an expected prevalence of 50% drug interactions, a 95% confidence level, a 5% margin of error, and a statistical power of 80%.

Data were analyzed using SPSS version 26. Descriptive statistics were presented as frequencies and percentages. For inferential analysis, the Chi-square test was applied to examine associations between categorical variables, and binary logistic regression was used to identify predictors of drug interactions. Model fitness was assessed using the Hosmer–Lemeshow goodness-of-fit test and ROC curve analysis to determine discriminative ability. Multicollinearity among predictors was checked using the Variance Inflation Factor (VIF). A p-value < 0.05 was considered statistically significant.

It is acknowledged that the convenience sampling method limits the generalizability of the findings, as pharmacy selection was not random and may not represent the entire population of Karachi.

3. RESULTS

A total of 100 prescriptions were analyzed for potential drug–drug interactions collected from community pharmacies across Karachi. Out of these, 43 (43%) prescriptions showed at least one drug–drug interaction, while 57 (57%) had no interaction detected. Table **1** presents the baseline characteristics of all prescriptions. Among those with interactions, 33% had 1-3 interactions, and 10% had more than three interactions.

Regarding the severity of interactions, 20% were minor, 30% were moderate, and 5% were severe (Fig. **1a**). Based on their mechanisms, 52% were pharmacodynamic, 38% pharmacokinetic, and 8% involved unknown mechanisms (Fig. **1b**). These proportions have been verified for consistency across text, tables, and figures.

The mean age of patients was 38.4 ± 13.7 years, and the average number of prescribed drugs per prescription was 4.2 ± 1.6. The frequency distribution of age groups, gender, comorbidities, and number of prescribed medications is shown in Table **1**.

Univariate logistic regression analysis revealed significant associations between drug interactions and age, gender, and number of prescribed drugs (Table **2**). Prescriptions of patients aged above 30 years had 3.17 times higher odds of containing an interaction (OR = 3.17, 95% CI 1.29–7.80, p = 0.012) compared to those aged 30 years or younger. Similarly, female patients had 2.68 times higher odds of drug interaction than males (OR = 2.68, 95% CI 1.19–6.07, p = 0.018). The presence of comorbidities showed increased odds (OR = 2.05, 95% CI 0.90–4.67, p = 0.089), although this association was not statistically significant.

The number of medications prescribed emerged as the most influential predictor. Prescriptions containing more than five drugs had 15.24 times higher odds of showing drug–drug interactions (OR = 15.24, 95% CI 4.68–49.58,

Table 1: Baseline characteristics of study prescriptions (n = 100).

Variable	Groups	Frequency (n)	Percentage (%)
Age (years)	1 – 17	15	15
	18 – 30	20	20
	31 – 45	29	29
	46 – 60	25	25
	> 60	11	11
Age category	≤ 30 years	35	35
	> 30 years	65	65
Gender	Female	49	49
	Male	51	51
Comorbidities	Present	37	37
	Absent	63	63
Number of prescribed drugs	< 5 drugs	73	73
	≥ 5 drugs	27	27
Presence of interaction	Yes	43	43
	No	57	57
Number of interactions	None	57	57
	1 – 3 interactions	33	33
	> 3 interactions	10	10

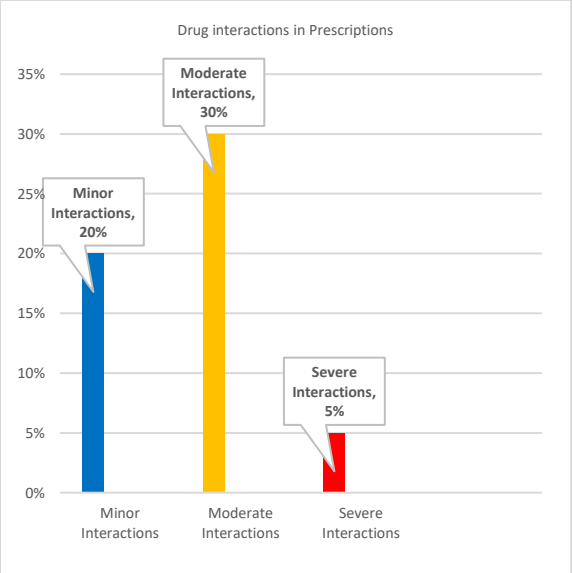

Figure 1a: Severity of drug-drug interactions among all prescriptions. Each bar represents the proportion of prescriptions classified by interaction severity: minor (20%), moderate (30%) and severe (5%).

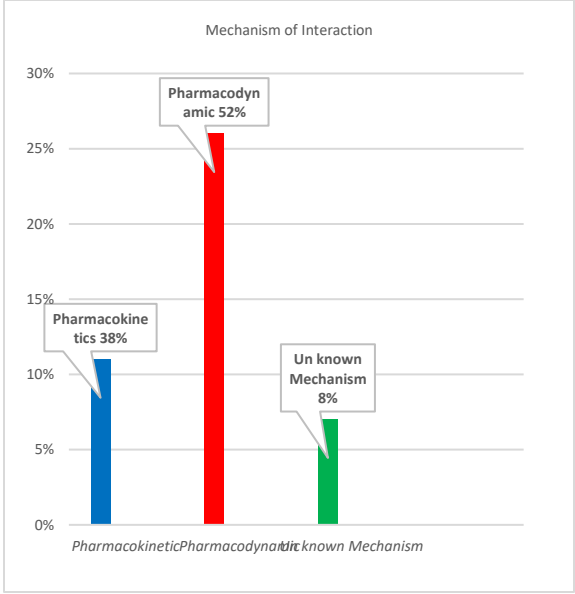

Figure 1b: Mechanisms of identified drug–drug interactions. Distribution of pharmacodynamic (52%), pharmacokinetic (38%), and unknown (8%) mechanisms detected through the Medscape Drug Interaction Checker.

$p < 0.001$). However, this finding should be interpreted with caution due to the small subgroup size (n = 27), which may contribute to sparse-data bias.

A multivariate logistic regression model including age, gender, comorbidities, and number of prescribed medications was subsequently applied. After adjustment, the number of drugs per prescription remained a statistically significant independent predictor (adjusted OR = 13.9, 95% CI 3.9–49.4, $p < 0.001$). Other factors such as age and gender did not retain statistical significance after adjustment. The model's Hosmer–Lemeshow goodness-of-fit test ($p = 0.42$) indicated acceptable fit, while the area under the ROC curve (AUC = 0.81) demonstrated good discrimination. Variance Inflation Factor (VIF) values for all predictors were below 2, confirming absence of multicollinearity.

Table 2: Relationship of drug interaction with independent variables using simple logistic regression (n = 100).

Predictor Variable	Interaction Present n (%)	Interaction Absent n (%)	p-value	Odds Ratio (95% CI)
Age (> 30 years)	34 (79.1)	31 (54.4)	0.012 *	3.17 (1.29 - 7.80)
Gender (Female)	27 (62.8)	22 (38.6)	0.018 *	2.68 (1.19 - 6.07)
Comorbidities (Present)	20 (46.5)	17 (29.8)	0.089	2.05 (0.90 - 4.67)
Number of drugs (≥ 5)	23 (53.5)	4 (7.0)	< 0.001 *	15.24 (4.68 - 49.58)

Further descriptive analysis showed that drug interactions were more frequent among females (55%) and among patients older than 30 years (65%). The mean number of drugs per prescription was higher in prescriptions with interactions (5.2 ± 1.3) compared to those without (3.5 ± 1.4).

Overall, polypharmacy (more than five drugs) and increasing age were found to be the strongest determinants of drug–drug interactions in this study. However, given the small sample size, non-probability sampling, and limited subgroup data, these findings should be interpreted with caution and validated in larger studies.

4. DISCUSSION

Writing prescriptions is a fundamental responsibility of physicians and an integral component of patient care. A prescription not only conveys medication instructions but also reflects the prescriber's clinical judgment and adherence to safety standards. Carelessness at this stage can result in avoidable errors and patient harm. Therefore, improving the quality of prescriptions remains a critical target for enhancing patient safety [11].

In this study, prescriptions were collected from community pharmacies in multiple localities, and both pharmacodynamic and pharmacokinetic drug–drug interactions (DDIs) were identified. Pharmacodynamic DDIs were more frequent (52%) than pharmacokinetic interactions (37.94%). Age and gender initially showed statistically significant associations with DDIs, whereas comorbidities were not significant. However, after adjustment, only polypharmacy remained a strong independent predictor, indicating that the number of drugs may mediate the effect of demographic factors.

The observed gender difference, with higher rates among females, aligns with trends reported in both local and international studies, although the biological and behavioral underpinnings of this association remain unclear. Consistent with other research, the current findings also reveal gaps in prescription quality, including a low rate of generic prescribing, which can increase treatment costs and reduce adherence [12].

Polypharmacy was the strongest predictor of potential DDIs, a finding that supports existing literature linking higher medication counts to increased interaction risk. While this observation is not novel, its demonstration in a community setting reinforces the importance of cautious prescribing and pharmacist involvement in reviewing complex regimens. Comparable local studies have reported interaction prevalence between 22% and 40%, with moderate-intensity and pharmacodynamic mechanisms predominating. This consistency across populations highlights the universal nature of interaction risks in healthcare systems with limited prescription monitoring.

Globally, DDIs contribute significantly to adverse outcomes, particularly in cardiovascular patients where drug–drug and drug–gene interactions influence therapeutic efficacy [13]. Létinier *et al*. observed a 2.5-fold increase in hospitalizations associated with contraindicated drug combinations, underscoring the importance of preventive strategies [14]. Similarly, Hatefi *et al*. reported clinically relevant DDIs in 92% of oncology patients, highlighting the need for multidisciplinary collaboration in complex cases [15].

In the current study, 43% of prescriptions demonstrated at least one DDI, most of which were moderate in severity and pharmacodynamic in nature. This aligns with findings from Karachi, where moderate interactions accounted for 66% and pharmacodynamic mechanisms for over half of all interactions [16]. Pharmacodynamic interactions, involving additive or opposing pharmacologic effects, are often more frequent than pharmacokinetic interactions that affect absorption, distribution, metabolism, or excretion. Although typically delayed in onset, moderate interactions can result in clinically significant harm with prolonged use.

Internationally, Jørring *et al*. reported a strong association between polypharmacy and increased mortality in older adults [17]. In tertiary hospitals in Pakistan, moderate and major DDIs were documented in 15.7% and 9.4% of cases respectively, particularly in pain management settings [18]. Rahman *et al*. emphasized ongoing surveillance, prescribing guidelines, and targeted training as key strategies for rational drug use [19]. Among elderly populations, DDIs have been linked to increased mortality and adverse outcomes [20-22].

DDIs remain a major challenge in combination therapy, particularly with the rise of complex treatment regimens. Integrating pharmacokinetic–pharmacodynamic modeling and artificial intelligence tools may help predict interactions more accurately, though experimental validation remains essential [23]. Bajracharya *et al*. reported that most DDIs were moderate in severity [24], while Alkhalid *et al*. showed that using multiple databases improves detection [25]. Farooqui *et al*. identified pharmacodynamic interactions as the most common (51.2%) [26], and Khan *et al*. highlighted the frequent prescribing of interacting analgesics without appropriate evaluation [27].

Although multivariate regression was applied, residual confounding from unmeasured factors such as drug classes, prescriber behavior, and pharmacy practices cannot be excluded. Future research should stratify results by therapeutic class and prescriber type to address this gap.

This study provides community-level evidence on the prevalence, pattern, and determinants of drug–drug interactions in Karachi, Pakistan—an area previously dominated by hospital-based data. By identifying pharmacodynamic interactions as the most common and demonstrating polypharmacy as a key independent predictor, these findings contextualize global trends within local prescribing practices. This adds practical insight for prescriber education, pharmacy-based screening, and rational medication use in primary care.

This study was limited by its small sample size (n = 100) and convenience sampling, which may restrict generalizability. The regression model may also have been prone to overfitting due to the low number of interaction events relative to predictors. Additionally, software-based detection identifies potential rather than clinically confirmed interactions.

Despite these limitations, the findings emphasize polypharmacy and increasing age as major contributors to DDIs, with possible gender effects. Strengthening prescriber awareness, routine use of interaction-checking tools, and continued professional education are recommended to minimize preventable adverse drug events.

5. CONCLUSION

This study identified potential drug–drug interactions in 43% of prescriptions collected from community pharmacies in Karachi. Most were of moderate severity, with pharmacodynamic mechanisms being the most frequent. Increasing age, female gender, and particularly polypharmacy was associated with a higher likelihood of interactions. These findings highlight the importance of rational prescribing practices, careful medication review, and the use of electronic interaction-checking tools to enhance patient safety.

While the study was limited by its sample size and software-based detection approach, it provides useful preliminary insight into prescribing trends in local pharmacy practice. Continued efforts toward prescriber education, digital prescription monitoring, and larger multicenter studies are recommended to reduce preventable adverse drug interactions and promote safer medication use.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the the Ethical Review Committee of Jinnah Medical & Dental College, Karachi, Pakistan (Protocol #000338/23).

Verbal consent was obtained from all participants, and the identities of both patients and prescribers were anonymized.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDING

The study received no financial support.

ACKNOWLEDGEMENTS

The authors acknowledge Dr. Shagufta Naqvi (Assoc. Professor-CHS) for her support.

AUTHOR CONTRIBUTIONS

SPK: Study design, manuscript writing, data analysis.

FN: Data collection, data interpretation.

SA: Data collection, data interpretation, manuscript writing.

FK: Data collection, data interpretation.

SI: Data collection.

SN: Data collection.

AW: Data collection.

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