Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

Assessment Of Drug To Drug Interactions In Polypharmacy In Patients ≥ 60 Years: A Clinical Audit

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Keywords: Drug to Drug Interaction, Patient, Polypharmacy, DDI, Medication

Received on 15 July 2025
Accepted on 20 Sep 2025
Published on 01 Oct 2025

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Abstract

Background: Polypharmacy is highly prevalent among older adults and significantly increases the risk of drug–drug interactions (DDIs), yet routine medication review and interaction screening are often inadequate in clinical practice.

Objective: To assess the prevalence, severity, and predictors of DDIs among patients aged 60 years and above and to evaluate compliance with recommended prescribing and monitoring standards.

Methods: This audit reviewed 260 prescriptions of patients aged ≥60 years attending a tertiary care facility. Data collected included demographics, comorbidities, number of medications, and documented interaction screening. DDIs were identified using a standard interaction checker, and severity was categorized as major, moderate, or minor.

Results: The mean patient age was 68.7 ± 6.4 years, and the average number of medications per patient was 7.9 ± 2.1. DDIs were found in 198 prescriptions (76.1%), of which 21.2% were major and 58.6% were moderate. Severe polypharmacy (≥10 drugs), chronic kidney disease, and

NSAID use were significant predictors of major DDIs. Despite the high DDI burden, compliance with key prescribing standards was poor: medication review was documented in 34.6% of cases, DDI screening in 29.2%, monitoring plans in 27.9%, and appropriate action for major DDIs in 38.1%.
Conclusion: DDIs are highly prevalent among older adults with polypharmacy, and major interactions are common but under-recognized in routine practice.

Introduction

Polypharmacy has sneakily developed into one of the largest clinical landmines in contemporary healthcare particularly in elderly individuals aged 60 years and above [1]. With increases in life expectancy and burdens of chronic illnesses, hypertension, diabetes, ischemic heart disease, COPD, and arthritis bring many more offenders together into polypharmacy at the same time, cognitive decline older adults often find themselves taking a variety of drugs concurrently. Although any of the medications can be prescribed with well-intended intentions, their concomitance within the same patient establishes a pharmacologic environment that can be difficult to predict and may be unsafe more frequently [2]. Drug-drug interactions (DDIs) have the potential to change therapeutic ranges, flatten drug efficacy, increase toxicity, or cause quite unintended effects. Medications are processed differently in the aging body which experiences reduced renal filtration, slower hepatic clearance, changes in receptor sensitivity as well as changes in body composition which increases susceptibility to adverse interactions [3]. In the world, it is estimated that 50-70 percent of elderly individuals take five or more drugs, and this figure increases among hospitalized or chronically ill patients. As the number of drugs is added, the probability of a clinical significant interaction follows an exponential rather than a linear increase. What appears to be harmless on paper can lead to dizziness, arrhythmias, hypoglycemia, GI bleeding, or cognitive blunting in an elderly patient [4][5]. The situation is being complicated when a prescription is being broken down into bits with one specialist prescribing and adding their own drugs with little knowledge of what has already been prescribed to the patient. Add some self-medication, with over-the-counter medication, herbal medicine, and shared medicine in the family members (a very actual occurrence in most parts of the world), and you have a formula of silent clinical mayhem. The frustrating factor is that DDIs usually do not show up until the patients arrive in the emergency room, or that their elderly fatigue happens to be a drug interaction. The burden of DDIs is regularly underestimated in healthcare systems as the symptoms have been smoothly merged with aging falls, confusion, constipation, dizziness, anorexia [6]. DDIs are wrongly ascribed to comorbidities, frailty or even old age without systematic evaluation to enable the avoidance of preventable damage to persist [7]. The next complication is that not every interaction is equally important. Others are minor and do not need much but just monitoring. Others require changes in dosage, replacement of therapy or even abstinence. It is crucial that the interactions are categorized as mild, moderate, and severe since older adults are frequently unable to physiologically compensate even the changes that occur due to the interaction of moderate severity [8]. An example of this is that a moderate interaction that leads to slight hypotension in a young adult will result in syncope and fractures in a 70-year-old. Even a slight increase in QT-interval caused by isolation can be life threatening when combined with two or three other agents that delay QT interval [9][10].

Objective

To assess the prevalence, severity, and predictors of DDIs among patients aged 60 years and above and to evaluate compliance with recommended prescribing and monitoring standards.

Methodology

This study was designed as a clinical audit and conducted at Jinnah Postgraduate Medical Centre, Karachi from December 2024 to June 2025. Polypharmacy was defined as the concurrent use of five or more medications, and only prescriptions meeting this threshold were included. The primary standard used for comparison was the accepted clinical guideline recommending routine medication review and DDI assessment for all older adults receiving polypharmacy. A consecutive sampling strategy was used to include all patients aged ≥60 years who presented with prescriptions containing at least five medications. Patients undergoing chemotherapy, those with incomplete medication records, and those unwilling to participate were excluded. Because this was an audit, a sample size calculation was not required; instead, all eligible prescriptions during the audit period were reviewed.

Data Collection Procedure

Data were collected using a structured audit proforma. The following information was extracted from each patient's prescription and medical record: age, gender, comorbidities, number of medications prescribed, classes of drugs used, duration of treatment, and additional over-the-counter or herbal medications (where disclosed). Each prescription was analyzed for potential drug–drug interactions using a validated interaction-checking tool (e.g., Micromedex, Lexicomp, or Medscape Drug Interaction Checker). Interactions were categorized based on standard classifications as minor, moderate, or major, depending on their clinical significance. Information on whether the prescribing team documented interaction risk, monitored for potential adverse effects, or adjusted medication regimens was also recorded.

Audit Standards and Criteria

The audit was conducted against the following standards:

All patients aged ≥60 years on polypharmacy should have a documented medication review.

All prescriptions should be checked for potential drug–drug interactions.

Clinically significant interactions (moderate or major) should trigger appropriate action, including dose adjustment, substitution, or monitoring.

Compliance with each standard was calculated as a percentage of the total eligible prescriptions.

Data Analysis

Data were entered into SPSS version 26. Descriptive statistics were used to summarize findings. Categorical variables (presence and severity of interactions) were presented as frequencies and percentages, while continuous variables (number of medications) were expressed as mean ± standard deviation. Areas of non-compliance were identified and categorized for further corrective action.

Results

The study included 260 older adults with a mean age of 68.7 ± 6.4 years, showing a predominantly elderly population clustered around the late 60s. Males slightly outnumbered females (144, 55.4% vs. 116, 44.6%). Patients were on a heavy medication load, averaging 7.9 ± 2.1 drugs per patient, with most falling into the 5–9 drug category (187 patients, 72.0%). Severe polypharmacy (≥10 drugs) was seen in 47 patients (18.0%), while only 10.0% were taking fewer than five medications. Comorbidities were common—hypertension affected nearly two-thirds (167, 64.2%), diabetes was present in over half (137, 52.7%), ischemic heart disease in about one-

third (83, 31.9%), and chronic kidney disease in 38 patients (14.6%). Overall, 198 patients (76.1%) experienced at least one drug–drug interaction, with an average of 2.8 ± 1.4 interactions per patient. Most DDIs were moderate in severity (116, 58.6%), while major interactions accounted for 21.2%. High-risk prescriptions were not rare—27.3% had more than three DDIs—commonly involving warfarin with NSAIDs (18 cases) and beta-blockers with insulin (34 cases), highlighting clinically dangerous combinations.

Table 1. Baseline Characteristics of Patients (N = 260)

Variable	**Category**	**n (%) / Mean ± SD**
Age (years)	Mean ± SD	68.7 ± 6.4
Gender	Male	144 (55.4)
	Female	116 (44.6)
Number of medications	Mean ± SD	7.9 ± 2.1
Polypharmacy category	5–9 drugs	187 (72.0)
	≥10 drugs	47 (18.0)
	<5 drugs	26 (10.0)
Hypertension	Present	167 (64.2)
Diabetes mellitus	Present	137 (52.7)
Ischemic heart disease	Present	83 (31.9)
Chronic kidney disease	Present	38 (14.6)
History of smoking	Present	62 (23.8)
DDI Parameters		
Patients with ≥1 DDI	Yes	198 (76.1)
	No	62 (23.9)
Severity of DDI	Major	42 (21.2)
	Moderate	116 (58.6)
	Minor	40 (20.2)
Mean number of DDIs per patient	Mean ± SD	2.8 ± 1.4
Prescriptions with >3 DDIs	Yes	71 (27.3)
Interaction Category		
Major	Warfarin + NSAIDs	18
	ACE inhibitor + K-sparing diuretic	11
	SSRI + Tramadol	13
Moderate	Metformin + Contrast agents	26
	Beta-blocker + Insulin	34
	Diuretic + ACE inhibitor	29

A clear dose–response relationship was evident between the number of medications and DDI occurrence. Among patients taking fewer than five drugs, only 9 out of 26 (34.6%) developed DDIs, whereas the majority (65.4%) remained interaction-free. This contrast flipped dramatically in patients receiving 5–9 drugs, where 152 of 187

patients (81.3%) had at least one DDI. Severe polypharmacy showed a similarly high burden, with 37 of 47 patients (78.7%) affected. All associations were statistically significant ($p < 0.001$ for <5 and 5–9 groups; $p = 0.002$ for ≥10 drugs), reinforcing the idea that as pill count rises, safety predictably drops.

Table 2. Association Between Polypharmacy Level and Presence of Drug–Drug Interactions (N = 260)

Polypharmacy Category	n (%)	Patients with DDI n (%)	Patients Without DDI n (%)	p-value
<5 drugs	26 (10.0)	9 (34.6)	17 (65.4)	<0.001
5–9 drugs	187 (72.0)	152 (81.3)	35 (18.7)	<0.001
≥10 drugs (severe polypharmacy)	47 (18.0)	37 (78.7)	10 (21.3)	0.002
Total	**260**	**198 (76.1)**	**62 (23.9)**	—

On univariate analysis, most demographic factors did not meaningfully predict major DDIs. Age ≥70 years showed comparable rates of major interactions (13.6%) versus absence (16.7%), and gender differences were negligible. Common conditions like diabetes (16.1% major DDIs) and hypertension (15.6%) also failed to reach significance. In contrast, chronic kidney disease stood out sharply—36.8% of CKD patients experienced major DDIs compared to 63.2% without, yielding strong statistical significance ($p = 0.001$). Severe polypharmacy was another major red flag, with 40.4% of patients on ≥10 drugs experiencing major interactions ($p < 0.001$). NSAID use further amplified risk, with one-third (33.3%) of NSAID users developing major DDIs ($p = 0.005$).

Table 3. Predictors of Major Drug–Drug Interactions (Univariate Analysis)

Variable	Category	Major DDI Present n (%)	Major DDI Absent n (%)	p-value
Age	≥70 yrs	21 (13.6)	31 (16.7)	0.18
Gender	Male	24 (16.7)	120 (83.3)	0.22
	Female	18 (15.5)	98 (84.5)	0.31
Diabetes	Present	22 (16.1)	115 (83.9)	0.09
Hypertension	Present	26 (15.6)	141 (84.4)	0.12
CKD	Present	14 (36.8)	24 (63.2)	0.001
Polypharmacy ≥10	Yes	19 (40.4)	28 (59.6)	<0.001
NSAID use	Yes	16 (33.3)	32 (66.7)	0.005

After adjustment, severe polypharmacy emerged as the strongest independent predictor of major DDIs, increasing risk nearly fourfold (adjusted OR 3.9, 95% CI 1.8–8.1; $p < 0.001$). Chronic kidney disease remained a significant contributor, doubling to tripling the odds of major interactions (OR 2.7, 95% CI 1.2–5.4; $p = 0.01$). NSAID use independently doubled the risk (OR 2.2, 95% CI 1.1–4.4; $p = 0.03$). Diabetes mellitus, older age (≥70 years), and male gender showed elevated odds numerically but did not reach statistical significance, suggesting their effects are secondary once medication burden and renal function are accounted for.

Table 4. Multivariate Logistic Regression for Predictors of Major DDIs

Predictor	Adjusted OR	95% CI	p-value
Severe polypharmacy (≥10 drugs)	3.9	1.8 – 8.1	<0.001

CKD	2.7	1.2 – 5.4	0.01
Diabetes mellitus	1.5	0.8 – 2.7	0.14
NSAID use	2.2	1.1 – 4.4	0.03
Age ≥70	1.3	0.7 – 2.5	0.28
Male gender	1.1	0.6 – 2.0	0.47

Discussion

This audit revealed that drug-drug interactions were very common amongst older adults who experience polypharmacy with 76.1% of all prescriptions having at least one potential drug-drug interaction and 21.2% of all prescriptions including major DDIs. These results illustrate a patient safety issue within a group of patients who are already at a high risk because of physiological, multimorbidity, and multifaceted treatment regimens. The fact that the average of almost eight drugs per patient is an anticipated trend in geriatric care is also indicative of the need to increase the prescribing care, but it also highlights the need to be more vigilant with the prescribing practices. The severity of polypharmacy turned out to be a significant risk of DDI [11]. The probability of major interactions was almost 4 times higher in patients taking 10 or more medications, which supports the good literature evidence that the probability of interaction can increase exponentially with the number of drugs taken. Another important predictor was chronic kidney disease as per the pharmacokinetic theory, which states that a compromised renal clearance increases the levels and toxicity of the drug. The NSAID-related interactions, in particular, with the warfarin and ACE inhibitors pre-eminence, can be viewed as a good indication of high-risk interactions that are not resolvable despite the warning of the guideline, which implies an absence of prescriber awareness or clinical decision support use [12][13]. It was also found in the analysis that compliance with key prescribing standards is suboptimal. Only 34.6% of the prescriptions contained a complete medication review, and less than one-third were documented to have undergone DDI screening, which is a serious problem in comparison to the recommended practice [14]. Even in cases when major interactions were detected, only 38.1% of cases were managed with corrective action taken. This is also clinically important as 6.9% of the patients had to be hospitalized due to DDI-related incidents and almost a quarter of them had to change therapy. Poor documentation of monitoring plans registered in less than 27.9% of cases also enhances the chances of avoidable harm especially when interacting drugs necessitate renal functions tests, INR tests or ECGs. The trend of the drugs used in DDIs is in line with the global evidence, where the anticoagulants, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, selective serotonin reuptake inhibitors, and tramadol are leading contributors [15]. Nevertheless, the prescribing environment in the locality is seen to increase some risks e.g. increase in the use of NSAIDs on older patients and regular use of ACE inhibitors and diuretics co-prescription. These regional prescribing patterns could explain some discrepancies with foreign datasets and support the fact that localized interventions should be introduced [16].

Notably, the audit has found system-level factors as opposed to prescriber behavior only. The lack of electronic interaction checkers, which are not inbuilt, the lack of uniformity in medication reconciliation in transition points, and the lack of involvement of pharmacists are likely causes of high rates of DDI. Since most interactions were avoidable, predictable, and some can be prevented, by using structured medication review, pharmacist-conducted rounds, and mandatory DDI screening tools, significant harm could be prevented [17]. This audit has a number of limitations that should be recognized when interpreting the results. Since it only depended on the documented prescriptions, drug to drug interactions might be under

reported as the over the counter medicines or herbal supplements as well as undocumented medicines were not recorded. The cross-sectional design is a constraint in order to make inferences about causality between DDIs and adverse clinical outcomes, as it allows only concluding on the observed associations. Critical confounding factors like liver functions status, H. pylori infection and gastroprotective drugs were not evaluated and may affect the clinical significance of found interactions. The information on medication doses and adherence is not detailed which restricts the capacity to assess the degree of interaction risk. Also, the audit was done only in one healthcare center, which is not as generalizable to other regions or institutions that have varying prescribing patterns. Regardless of these drawbacks, the audit offers a great insight into the prescribing practices, and identified the most important areas that require the improvement of quality.

Conclusion

The findings of this audit demonstrate that drug–drug interactions are highly prevalent among patients aged 60 years and above receiving polypharmacy, with more than three-quarters of all reviewed prescriptions containing at least one interaction and over one-fifth involving a major, potentially harmful interaction. Severe polypharmacy, chronic kidney disease, and NSAID use emerged as the most important predictors of clinically significant interactions, underscoring the heightened vulnerability of older adults. Despite the high-risk profile of this population, documentation of medication review, DDI screening, and appropriate monitoring was notably suboptimal, reflecting gaps in adherence to recommended prescribing standards.

Recommendations / Action Plan

To address the identified deficiencies and improve medication safety for older adults receiving polypharmacy, several targeted actions are recommended. First, mandatory and documented medication reviews should be implemented for all patients aged 60 years and older prescribed five or more medications, ideally supported by pharmacist-led reconciliation at key care transitions. Second, the integration of electronic drug–drug interaction screening tools within the hospital prescribing system is essential, accompanied by a requirement for clinicians to document actions taken in response to major interaction alerts. Third, high-risk prescribing protocols involving NSAIDs, anticoagulants, ACE inhibitors, SSRIs, and potassium-sparing diuretics should be established, with standardized monitoring plans for laboratory parameters and clinical follow-up.

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