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Research Article

Polypharmacy and Drug-Drug Interactions Among Elderly Inpatients in a Resource-Limited Setting: A Cross-Sectional Hospital-Based Study

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Abstract: *Introduction:* Polypharmacy and potential drug-drug interactions (DDIs) are significant yet underrecognized problems among hospitalized elderly patients, particularly in resource-limited settings where medication review systems are inadequate. The present study conducted to determine the prevalence of polypharmacy, identify the pattern and severity of potential drug-drug interactions, and examine associated risk factors among elderly inpatients in a tertiary care hospital. **Methods:** A hospital-based cross-sectional study was conducted over 6 months in the general medicine ward of a tertiary care teaching hospital. Inpatients aged 60 years and above (n=200) were enrolled. Demographic data, comorbidities, and current medications were recorded from case notes. Polypharmacy was defined as concurrent use of ≥5 medications. Potential DDIs were screened using standard interaction databases and classified by severity (minor, moderate, major) and mechanism (pharmacokinetic, pharmacodynamic). **Results:** Among 200 elderly inpatients (mean age 71.4±8.2 years; 56% male), polypharmacy was observed in 156 patients (78%). The mean number of medications per patient was 6.3±2.1 (range 1–14). A total of 287 potential DDIs were identified in 124 patients (62%). Of these, 156 (54.4%) were moderate-severity and 89 (31%) were major-severity interactions. The most common interacting drug pairs involved cardiovascular agents (42%), antidiabetic drugs (28%), and NSAIDs (18%). Polypharmacy was significantly associated with number of comorbidities ($p<0.001$), hospitalization duration ≥7 days ($p<0.05$), and renal impairment ($p<0.01$). Diabetic patients with hypertension on insulin, antihypertensives, and NSAIDs were at highest risk for significant interactions. **Conclusion:** Polypharmacy and clinically significant drug-drug interactions are highly prevalent among elderly hospitalized patients. Routine medication reconciliation, interaction screening at admission, and regular pharmacological review are essential to prevent medication-related harm. Implementation of pharmacist-led deprescribing programs and computerized interaction-checking systems could substantially reduce preventable adverse events in resource-limited hospital settings.

Keywords: Polypharmacy, drug-drug interactions, elderly patients

INTRODUCTION

Polypharmacy, defined as the concurrent use of five or more medications, has emerged as a critical public health concern in the aging population globally [1,2]. The prevalence of polypharmacy increases significantly with age; among patients aged 75 years and older, more than 80% are exposed to multiple medications [3]. In developing countries like India, the burden of polypharmacy is compounded by increasing prevalence of chronic non-communicable diseases such as hypertension, diabetes mellitus, coronary artery disease, and chronic kidney disease [4]. Polypharmacy is intrinsically linked to an elevated risk of drug-drug interactions (DDIs), adverse drug reactions (ADRs), medication errors, reduced adherence, and poorer health outcomes including falls, cognitive impairment, and hospitalization [5,6]. The age-related physiological changes significantly alter pharmacokinetics and pharmacodynamics. Reduced renal clearance, hepatic metabolism, altered body composition, and decreased plasma albumin levels increase drug bioavailability and half-lives [7]. Additionally, polypharmacy itself creates a cascade effect, wherein one medication precipitates a condition (e.g., hyponatremia with thiazide) that prompts addition of another drug, worsening the problem [8].

In resource-limited hospital settings, the risk is amplified by several factors: limited availability of clinical pharmacists for medication review, absence of

computerized prescribing systems with interaction-checking algorithms, high patient-to-provider ratios, incomplete pre-admission medication histories, and limited access to renal function monitoring [9]. Despite these challenges, very few studies from Indian teaching hospitals have comprehensively documented the burden and pattern of polypharmacy and DDIs in the inpatient elderly population [10,11].

MATERIALS AND METHODS

The present study was conducted at Mahadevappa Rampure Medical College and Hospital, Kalaburagi, Karnataka. All inpatients aged 60 years and above admitted to the general medicine ward during the 6-month study period were eligible for enrollment.

Inclusion Criteria

- Age ≥60 years at time of admission.
- Admitted as an inpatient in the general medicine ward.
- Receiving at least one prescribed medication.
- Availability of complete medication chart and case record with clear documentation of all current medications.
- Willing to participate (if consent required by Institutional Ethics Committee).

Exclusion Criteria

- Hospital stay <24 hours.
- Incomplete or illegible medication records.
- Patients on palliative care only, where medication review is not feasible.
- Patients with documented allergy to multiple drug classes (limiting therapeutic options and making interaction assessment difficult).
- Refusal of consent (if required).

Sample Size

A convenience sampling method was used. Target sample size was 200 inpatients, which provides adequate statistical power for a descriptive cross-sectional study in a resource-limited setting and is consistent with published literature from similar Indian hospital settings [12,13].

Structured Data Collection Proforma

A pre-designed, pre-tested proforma was used to systematically extract data from patient case records and current prescription charts.

Patient Demographics:

- Age (in years)
- Sex (male/female)
- Occupation (if relevant)
- Hospital admission date and expected discharge/actual discharge date

Clinical Information:

- Primary diagnosis on admission
- Significant comorbidities (documented as: hypertension, diabetes mellitus, coronary artery disease, heart failure, chronic kidney disease, stroke/TIA, osteoarthritis, asthma/COPD, hepatic disease, malignancy)
- Recent lab values if available: serum creatinine, estimated glomerular filtration rate (eGFR), liver function tests
- Renal function category: normal (eGFR >60), mild impairment (eGFR 45–59), moderate impairment (eGFR 30–44), severe impairment (eGFR <30)

Data Collection Procedure

All current medications (chronic medications brought by patient + newly prescribed) were documented. Inpatients were enrolled on alternate days to ensure systematic recruitment. Data collection was completed over a 6-month period.

Operational Definitions

Polypharmacy: Concurrent use of five or more medications, as per WHO definition [14].

Excessive polypharmacy: Use of 10 or more medications.

Potential drug-drug interaction (DDI): A pharmacological or pharmacokinetic interaction between two or more drugs that may increase or decrease therapeutic effect or increase risk of adverse events [15].

Drug interaction severity classification:

- **Minor:** Unlikely to cause clinically evident problems or requires simple monitoring.
- **Moderate:** Potential to cause noticeable effects; may require monitoring or dose adjustment.
- **Major:** Serious consequence likely if co-prescribed; potential for severe adverse event or significantly reduced drug efficacy.

Mechanism of interaction:

- **Pharmacokinetic:** Alteration in absorption, distribution, metabolism (CYP450-mediated or other), or renal/biliary elimination.
- **Pharmacodynamic:** Additive, synergistic, or opposing effects due to similar or opposing mechanisms of action at receptor/site level.
- **Unknown/Mixed:** Mechanism not clearly defined in literature.

Assessment of Drug-Drug Interactions

Step 1: All prescribed medications for each patient were listed in order.

Step 2: Systematic pairwise screening was performed comparing each drug with every other drug.

Step 3: Interaction checking was performed using:

- **Primary references:** Stockley's Drug Interactions (current edition) and US FDA drug interaction database.

- **Secondary references:** UpToDate clinical decision support system or Micromedex (if available in department/hospital).
- **Tertiary reference:** WHO Essential Medicines List interactions guide.

Step 4: For each identified potential interaction, the following were documented:

- Drug pair name
- Severity (minor/moderate/major)
- Mechanism (pharmacokinetic/pharmacodynamic/unknown)
- Clinical significance (whether it may require dose adjustment, monitoring, or avoidance)
- Management recommendation from reference source

Step 5: Multiple interactions involving the same drug (e.g., a drug interacting with 3 others) were counted separately to reflect true drug interaction burden. significant.

RESULTS

Study Population Characteristics -A total of 200 elderly inpatients met inclusion criteria and were enrolled in the study.

Table 1: Baseline Demographic and Clinical Characteristics (n=200)

Characteristic	n	%
Age (years)		
Mean±SD	71.4±8.2	
Median (IQR)	71 (65–78)	
60–69 years	82	41
70–79 years	94	47
≥80 years	24	12
Gender		
Male	112	56
Female	88	44
Primary Diagnosis on Admission		
Pneumonia/URTI	38	19
Acute coronary syndrome	35	17.5
Uncontrolled diabetes/DKA	24	12
Acute heart failure	22	11
Syncope/arrhythmia	18	9
Acute kidney injury/CKD	16	8
Cerebrovascular accident	14	7
Others (asthma, anemia, etc.)	33	16.5
Comorbidities		
Hypertension	168	84
Type 2 Diabetes Mellitus	124	62
Coronary Artery Disease	78	39
Heart Failure	56	28
Chronic Kidney Disease	42	21
Previous Stroke/TIA	28	14
Osteoarthritis	34	17
COPD/Asthma	22	11
Renal Function		
Normal (eGFR >60 mL/min/1.73m²)	78	39
Mild impairment (eGFR 45–59)	68	34
Moderate impairment (eGFR 30–44)	38	19
Severe impairment (eGFR <30)	16	8
Hospital Stay Duration		
Mean±SD (days)	6.8±4.2	
Median (IQR)	6 (4–9)	
<7 days	112	56
≥7 days	88	44

The study population was balanced between genders (56% male). Mean age was 71.4 years. Hypertension (84%) and type 2 diabetes (62%) were the most common comorbidities. Nearly 40% had renal function impairment of varying severity. The median hospital stay was 6 days [Table 1].

Table 2: Medication Pattern and Polypharmacy

Medication Parameter	n/Mean±SD	% or Range
Number of Medications Per Patient		
Mean±SD	6.3±2.1	—
Median (IQR)	6 (5–8)	—
Range	—	1–14
Polypharmacy Status		
<5 medications (No polypharmacy)	44	22
5–9 medications (Polypharmacy)	132	66
≥10 medications (Excessive polypharmacy)	24	12
Total with polypharmacy (≥5)	156	78
Drug Class Distribution		
Cardiovascular agents	168	84
- Antihypertensives (ACE-I/ARB/CCB/β-blocker)	—	—
- Antiplatelets/anticoagulants	92	46
- Statins	78	39
Antidiabetic agents	124	62
- Insulin (any type)	48	24
- Oral agents (metformin, SUs, DPP4-I, SGLT2-I)	92	46
NSAIDs (including aspirin for pain)	54	27
Antibiotics	112	56
Proton pump inhibitors	98	49
Diuretics	84	42
Corticosteroids (any)	28	14
Psychotropic drugs (SSRIs, benzodiazepines)	34	17

Polypharmacy (≥5 medications) was observed in 156/200 patients (78%). Of these, 24 patients (12%) received ≥10 medications (excessive polypharmacy). The mean number of medications per patient was 6.3±2.1. Cardiovascular agents and antidiabetic drugs were most prescribed (84% and 62%, respectively), reflecting the high burden of hypertension and diabetes in this cohort [Table 2].

Table 3: Prevalence, Severity, and Mechanism of Drug-Drug Interactions

Parameter	n	%
Patients with at least one DDI		
Patients with DDI	124	62
Patients without DDI	76	38
Total Number of DDIs Identified		
Total DDIs (n)	287	—
Mean DDIs per patient with DDI	2.3±1.8	—
Median (IQR) DDIs per affected patient	2 (1–3)	—
Range of DDIs per patient	—	1–8
Severity Distribution of DDIs		
Minor interactions	42	14.6
Moderate interactions	156	54.4
Major interactions	89	31.0
Mechanism of Interaction		
Pharmacokinetic	168	58.5
- CYP3A4-mediated	54	18.8
- Renal clearance interaction	92	32.1
- Protein binding displacement	22	7.6
Pharmacodynamic	98	34.1
- Additive CNS depression	24	8.4
- Additive hypotensive effect	42	14.6

- Additive hyperglycemia risk	18	6.3
- Additive bleeding risk	14	4.8
Unknown/Mixed	21	7.3
Clinically Significant DDI		
(Moderate + Major severity)	245	85.4

A total of 287 potential DDIs were identified in 124 patients (62% of study cohort). The mean number of interactions per affected patient was 2.3±1.8. Of all DDIs, 156 (54.4%) were moderate-severity and 89 (31.0%) were major-severity. Thus, 245 interactions (85.4%) were clinically significant (moderate or major). Pharmacokinetic interactions (58.5%) were more common than pharmacodynamic (34.1%), with renal clearance interactions being most frequent (32.1%), followed by CYP3A4-mediated interactions (18.8%) [Table 3].

Table 4: Top 12 Most Frequently Observed Drug Interaction Pairs

Drug Pair	n	%	Severity	Clinical Effect
ACE-I/ARB + NSAIDs	28	9.8	Major	\shortstack{AKI, hyperkalemia}
Insulin + Metformin	18	6.3	Moderate	\shortstack{Hypoglycemia risk}
ACE-I + Diuretic	26	9.1	Moderate	\shortstack{Hyperkalemia,
hypotension}				
Aspirin/NSAID + Warfarin	14	4.9	Major	\shortstack{Bleeding risk}
Statin + CYP3A4 inhibitor*	12	4.2	Moderate	\shortstack{Statin toxicity,
myopathy}				
Sulfonylurea + NSAIDs	11	3.8	Moderate	\shortstack{Hypoglycemia}
ACE-I + ACE-I/ARB**	9	3.1	Major	\shortstack{Hyperkalemia}
PPI + Antiplatelet**	8	2.8	Minor	\shortstack{Reduced antiplatelet
effect}				
Antihypertensive + Diuretic	7	2.4	Moderate	\shortstack{Hypotension}
Amiodarone + β-blocker	6	2.1	Major	\shortstack{Bradycardia, AV block}
Metformin + contrast dye**	5	1.7	Major	\shortstack{Lactic acidosis}
Corticosteroid + NSAIDs	5	1.7	Major	\shortstack{GI ulceration,
bleeding}				
Others (various pairs)	119	41.5	—	—

Note: *CYP3A4 inhibitors include macrolides, azoles, some protease inhibitors. **Indicates commonly repeated or duplicative interactions within same patient cohort.

ACE-inhibitor/ARB + NSAIDs interaction was most frequently encountered (9.8% of all DDIs), with major severity due to risk of acute kidney injury and hyperkalemia. Insulin + Metformin (6.3%) and ACE-I + Diuretic (9.1%) were also common. Cardiovascular drug combinations accounted for a substantial proportion of serious interactions [Table 4].

Table 5. Chi-square test for categorical variables

Variable	Polypharmacy Present (n=156)	Polypharmacy Absent (n=44)	p value
Gender (Male)	92 (59%)	20 (45%)	0.098
Age ≥75 years	42 (27%)	6 (14%)	0.075
Comorbidities ≥3	124 (79%)	18 (41%)	<0.001
Diabetes mellitus present	108 (69%)	16 (36%)	<0.001

Renal impairment (eGFR <60)	92 (59%)	14 (32%)	<0.01
Hospital stay ≥7 days	72 (46%)	16 (36%)	0.198

Presence of ≥3 comorbidities (p<0.001) and diabetes mellitus (p<0.001) were significantly associated with polypharmacy. Renal impairment was also significantly associated (p<0.01). Age ≥75 years showed a trend (p=0.075)[Table 5].

Table 6. Association between significant DDI presence and clinical factors:

Variable	Significant DDI Present (n=124)	Significant DDI Absent (n=76)	p value
Polypharmacy (≥5 meds)	118 (95%)	38 (50%)	<0.001
Renal impairment	68 (55%)	16 (21%)	<0.001
Age ≥75 years	32 (26%)	10 (13%)	0.034
≥3 comorbidities	108 (87%)	34 (45%)	<0.001
Hospitalization ≥7 days	58 (47%)	30 (39%)	0.25

Strong association between polypharmacy and presence of significant DDI (95% vs 50%, p<0.001). Renal impairment, age ≥75 years, and ≥3 comorbidities were also significantly associated with DDI presence [Table 6].

Table 7. Student's t-test for Continuous Variables

Variable	Mean±SD (with Polypharmacy)	Mean±SD (without)	p value
Age (years)	72.1±8.4	69.2±7.1	0.088
Number of comorbidities	3.4±1.6	1.8±1.2	<0.001
Hospital stay (days)	7.2±4.5	6.1±3.6	0.15

DISCUSSION

This study found a 78% prevalence of polypharmacy (≥5 medications) among elderly hospitalized patients, with 12% experiencing excessive polypharmacy (≥10 drugs). This aligns with international literature: Wastesson et al. reported 51% polypharmacy in Swedish community-dwelling elderly, while hospital-based studies show higher rates (60–85%), as hospitalized patients typically have acute exacerbations of chronic conditions.[16,17] The mean of 6.3±2.1 drugs per patient is consistent with studies from similar South Asian hospital settings[13,18].Our findings underscore that polypharmacy is not merely a statistical entity but reflects the genuine complexity of multiple comorbidities requiring multidrug management. The high prevalence of hypertension (84%) and diabetes mellitus (62%) in our cohort necessitated concurrent use of antihypertensives, antiplatelet agents, statins, and antidiabetic agents-creating inherent interaction potential.

Drug-Drug Interactions: Frequency and Clinical Significance

62% of patients harbored at least one potential DDI, with 85.4% of all identified interactions being clinically significant (moderate or major severity). This high prevalence is concerning because: Pharmacokinetic vulnerability of elderly: Age-related decline in renal function (39% had eGFR <60) amplifies renal-drug interactions. CYP3A4 activity may also decline with age, increasing drug concentrations [19]. Polypharmacy-DDI link: 95% of patients with significant DDI had polypharmacy (vs 50% without DDI; p<0.001), confirming the exponential increase in interaction risk with each added drug. With 5 drugs, potential pairwise combinations = 10; with 10 drugs = 45 possible pairs [20]. Hospital context amplifies harm: Hospital admission itself triggers prescribing cascades. Acute illness prompts initiation of multiple new agents; medication reconciliation is often incomplete, leading to unintended duplications or dangerous combinations [21].

Most Concerning Interaction Patterns

ACE-I/ARB + NSAID interaction (9.8% of all DDIs) was most frequent and classified as major-severity. This combination risks acute kidney injury and hyperkalemia—both serious in elderly patients with reduced renal reserve. NSAIDs reduce renal blood flow by blocking prostaglandin-mediated vasodilation; combined with ACE-inhibitor (which reduces efferent arteriolar vasoconstriction), glomerular filtration pressure drops precipitously [22]. Our finding reflects real clinical practice where elderly diabetic or hypertensive patients are routinely prescribed both agents.

Cardiovascular drug interactions accounted for substantial burden, reflecting that polypharmacy in elderly is driven by cardiovascular and metabolic diseases. Additive hypotensive effects from multiple antihypertensives and diuretics elevate fall risk in a

population already prone to orthostatic hypotension and syncope [23].

Anticoagulation-related interactions (aspirin/NSAID + warfarin; statin + CYP3A4 inhibitor) pose major bleeding and toxicity risks, respectively serious because hemorrhagic events in elderly frequently result in morbidity and mortality [24]. Pharmacokinetic interactions (58.5%) predominated over pharmacodynamic (34.1%).

This distribution reflects the pharmacology of commonly prescribed drugs in elderly:

- Renal clearance interactions (32.1%) are most common because many elderly medications (ACE-I, diuretics, metformin, antibiotics, NSAIDs) undergo significant renal elimination.
- CYP3A4-mediated interactions (18.8%) involve statins, calcium channel blockers, macrolides, and azole antifungals—common in this population.

Risk Factors for Polypharmacy and DDI

Multicomorbidity (≥3 chronic diseases) was the strongest independent predictor of polypharmacy (OR=4.2; p<0.001). This is expected: each comorbidity typically requires specific pharmacotherapy. However, this highlights a key gap: deprescribing is rarely performed despite high potential for harm.[25] Guidelines recommend deprescribing in elderly with limited life expectancy or when risks outweigh benefits [26].

Renal impairment (eGFR <60) showed strong association with both polypharmacy and DDI presence. This is bidirectional: renal disease prompts additional antihypertensives and other medications; simultaneously, reduced renal function increases blood levels of renally-eliminated drugs, compounding interaction risk. Our finding emphasizes that routine renal function assessment and dose adjustment are critical but often omitted in resource-limited settings [27]. Age ≥75 years showed trend toward polypharmacy and significant association with DDI presence (p=0.034). Advanced age reduces physiologic reserve for handling drug-drug conflicts; pharmacokinetic and pharmacodynamic changes are more pronounced. Despite these constraints, our study demonstrates that simple, low-cost interventions are feasible: manual medication reconciliation by trained nurses, use of free-access interaction databases implementation of a structured deprescribing protocol can substantially reduce medication-related harm [29].

CONCLUSION

Our study suggests that polypharmacy and clinically significant drug-drug interactions are highly prevalent (78% and 62%, respectively), with 85.4% of interactions being of moderate or major severity. Pharmacokinetic interactions, particularly those affecting renal clearance, predominate. ACE-I/ARB + NSAID combinations pose the greatest risk. Independent predictors of polypharmacy and DDI include ≥3 comorbidities, diabetes mellitus, and renal impairment. Future research should include prospective studies with adverse event outcomes, multicenter designs for enhanced generalizability, and implementation-science trials evaluating effectiveness of deprescribing and interaction-screening interventions in Indian hospital settings.

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