RESEARCH PAPER

Polypharmacy and Drug-Drug Interactions in Chronic Disease Prescriptions - A Community Pharmacy Study

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ABSTRACT

Background: Rising multimorbidity and chronic disease burden have increased multidrug exposure in ambulatory populations, thereby elevating the risk of potential drug–drug interactions (pDDIs). Community pharmacies serve as important medication-safety checkpoints before drug utilization.

Objective: To evaluate the prevalence, severity, therapeutic contributors, and predictors of potential drug–drug interactions among chronic disease prescriptions dispensed from community pharmacies in South India.

Materials and Methods: A community pharmacy-based cross-sectional analytical study was conducted using 300 chronic disease prescriptions collected from registered pharmacies in Anantapur, Andhra Pradesh, India. Adult prescriptions containing at least two concurrent medications were included. Potential drug–drug interactions were screened using LexiDrug, Medscape Drug Interaction Checker, and Drugs.com databases. Polypharmacy and excessive polypharmacy were defined as ≥5 and ≥10 medications, respectively. Interaction severity was categorized as minor, moderate, major, or contraindicated. Associations between medication burden and pDDIs were analyzed using odds ratios and Wald z-test.

Results: Polypharmacy occurred in 42.3% of prescriptions, while 27.7% demonstrated at least one pDDI. Among 116 identified interactions, moderate interactions predominated (74.1%), followed by major (21.6%) and minor interactions (4.3%). Polypharmacy showed strong association with overall pDDIs (OR: 4.60; 95% CI: 2.67–7.93; $p<0.001$) and major pDDIs (OR: 6.28; 95% CI: 2.29–17.24; $p<0.001$). Cardiovascular and antidiabetic combinations contributed substantially to interaction burden.

Conclusion: Potential drug–drug interactions are highly prevalent among chronic disease prescriptions in community pharmacies. Increasing prescription complexity significantly elevates clinically important interaction risk, emphasizing the importance of pharmacist-led prescription review and medication-safety interventions.

Keywords: *Chronic Disease; Community Pharmacy; Drug Interactions; Medication Safety; Polypharmacy; Prescription Drug Interactions*

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1. INTRODUCTION

The global rise in multimorbidity has substantially increased long-term exposure to multidrug pharmacotherapy, particularly among patients with diabetes mellitus, hypertension, cardiovascular disorders, chronic kidney disease, and metabolic syndromes[1,2]. Contemporary chronic disease management frequently requires simultaneous use of antihypertensives, antidiabetic agents, antiplatelets, lipid-lowering agents, gastroprotective drugs, and symptomatic therapies[2,3]. Although multidrug regimens are often clinically justified, increasing prescription complexity simultaneously expands the probability of pharmacokinetic and pharmacodynamic drug–drug interactions[3,4].

Potential drug–drug interactions represent a major contributor to preventable medication-related morbidity

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worldwide[4,5]. Interaction-associated complications may alter therapeutic response, impair treatment efficacy, precipitate electrolyte disturbances, prolong ventricular repolarization, increase bleeding tendency, worsen renal function, and elevate hospitalization risk[5,6]. The interaction burden becomes particularly pronounced among elderly individuals and patients receiving cardiometabolic polypharmacotherapy because the number of possible drug combinations increases exponentially with medication count[6,7].

Cardiovascular and antidiabetic regimens constitute major sources of clinically relevant pDDIs[7,8]. Renin–angiotensin system inhibitors combined with potassium-sparing diuretics may synergistically impair renal potassium excretion, predisposing susceptible individuals to hyperkalemia[8]. Similarly, beta-adrenergic blockade may attenuate sympathetic manifestations of hypoglycemia during sulfonylurea therapy, thereby delaying recognition of declining glucose levels[9]. Concurrent administration of QT-prolonging agents such as macrolides and prokinetic drugs may further increase arrhythmogenic susceptibility through additive ventricular repolarization abnormalities[10].

Despite growing awareness regarding medication safety, community pharmacy-based evidence from semi-urban South Indian settings remains limited[11,12]. Most Indian pDDI investigations originate from tertiary-care hospitals, where medication patterns differ considerably from ambulatory chronic disease practice[12]. Community pharmacists, however, function as the final prescription-level safety checkpoint before medication utilization and therefore occupy a strategically important role in identifying high-risk combinations, counselling patients, and communicating clinically significant interactions to prescribers[13].

The present study was therefore designed to evaluate the prevalence, severity distribution, therapeutic contributors, and predictors of potential drug–drug interactions among chronic disease prescriptions dispensed from community pharmacies in Anantapur town, Andhra Pradesh.

2. MATERIALS AND METHODS

2.1 Study Design and Setting
The investigation adopted a community pharmacy-based cross-sectional analytical design to evaluate medication-related interaction burden among ambulatory chronic disease prescriptions[14,15] dispensed in Anantapur town, Andhra Pradesh, India.

2.2 Study Duration
Prescription collection and analysis were performed over a three-month study period.

2.3 Study Population
The study included adult patients receiving chronic disease prescriptions from participating registered community pharmacies.

2.4 Inclusion Criteria
- Adult prescriptions corresponding to patients aged ≥18 years
- Prescriptions containing at least two concurrently prescribed medications
- Chronic disease prescriptions involving long-term pharmacotherapy
- Prescriptions with adequately documented medication details

2.5 Exclusion Criteria
- Prescriptions intended exclusively for acute illnesses
- Illegible or incomplete prescriptions
- Prescriptions containing only over-the-counter medicines
- Non-allopathic prescriptions

2.6 Sample Size
The sample size was calculated using the standard single-population proportion formula based on expected prevalence, 95% confidence interval, and acceptable precision margin[16,17]. A total of 300 eligible prescriptions underwent final analysis.

2.7 Data Collection Procedure
Eligible prescriptions were consecutively screened during pharmacy operating hours using a structured data collection format. Demographic variables, comorbidities, medication count, therapeutic categories, and concomitant medication patterns were systematically documented.

2.8 Operational Definition of Polypharmacy
The current study operationally categorized prescriptions containing five or more concurrent medications as polypharmacy, whereas prescriptions containing ten or more medications were categorized as excessive polypharmacy[3,18].

2.9 Potential Drug–Drug Interaction Screening
Interaction screening was independently performed using LexiDrug, Medscape Drug Interaction Checker, and Drugs.com databases. Identified interactions were classified according to severity[19,20] into: (a) Minor, (b) Moderate, (c) Major, and (d) Contraindicated. Previous south Indian studies have demonstrated the utility of mobile-based drug interaction screening applications in improving identification of clinically relevant pDDIs[21].

2.10 Statistical Analysis
Prescription variables underwent coding, tabulation, and statistical interpretation using spreadsheet-assisted analytical methods. Descriptive statistics were used to summarize frequencies and prevalence. Odds ratios, risk ratios, prevalence differences, and 95% confidence intervals quantified associations between medication burden and pDDIs[22]. Associations demonstrating probability values below the predefined alpha threshold of 0.05 were interpreted as statistically meaningful.

3. RESULTS

3.1 Demographic and Clinical Characteristics

Among 300 evaluated prescriptions, polypharmacy occurred in 127 prescriptions (42.3%), whereas excessive polypharmacy was identified in 20 prescriptions (6.7%). Most patients belonged to the 40–59-year and 60–74-year age categories, reflecting the predominance of chronic cardiometabolic disease among middle-aged and elderly ambulatory populations (Table 1). Diabetes mellitus and hypertension represented the dominant clinical conditions contributing to multidrug exposure.

Table 1. Demographic and Clinical Characteristics

Variable	Frequency (%)
Male patients	74 (58.3)
Age 40–59 years	60 (47.2)
Age 60–74 years	55 (43.3)
Type 2 diabetes mellitus	80 (63.0)
Hypertension	42 (33.1)
OTC/supplement use	98 (77.2)

3.2 Prevalence and Severity of Potential Drug–Drug Interactions

Interaction screening identified 116 pDDIs distributed across 83 prescriptions, yielding an overall prevalence of 27.7%. Moderate-severity interactions dominated the interaction spectrum, indicating substantial monitoring requirements during chronic pharmacotherapy (Table 2).

Table 2. Severity Distribution of Potential Drug–Drug Interactions

Severity Category	Frequency (%)
Moderate	86 (74.1)
Major	25 (21.6)
Minor	5 (4.3)
Contraindicated	0 (0)

3.3 Frequently Identified Interaction Combinations

Cardiovascular and antidiabetic combinations contributed prominently to the observed interaction burden (Table 3).

Table 3. Frequently Identified Potential Drug–Drug Interactions

Drug Combination	Frequency	Highest Severity
Amlodipine + Metoprolol	21	Moderate
Aspirin + Clopidogrel	20	Moderate
Azithromycin + Domperidone	10	Major
Glimepiride + Metoprolol	10	Moderate
Losartan + Spironolactone	6	Major

3.4 Association Between Medication Burden and pDDIs

Interaction prevalence demonstrated a pronounced upward gradient across increasing medication categories. Polypharmacy substantially amplified both overall and clinically significant interaction probability (Table 4).

Table 4. Association Between Polypharmacy and pDDIs

Outcome	Odds Ratio (95% CI)	Risk Ratio	p-value
Any pDDI	4.60 (2.67–7.93)	2.99	<0.001
Major pDDI	6.28 (2.29–17.24)	5.45	<0.001

3.5 Therapeutic Drug Class Contribution

Antiplatelets, beta blockers, NSAIDs, calcium channel blockers, ARBs, and macrolide antibiotics contributed substantially to interaction occurrence (Table 5).

Table 5. Therapeutic Drug Classes Contributing to pDDIs

Therapeutic Class	Contribution (%)
Antiplatelets	19.0
Beta blockers	13.4
NSAIDs	10.3
Calcium channel blockers	9.9
ARBs	8.2
Macrolide antibiotics	7.8

4. DISCUSSION

The present investigation demonstrates a clinically meaningful burden of potential drug–drug interactions among chronic disease prescriptions dispensed from community pharmacies in South India. More than one-fourth of evaluated prescriptions carried at least one interaction risk, indicating substantial exposure to preventable medication-related complications within ambulatory chronic disease populations[4,11].

Similar findings have been reported in Indian ambulatory care settings, where chronic cardiometabolic prescriptions demonstrated a substantial burden of moderate and clinically significant potential drug–drug interactions, particularly among patients receiving multidrug therapy for diabetes and hypertension[1,7,23]. Recent evidence has additionally linked polypharmacy with xerostomia and other medication-related quality-of-life impairments among elderly patients receiving chronic multi-drug therapy[24]. The observed interaction prevalence likely reflects increasing multidrug cardiometabolic management among patients with coexisting diabetes mellitus, hypertension, and cardiovascular disease[1,7].

Such populations frequently receive overlapping antihypertensive, antiplatelet, antidiabetic, and symptomatic therapies, thereby increasing opportunities for pharmacodynamic and pharmacokinetic interaction pathways[25-27]. The predominance of moderate-severity interactions suggests that many identified combinations may not require immediate discontinuation but nevertheless warrant close monitoring, dose optimization, therapeutic review, and structured patient counselling[13,28].

Escalating medication burden markedly amplified interaction probability in the present dataset. Interaction prevalence increased sharply among prescriptions containing ≥5 medications and became particularly pronounced in excessive polypharmacy categories. This relationship possesses strong pharmacological plausibility because the number of possible interaction pairs expands exponentially with increasing medication count[3,6,18]. Comparable observations from Indian hospital-based investigations have likewise demonstrated a strong association between increasing medication count and heightened interaction risk, reinforcing polypharmacy as an independent predictor of clinically important pDDIs[29].

Cardiovascular combinations contributed substantially to the observed interaction burden. Concurrent administration of amlodipine and metoprolol may potentiate additive hemodynamic suppression, thereby increasing susceptibility to bradycardia, hypotension, dizziness, and fatigue among vulnerable individuals[30]. Similarly, aspirin combined with clopidogrel reflects extensive utilization of dual antiplatelet therapy in chronic cardiovascular prevention. Although clinically justified in selected populations, this combination may amplify gastrointestinal and systemic bleeding risk, particularly among elderly patients and those concurrently exposed to NSAIDs[31].

The interaction involving glimepiride and metoprolol deserves particular clinical attention because beta-adrenergic blockade may attenuate adrenergic manifestations of hypoglycemia[9], including tremors and palpitations, thereby delaying recognition of declining glucose levels. Likewise, combinations involving losartan or enalapril with spironolactone may synergistically impair renal potassium excretion through renin–angiotensin–aldosterone system modulation, predisposing susceptible patients to hyperkalemia and cardiac conduction abnormalities[8].

QT interval-related combinations also emerged prominently within the present study. Combined exposure to azithromycin and domperidone may increase ventricular repolarization abnormalities through additive electrophysiological effects[10].

Such combinations may become clinically significant among elderly individuals, patients with electrolyte imbalance, and those with underlying cardiovascular disease[32,33].

NSAID-associated interactions represented another clinically relevant observation. NSAID exposure may reduce renal perfusion through prostaglandin inhibition, thereby attenuating antihypertensive response and potentiating nephrotoxic risk when combined with renin–angiotensin system inhibitors and diuretics[34]. Because many analgesics remain readily accessible without prescription, the actual interaction burden in community settings may exceed documented estimates[34,35].

The therapeutic class distribution observed in the present investigation highlights the dominant contribution of cardiometabolic pharmacotherapy to interaction burden in ambulatory practice. These findings reinforce the need for targeted pharmacist-led medication review focusing particularly on patients receiving cardiovascular combinations, antiplatelet therapy, antidiabetic agents, QT-prolonging drugs, and NSAID-containing regimens.

Previous studies evaluating healthcare professionals' perceptions toward drug–drug interactions have further emphasized the importance of pharmacist-led surveillance, interprofessional communication, and continuous medication review in minimizing preventable interaction-related harm.[13,36,37]. Community pharmacists can substantially reduce preventable medication-related harm through routine interaction screening, individualized patient counselling, therapeutic duplication assessment, and collaborative communication with prescribers[13,36] regarding clinically important combinations. Prioritizing prescriptions containing five or more medications may further improve the efficiency of medication safety interventions in high-volume community pharmacy settings.

5. LIMITATIONS

The present study evaluated potential rather than clinically confirmed drug–drug interactions; therefore, the findings represent interaction risk rather than verified adverse

outcomes. Laboratory parameters, renal function, hepatic function, alcohol use, herbal medicine exposure, and adherence-related variables were not comprehensively evaluated.

Additionally, undocumented over-the-counter medication use may have contributed to underestimation of the actual interaction burden.

6. CONCLUSION

Potential drug–drug interactions remain highly prevalent among chronic disease prescriptions encountered in community pharmacy settings. Increasing medication burden substantially amplifies the probability of clinically important interactions, particularly among patients receiving multidrug cardiometabolic therapy. Moderate-severity interactions predominated; however, major interactions constituted a clinically meaningful proportion requiring active pharmacist intervention and monitoring. Cardiovascular agents, antiplatelets, beta blockers, NSAIDs, renin–angiotensin system inhibitors, and macrolide antibiotics contributed prominently to interaction burden. Systematic pharmacist-led prescription review, real-time interaction screening, and collaborative medication management strategies may significantly reduce preventable medication-related harm in ambulatory chronic disease care.

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CONFLICTS OF INTERESTS (IF ANY)

There are no conflicts of interest.

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ABBREVIATIONS

ACE: Angiotensin-Converting Enzyme; ADA: American Diabetes Association; AKI: Acute Kidney Injury; ARBs: Angiotensin Receptor Blockers; BMJ: British Medical Journal; DASH: Dietary Approaches to Stop Hypertension; DDI: Drug–Drug Interaction; ESC: European Society of Cardiology; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; pDDIs: Potential Drug–Drug Interactions; QT: Ventricular Depolarization and Repolarization Interval on Electrocardiography

RAAS: Renin–Angiotensin–Aldosterone System; WHO: World Health Organization.

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