e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(7); 2057-2062

Original Research Article

Prospective Evaluation of Drug–Drug Interactions in Patients Receiving Antihypertensive Therapy

Rachana Raina[1], Roohi sharma[2], Shivani Rani[3], Sharminder Kaur[4], Vishal R. Tandon[5]

[1]Senior Resident, Department of Pharmacology, GMC Jammu, India
[2]Associate Professor, Department of Pharmacology, GMC Udhampur, India
[3]Assistant Professor, Acharya Shri Chander College of Medical Sciences, Sidra Jammu, India
[4]Associate Professor, Department of Pharmacology, GMC Jammu, India
[5]Professor, Department of Pharmacology, GMC Jammu, India

Received: 13-05-2025 / Revised: 12-06-2025 / Accepted: 13-07-2025
Corresponding Author: Dr. Shivani Rani
Conflict of interest: Nil

Abstract:

Background: Hypertension is a prevalent chronic disorder that often requires long-term multidrug therapy for effective control. The concomitant use of multiple antihypertensive agents and medications for comorbid conditions increases the risk of drug–drug interactions (DDIs), which can compromise therapeutic outcomes and patient safety. Evaluating these interactions prospectively in real-world clinical settings is essential for identifying at-risk populations and promoting rational prescribing practices.

Aim: The present study aimed to prospectively evaluate the prevalence, pattern, severity, and determinants of potential drug–drug interactions in patients receiving antihypertensive therapy at a tertiary care hospital.

Materials and Methods: This prospective, observational study was conducted in the Department of Pharmacology in collaboration with the Medicine Department at a tertiary care hospital. Ninety-two hypertensive patients receiving at least one antihypertensive medication were enrolled. Data were collected using a predesigned case record form that included demographic details, comorbidities, and complete prescription profiles. Drug–drug interactions were identified using standard databases such as Lexicomp®, Micromedex®, and Medscape Drug Interaction Checker, and were categorized based on severity (major, moderate, minor) and mechanism (pharmacokinetic, pharmacodynamic).

Results: Out of 92 patients, 57.61% were male and 42.39% were female, with a mean age of 56.43 ± 11.28 years. A total of 92 potential DDIs were identified (mean 1.00 ± 0.42 per patient). Moderate interactions were most frequent (52.17%), followed by major (23.91%) and minor (23.91%) types. Pharmacodynamic interactions predominated (61.96%). A significant association was observed between polypharmacy and DDIs ($p = 0.001$), and between comorbidities such as diabetes and chronic kidney disease with DDI occurrence ($p = 0.004$).

Conclusion: The study demonstrates that DDIs are common among patients on antihypertensive therapy, particularly in those with multiple comorbidities and complex medication regimens. Regular medication review, pharmacist intervention, and the use of interaction-checking tools are recommended to minimize potential risks and optimize therapeutic safety.

Keywords: Drug–drug interactions, Hypertension, Antihypertensive therapy, Polypharmacy, Comorbidities.

Introduction

Hypertension remains one of the most pervasive noncommunicable diseases worldwide and a leading, modifiable driver of cardiovascular morbidity and mortality. Despite wide availability of effective treatment, control rates remain suboptimal in many regions, with millions of adults either undiagnosed, untreated, or inadequately treated. This treatment gap, coupled with demographic aging and rising cardiometabolic risk, sustains a large pool of patients who require long-term pharmacotherapy and regular regimen adjustments over the life course. [1]

Over the last three decades, population estimates have highlighted both the magnitude and the uneven progress in detection, treatment, and control of hypertension across countries. Global analyses suggest that well over a billion adults live with elevated blood pressure and that substantial proportions in low- and middle-income countries remain untreated. These trends are crucial for pharmacotherapy planning because they translate into a vast and growing exposure to antihypertensive drugs, combination regimens, and—inevitably—opportunities for drug–drug interactions (DDIs). [2]

Clinical practice guidelines emphasize earlier identification, accurate measurement, and timely intensification of therapy, often via combinations that target complementary mechanisms. In contemporary care, multiple classes—renin–angiotensin system (RAS) blockers, calcium channel blockers (CCBs), thiazide-type diuretics, beta-blockers, and mineralocorticoid receptor antagonists—are deployed based on comorbidities and risk. The 2017 ACC/AHA recommendations, for example, codified lower diagnostic thresholds and widespread use of combination therapy to attain targets efficiently, changes that have expanded real-world polypharmacy in hypertension care. [3]

Parallel global guidance from the World Health Organization (WHO) underscores standardized treatment protocols, rational fixed-dose combinations, and team-based care to improve control rates. These strategies, while necessary for population impact, increase the prevalence of multi-drug regimens in routine practice—making systematic surveillance for DDIs a critical safety task in outpatient and inpatient settings alike. [4]

DDIs in antihypertensive therapy can be pharmacokinetic (altered absorption, metabolism, or excretion) or pharmacodynamic (additive or antagonistic physiologic effects). Reviews focused on antihypertensive pharmacotherapy have cataloged interaction patterns that arise commonly when blood pressure agents intersect with cardiometabolic, renal, and neurologic medications used for multimorbidity. Mechanistically, these include CYP-mediated changes to statin exposure by CCBs, renal hemodynamic effects when RAS blockers and diuretics are combined with nonsteroidal anti-inflammatory drugs (NSAIDs), and conduction or inotropy effects when rate-limiting CCBs are paired with beta-blockers. In real-world care, the breadth of such combinations makes pre-emptive identification and mitigation vital. [5]

Specific, widely encountered interaction pairs illustrate the clinical stakes. Simvastatin exposure, for instance, increases when co-administered with amlodipine, prompting dose limitations to reduce myopathy risk; regulators explicitly recommend that simvastatin not exceed 20 mg daily when used with amlodipine or certain other interacting agents. Such labeling changes reinforce the need to reconcile cardiovascular regimens against lipid-lowering therapy at every visit. [6]

Renally mediated interactions are equally salient. The so-called “triple whammy”—concurrent use of a RAS inhibitor (ACE inhibitor or ARB), a diuretic, and an NSAID—can precipitate acute kidney injury (AKI) by compounding afferent and efferent arteriolar effects and intravascular volume changes. Signal detection and pharmacoepidemiologic studies have associated this combination with earlier and higher risk of AKI, underscoring that common, over-the-counter analgesic choices can tip otherwise stable antihypertensive regimens into harm. [7]

Diet–drug interactions further complicate antihypertensive care. Grapefruit—through intestinal CYP3A4 inhibition—raises exposure to several dihydropyridine CCBs (notably felodipine), with clinically relevant increments in blood levels and hemodynamic effects documented in controlled studies. For patients on multi-drug regimens, such food effects can masquerade as resistant hypertension or adverse reactions, unless proactively addressed during counseling and medication review.

Materials and Methods

This was a prospective, observational study conducted in the Department of Pharmacology in collaboration with the Medicine Department at a tertiary care hospital. The study aimed to evaluate potential and clinically significant drug–drug interactions (DDIs) among patients receiving antihypertensive therapy. Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the study, and written informed consent was collected from all participants before enrollment. A total of 92 patients who were receiving at least one antihypertensive medication were included in the study. Patients were enrolled from both inpatient and outpatient departments. Inclusion criteria comprised adult patients (≥18 years) of either gender, diagnosed with hypertension and receiving antihypertensive drugs either as monotherapy or combination therapy. Patients receiving antihypertensive therapy for any comorbid condition, such as diabetes mellitus, ischemic heart disease, or chronic kidney disease, were also included. Patients who were unwilling to participate or had incomplete prescription data were excluded.

Methodology: Data were collected prospectively using a predesigned case record form. The form captured demographic details (age, gender, weight, and BMI), clinical data (diagnosis, comorbidities, blood pressure readings, and laboratory values), and complete prescription details, including drug name, dose, route, frequency, and duration. Concomitant medications other than antihypertensive agents were also documented to identify potential DDIs. The prescribing pattern of antihypertensive agents was classified according to therapeutic class such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), beta-blockers, diuretics, and others.

Assessment of Drug–Drug Interactions: All prescriptions were screened for potential drug–drug interactions using an updated, standard interaction-checking database such as Lexicomp®,

Micromedex®, or Medscape Drug Interaction Checker. The identified DDIs were categorized based on severity (major, moderate, or minor) and mechanism (pharmacokinetic or pharmacodynamic). The clinical relevance of potential interactions was evaluated in consultation with the treating physician and verified through available literature evidence.

Parameters Evaluated: The parameters assessed included the frequency and pattern of DDIs, number of antihypertensive drugs prescribed per patient, severity level of interactions, and drug classes most commonly involved. Additional parameters such as association between the number of drugs prescribed and the likelihood of DDIs, correlation between comorbidities and DDIs, and impact of polypharmacy were also evaluated. Demographic factors such as age group, gender, and comorbidity profile were analyzed for their relationship with the occurrence of DDIs.

Statistical Analysis: All collected data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Descriptive statistics such as mean ± standard deviation (SD) and frequency (%) were used for continuous and categorical variables, respectively. The association between the occurrence of DDIs and variables such as age, gender, number of drugs prescribed, and comorbidities was tested using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics: A total of 92 patients receiving antihypertensive therapy were enrolled in the study. Among them, males constituted a slightly higher proportion (57.61%) compared to females (42.39%), indicating a modest male predominance among hypertensive patients. The majority of participants (47.83%) were in the age group of 41–60 years, followed by 36.96% aged above 60 years, suggesting that middle-aged and elderly individuals formed the predominant group affected by hypertension. Only 15.22% of patients were aged between 18 and 40 years. The mean age of the study population was 56.43 ± 11.28 years, indicating that most participants were in the late middle-age range.Regarding comorbid conditions, 33.70% of patients had diabetes mellitus, 19.57% had ischemic heart disease, and 11.96% were suffering from chronic kidney disease. About 34.78% of the patients did not present with any comorbid condition. The mean body mass index (BMI) was 25.67 ± 3.41 kg/m², showing that most participants were in the overweight range. These findings reflect that hypertension is commonly associated with metabolic and cardiovascular comorbidities in the tertiary care setting.

Prescribing Pattern of Antihypertensive Agents: The prescribing pattern revealed that angiotensin receptor blockers (ARBs) were the most commonly prescribed class of antihypertensive drugs, used by 41.30% of patients. This was followed by calcium channel blockers (CCBs) in 34.78%, ACE inhibitors (ACEIs) in 29.35%, and beta-blockers in 26.09% of patients. Diuretics were prescribed to 21.74%, while alpha-blockers and other centrally acting antihypertensive agents were less frequently prescribed (8.70% and 6.52%, respectively). The mean number of antihypertensive drugs per prescription was 2.14 ± 0.93, indicating that combination therapy was common in this population. The preference for ARBs and CCBs aligns with current hypertension management guidelines, which favor these classes due to their favorable side-effect profile and effectiveness in comorbid conditions such as diabetes and renal impairment.

Distribution of Drug–Drug Interactions by Severity and Mechanism: A total of 92 potential drug–drug interactions (DDIs) were identified in the prescriptions analyzed, averaging 1.00 ± 0.42 DDIs per patient. Based on severity, moderate interactions were the most prevalent, accounting for 52.17%, followed by major and minor interactions, each constituting 23.91%. The predominance of moderate DDIs indicates that while most interactions may not be immediately life-threatening, they possess the potential to alter therapeutic outcomes if not properly monitored.When classified by mechanism, pharmacodynamic interactions were more common (61.96%) than pharmacokinetic interactions (38.04%). This suggests that the majority of DDIs occurred due to additive or antagonistic effects on blood pressure, heart rate, or electrolyte balance, rather than from altered drug absorption or metabolism. This pattern is consistent with the nature of antihypertensive drugs, many of which share overlapping mechanisms affecting vascular tone and cardiac function.

Association Between Number of Drugs Prescribed and Occurrence of DDIs: A clear association was observed between the number of drugs prescribed and the occurrence of DDIs. Among patients receiving ≤3 drugs, DDIs were noted in 31.58% of cases, while those receiving 4–6 drugs had a higher incidence of 72.97%, and patients on ≥7 drugs showed the highest DDI occurrence at 88.24%. The relationship between polypharmacy and DDIs was found to be statistically significant ($p = 0.001$). This finding highlight that the risk of drug–drug interactions rises sharply with an increasing number of prescribed medications. It emphasizes the importance of rational prescribing and regular medication review, particularly in elderly and multimorbid patients who often require multiple therapeutic agents.

Association Between Comorbidities and Occurrence of Drug–Drug Interactions: Comorbidity was found to be a significant factor influencing the incidence of DDIs. Patients with chronic kidney disease (CKD) had the highest proportion of DDIs (90.91%), followed by those with diabetes mellitus (80.65%) and ischemic heart disease (77.78%). In contrast, only 43.75% of patients without comorbidities exhibited potential DDIs. Statistical analysis revealed a significant association between the presence of comorbidities and the occurrence of DDIs ($p = 0.004$). This suggests that patients with chronic diseases are more vulnerable to DDIs, likely due to the need for multiple concomitant medications to manage both hypertension and associated conditions. These findings underscore the need for cautious selection and monitoring of drug regimens in patients with multiple comorbidities to minimize adverse outcomes.

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 92)

Parameter	Category	Frequency (n)	Percentage (%)
Gender	Male	53	57.61
	Female	39	42.39
Age Group (years)	18–40	14	15.22
	41–60	44	47.83
	>60	34	36.96
Comorbidities	Diabetes Mellitus	31	33.70
	Ischemic Heart Disease	18	19.57
	Chronic Kidney Disease	11	11.96
	None	32	34.78

Mean age: 56.43 ± 11.28 years; Mean BMI: 25.67 ± 3.41 kg/m²

Table 2: Prescribing Pattern of Antihypertensive Agents

Antihypertensive Class	No. of Patients Receiving	Percentage (%)
ACE Inhibitors (ACEIs)	27	29.35
Angiotensin Receptor Blockers (ARBs)	38	41.30
Calcium Channel Blockers (CCBs)	32	34.78
Beta-Blockers	24	26.09
Diuretics	20	21.74
Alpha-Blockers	8	8.70
Others (e.g., central acting, vasodilators)	6	6.52

Mean number of antihypertensive drugs per patient: 2.14 ± 0.93

Table 3: Distribution of Drug–Drug Interactions by Severity and Mechanism

Type of Interaction	Frequency (n)	Percentage (%)
Severity		
Major	22	23.91
Moderate	48	52.17
Minor	22	23.91
Mechanism		
Pharmacodynamic	57	61.96
Pharmacokinetic	35	38.04

Total potential DDIs identified: 92 (mean 1.00 ± 0.42 per patient)

Table 4: Association Between Number of Drugs Prescribed and Occurrence of DDIs

No. of Drugs per Prescription	Patients (n)	DDIs Present (n, %)	p-value
≤3 drugs	38	12 (31.58%)	
4–6 drugs	37	27 (72.97%)	
≥7 drugs	17	15 (88.24%)	**0.001***

Table 5: Association Between Comorbidities and Occurrence of Drug–Drug Interactions (n = 92)

Comorbidity	Total Patients (n)	Patients with DDIs (n)	Percentage with DDIs (%)	p-value
Diabetes Mellitus	31	25	80.65	
Ischemic Heart Disease	18	14	77.78	
Chronic Kidney Disease	11	10	90.91	
Without Comorbidity	32	14	43.75	**0.004***

Discussion

In this study, the cohort showed a modest male predominance (57.61%) and a mean age of 56.43 ± 11.28 years, with most participants in the 41–60 (47.83%) and >60 (36.96%) age groups. This demographic profile mirrors hospital data in hypertensive patients where clinically significant DDIs were more frequent in men (62.5%) and were concentrated in the 50–60-year band (37.49%), as reported by Sivva et al. (2015). [8]

Our prescribing pattern was ARB-forward (41.30%), followed by CCBs (34.78%) and ACEIs (29.35%), with combination therapy reflected by a mean of 2.14 ± 0.93 antihypertensive agents per patient. This aligns closely with a western India prescription audit in which Narkar et al. (2021) observed ARBs as the most commonly used class (41.5%) and documented substantial multidrug use (56%)—particularly triple therapy with ARB+CCB+diuretic (35.7%)—supporting the generalizability of our ARB-leading pattern. [9]

At the same time, variation across centers persists: while our practice leaned toward ARBs, another OPD audit found overall utilization dominated by CCBs (58.11%) with widespread combination therapy (~69.76%). These data from Sinha et al. (2024) still corroborate our core observation that multidrug regimens are common and guideline-concordant, even if the leading class differs locally. [10]

Regarding interaction burden, we identified 92 potential DDIs (1.00 ± 0.42 per patient). This density is very similar to Subramanian et al. (2018), who recorded 123 DDIs across 125 hypertensive patients (~0.98/patient) with 48% of patients experiencing at least one potential interaction—differences likely reflect case-mix (our mixed OPD/IPD) and the range of concomitant therapies. [11]

By severity, moderate interactions predominated in this study (52.17%), with major and minor each at 23.91%. A larger internal-medicine cohort from Sudan showed an even higher moderate share (70.1%) among potential DDIs, as reported by Hamadouk et al. (2023), emphasizing that hospital case severity and longer medication lists can shift distributions toward moderate-risk combinations that still require active monitoring. [12]

Polypharmacy strongly predicted DDIs in this study (31.58% with ≤3 drugs vs 72.97% with 4–6 vs 88.24% with ≥7; p = 0.001). A prospective cardiology-ward study by Akbar et al. (2021) likewise quantified a steep risk gradient, with patients taking >12 drugs having OR 4.187 (p = 0.009) for serious (Class D/X) interactions, reinforcing the dose-response relationship between drug count and interaction risk. [13]

Mechanistically, pharmacodynamic interactions were more frequent in this study (61.96%) than pharmacokinetic (38.04%). D'Souza et al. (2017) reported a similar pattern in hypertensive outpatients—55.47% pharmacodynamic vs 40.87% pharmacokinetic across 411 PDDIs—supporting the notion that additive or antagonistic hemodynamic/electrolyte effects underpin most interaction flags in antihypertensive polytherapy. [14]

Comorbidity magnified risk in this study: CKD patients had DDIs in 90.91%, compared with 80.65% in diabetes and 77.78% in IHD; patients without comorbidity had 43.75% interactions (p = 0.004). A nephrology cohort from Spain by Santos-Díaz et al. (2020) found 91% of CKD patients carried at least one potential DDI and 77.3% of interactions were moderate (Type C), closely matching our CKD signal and underscoring the high-alert status of renal disease for interaction surveillance. [15]

Conclusion

In this study, a significant proportion of patients receiving antihypertensive therapy were found to have potential drug–drug interactions, emphasizing the clinical importance of regular medication review. The majority of interactions were moderate in severity and predominantly pharmacodynamic in nature, reflecting additive effects among commonly co-prescribed agents. Polypharmacy and the presence of comorbidities such as diabetes and chronic kidney disease were major predictors of interaction risk. These findings underscore the need for vigilant prescription monitoring, pharmacist involvement, and the use of interaction-checking tools to enhance the safety and effectiveness of antihypertensive therapy in tertiary care settings.

References

1. World Health Organization. Hypertension – Fact sheet. 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/hypertensionWorld Health Organization
2. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence, detection, treatment, and control from 1990 to 2019. Lancet. 2021;398(10304):957–80. Available from: https://www.thelancet.com/article/S0140-6736(21)01330-1/fulltextThe Lancet
3. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA Guideline for High Blood Pressure in Adults. JAMA Cardiol. 2018;3(4):351–8. Available from: https://jamanetwork.com/journals/jamacardiology/fullarticle/2672947JAMA Network

4. World Health Organization. Guideline for the pharmacological treatment of hypertension in adults. 2021. Available from: https://www.who.int/publications/i/item/9789240033986World Health Organization
5. Fravel M, Ernst ME. Drug interactions with antihypertensives. Curr Hypertens Rep. 2021;23:62. Available from: https://link.springer.com/article/10.1007/s11906-021-01131-ySpringerLink
6. U.S. Food and Drug Administration. FDA Drug Safety Communication: Dose limitations for Zocor (simvastatin) to reduce muscle injury risk. 2011 (updated). Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-new-restrictions-contraindications-and-dose-limitations-zocorU.S. Food and Drug Administration
7. Kunitsu Y, Hira D, Morikochi A, et al. Time until onset of acute kidney injury by combination therapy with "triple whammy" drugs. PLoS One. 2022;17(2):e0263682. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0263682PLOS
8. Sivva D, Mateti UV, Neerati VM, Thiruthopu NS, Martha S. Assessment of drug–drug interactions in hypertensive patients at a superspeciality hospital. Avicenna J Med. 2015;5(2):29–35.
9. Narkar N, et al. Pattern of Antihypertensive Drugs Prescribed in a Tertiary Care Hospital in Western India. Biomed Pharmacol J. 2021;14(2).
10. Sinha DP, Kumar A, Sinha KK. Study of prescription pattern of antihypertensive drugs in a tertiary care hospital. Int J Acad Med Pharm. 2024;6(4):1079–1082.
11. Subramanian A, Adhimoolam M, Kannan S. Study of drug–drug interactions among hypertensive patients in a tertiary care teaching hospital. Perspect Clin Res. 2018;9(1):9–14.
12. Hamadouk RA, Mustafa AT, Shuaib N, Abdelrahman AA. The prevalence and severity of potential drug–drug interactions in internal medicine patients: a cross-sectional study. Drug Healthc Patient Saf. 2023;15:—.
13. Akbar Z, Rehman S, Khan A, et al. Potential drug–drug interactions in patients with cardiovascular diseases: findings from a prospective observational study. J Pharm Policy Pract.2021;14:63.
14. D'Souza VR, Udaykumar P. Potential drug interactions in hypertensive outpatients – A cross-sectional study. IOSR-JPBS. 2017;12(5):83–86.
15. Santos-Díaz G, Pérez-Pico AM, Suárez-Santisteban MÁ, et al. Prevalence of Potential Drug–Drug Interaction Risk among Chronic Kidney Disease Patients in a Spanish Hospital. Pharmaceutics. 2020;12(8):713.