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Original Research Article

Evaluation of Adverse Drug Reactions among Patients Receiving Antihypertensive Therapy in a Tertiary Care Hospital: A Prospective Observational Study

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Abstract

Background: Hypertension requires sustained pharmacotherapy, and adverse drug reactions (ADRs) can reduce tolerability, adherence, and continuity of treatment. Systematic ADR monitoring is therefore important in routine antihypertensive care.

Objectives: To determine the incidence and pattern of ADRs among patients receiving antihypertensive therapy and to assess their severity, causality, and association with selected patient and treatment characteristics.

Methods: This prospective observational study included 100 adults receiving antihypertensive therapy at Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh, India, from July 2025 to April 2026. Demographic characteristics, comorbidities, antihypertensive regimens, and suspected ADRs were prospectively documented. Causality was assessed using the Naranjo algorithm and severity using the modified Hartwig and Siegel scale. Categorical variables were compared using chi-square tests, with $p<0.05$ considered statistically significant.

Results: The mean age was 56.8 ± 11.9 years; 54% were male. Monotherapy was used in 58%, dual therapy in 34%, and triple therapy in 8%. Calcium channel blockers were the most frequently prescribed class. Twenty-eight patients developed at least one ADR, yielding an incidence proportion of 28.0%, and 34 ADR events were recorded. Peripheral/ankle edema was most frequent, followed by dizziness and dry cough. Most ADRs were mild (61.8%) or moderate (35.3%); 70.6% were categorized as probable. ADR occurrence was significantly higher among patients aged ≥60 years and increased with the number of antihypertensive drugs, whereas sex was not significantly associated.

Conclusion: ADRs were common but predominantly mild to moderate. Older age and multidrug antihypertensive therapy were associated with greater ADR occurrence, supporting active pharmacovigilance and individualized treatment review.

Keywords: Adverse Drug Reaction; Antihypertensive Therapy; Pharmacovigilance; Hypertension; Causality Assessment; Drug Safety.

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Introduction

Hypertension is a major modifiable determinant of cardiovascular, cerebrovascular, and renal disease and remains a substantial public-health challenge in India. Population-based evidence has demonstrated a high burden of hypertension with important gaps in awareness and control, while international guidelines emphasize sustained blood-pressure reduction to prevent target-organ damage and cardiovascular events [1-3]. Because hypertension is usually asymptomatic and treatment is continued for years, the safety and tolerability of pharmacotherapy are central to long-term treatment success. Calcium channel blockers (CCBs), angiotensin receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, thiazide or thiazide-like diuretics, and beta-blockers are frequently used either alone or in combination according to the patient's age, comorbidities, blood-pressure level, and clinical indications [2,3]. Adverse drug reactions (ADRs) are an important limitation of antihypertensive therapy. Reactions such as pedal edema, dizziness, postural hypotension, headache, electrolyte disturbances, fatigue, bradycardia, and ACE-inhibitor-associated cough can interfere with daily

functioning and discourage continued medication use. Indian pharmacovigilance studies have shown that ADRs occur across the major antihypertensive classes and that combination therapy can be associated with a greater burden of reactions than monotherapy [4,5]. In addition, clinical observations from other settings suggest that older patients and individuals exposed to multiple drugs are particularly vulnerable because of altered pharmacokinetics, pharmacodynamic sensitivity, multimorbidity, and the potential for drug-drug interactions [6,7,12].

The adverse-effect profile also differs by drug class. Dihydropyridine CCBs can produce peripheral edema through preferential arteriolar dilatation and increased intracapillary hydrostatic pressure; meta-analytic evidence confirms a higher occurrence of edema with CCB therapy, particularly with higher doses and longer exposure [8,9]. Dry cough is a characteristic adverse effect of ACE inhibitors, and recent comparative evidence demonstrates a substantially higher risk of cough with ACE inhibitors than with ARBs or CCBs [10]. Recognition of these predictable patterns helps clinicians distinguish drug-related symptoms from manifestations of comorbidity and allows timely dose modification, substitution, or supportive management.

Despite widespread antihypertensive use, real-world ADR patterns vary with prescribing practices, patient characteristics, and local monitoring systems. Prospective observation within a tertiary-care setting can identify clinically relevant reactions that are not always captured by spontaneous reporting alone and can support safer prescribing. Therefore, the present study was undertaken to prospectively evaluate ADRs among patients receiving antihypertensive therapy at ASRAM Medical College, Elluru, Andhra Pradesh. The objectives were to determine the incidence and clinical pattern of ADRs, characterize the antihypertensive regimens associated with these events, assess ADR causality and severity using standardized tools, and examine associations between ADR occurrence and age, sex, and the number of antihypertensive drugs prescribed.

Materials and Methods

Study Design and Setting: A prospective observational study was conducted at Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh, India, from July 2025 to April 2026. The study was undertaken in patients receiving care through the tertiary-care clinical services where hypertension and associated medical comorbidities are routinely evaluated and treated. The study was observational; treatment selection, dose changes, investigations, and clinical management remained entirely under the discretion of the treating physician.

Study Population and Eligibility: Adult patients aged 18 years or older with a diagnosis of hypertension and receiving at least one antihypertensive medicine were eligible. Patients were included irrespective of the presence of common comorbidities such as diabetes mellitus, dyslipidemia, ischemic heart disease, or chronic kidney disease. Patients who were unwilling to participate, had insufficient treatment information, or could not provide reliable information regarding suspected reactions were excluded. Consecutive eligible patients were approached until the required sample was obtained.

Sample Size: A previous Indian pharmacovigilance study reported 34 ADRs among 250 patients receiving antihypertensive medicines, corresponding to an observed proportion of approximately 13.6% [4]. Using the single-proportion formula $n=Z^2p(1-p)/d^2$, a 95% confidence level, an expected proportion of 13.6%, and absolute precision of 7.5%, the minimum estimated sample was approximately 81. Allowing for incomplete follow-up or unusable records and rounding upward for adequate representation, the final planned sample was 100 patients.

Data Collection and ADR Assessment: After enrolment, demographic data, duration of hypertension, comorbidities, and current antihypertensive medicines were recorded in a structured case-record form. Therapy was categorized as monotherapy, two-drug therapy, or three-drug therapy. Patients were prospectively assessed during routine clinical follow-up for new symptoms, clinically detected reactions, relevant laboratory abnormalities, and treatment changes suggestive of an ADR. Each suspected ADR was documented with the implicated drug class, clinical manifestation, temporal relationship, management, and outcome. When a patient experienced more than one distinct reaction, each event was counted separately. The Naranjo adverse drug reaction probability scale was used for causality assessment [13], and severity was graded according to the modified Hartwig and Siegel approach [14].

Ethical Considerations: Necessary Permissions were obtained before starting the study. Written informed consent was obtained from participants before enrolment. Confidentiality was maintained by using coded study records.

Statistical Analysis: Data were summarized using mean and standard deviation for continuous variables and frequency with percentage for categorical variables. The occurrence of ADRs was compared across age group, sex, and number of antihypertensive drugs. Continuity-corrected chi-square testing was used for 2×2 comparisons, and

Pearson's chi-square test was used for larger contingency tables. A two-sided p value <0.05 was considered statistically significant.

Results

Participant Characteristics: A total of 100 patients receiving antihypertensive therapy were prospectively evaluated during the study period. The mean age of the study population was 56.8 ± 11.9 years, with ages ranging from 31 to 82 years. Patients aged ≥60 years constituted 42% of the cohort.

There were 54 (54.0%) males and 46 (46.0%) females. The mean duration of hypertension was 7.4 ± 5.1 years. Diabetes mellitus was the most frequent associated comorbidity, observed in 38 (38.0%) patients, followed by dyslipidemia in 24 (24.0%), ischemic heart disease in 12 (12.0%), and chronic kidney disease in 8 (8.0%) patients (Table 1).

Table 1: Baseline characteristics of the study population (n=100)

Characteristic	n (%) / Mean ± SD
Age, years	56.8 ± 11.9
Age <60 years	58 (58.0)
Age ≥60 years	42 (42.0)
Male	54 (54.0)
Female	46 (46.0)
Duration of hypertension, years	7.4 ± 5.1
Diabetes mellitus	38 (38.0)
Dyslipidemia	24 (24.0)
Ischemic heart disease	12 (12.0)
Chronic kidney disease	8 (8.0)

Pattern of antihypertensive therapy: Monotherapy was prescribed to 58 (58.0%) patients, while 34 (34.0%) patients received two antihypertensive drugs and 8 (8.0%) received three-drug therapy. Calcium channel blockers were the most frequently prescribed drug class, being used in 52 (52.0%) patients, followed by angiotensin receptor blockers in 41 (41.0%), beta-blockers in 22 (22.0%), thiazide/thiazide-like diuretics in 18 (18.0%), and ACE inhibitors in 15 (15.0%) patients. Individual patients receiving combination therapy contributed to more than one drug-class category (Table 2).

Table 2: Pattern of antihypertensive therapy

Treatment characteristic	n (%)
Number of antihypertensive drugs	
Monotherapy	58 (58.0)
Two-drug therapy	34 (34.0)
Three-drug therapy	8 (8.0)
Antihypertensive drug class*	
Calcium channel blockers	52 (52.0)
Angiotensin receptor blockers	41 (41.0)
Beta-blockers	22 (22.0)
Thiazide/thiazide-like diuretics	18 (18.0)
ACE inhibitors	15 (15.0)

*Drug-class percentages are not mutually exclusive because patients receiving combination therapy were counted under each prescribed class. ACE: angiotensin-converting enzyme.

Incidence and pattern of adverse drug reactions: During prospective follow-up, 28 of the 100 patients developed at least one adverse drug reaction (ADR), giving an overall incidence proportion of 28.0%.

A total of 34 individual ADR events were documented because six patients experienced more than one reaction.

Peripheral or ankle edema was the most commonly observed ADR, accounting for 9 (26.5%) of the 34 reactions. This was followed by dizziness in 6 (17.6%), dry cough in 5 (14.7%), fatigue or bradycardia in 4 (11.8%), headache in 3 (8.8%), electrolyte abnormalities in 3 (8.8%), postural hypotension in 2 (5.9%), and other reactions in 2 (5.9%) cases (Table 3).

Calcium channel blockers accounted for the largest proportion of ADRs, predominantly peripheral edema and headache. ACE inhibitors were principally associated with dry cough, whereas beta-blockers were associated with fatigue and bradycardia. Dizziness and postural hypotension were observed across several antihypertensive drug classes.

Severity and causality assessment: According to severity assessment, 21 (61.8%) ADRs were mild, 12 (35.3%) were moderate, and 1 (2.9%) was classified as severe. No ADR-related mortality

occurred. The severe reaction required temporary withdrawal of the suspected drug and additional clinical monitoring. On causality assessment, 24 (70.6%) reactions were categorized as probable and 10 (29.4%) as possible. None fulfilled the criteria for a definite causal relationship because intentional rechallenge was not performed. Most reactions improved after dose modification, withdrawal of the suspected medication, or substitution with another antihypertensive agent (Table 4).

Table 3: Distribution of adverse drug reactions (n=34 ADR events)

Adverse drug reaction	n (%)
Peripheral/ankle edema	9 (26.5)
Dizziness	6 (17.6)
Dry cough	5 (14.7)
Fatigue/bradycardia	4 (11.8)
Headache	3 (8.8)
Electrolyte abnormality	3 (8.8)
Postural hypotension	2 (5.9)
Other reactions	2 (5.9)
Total	34 (100.0)

Table 4: Severity and causality assessment of ADRs

Assessment	n (%)
Severity	
Mild	21 (61.8)
Moderate	12 (35.3)
Severe	1 (2.9)
Causality	
Probable	24 (70.6)
Possible	10 (29.4)

Factors associated with adverse drug reactions: ADRs occurred in 18 of 42 patients aged ≥60 years (42.9%), compared with 10 of 58 patients aged <60 years (17.2%). This difference was statistically significant (continuity-corrected χ^2=6.71, p=0.010). The occurrence of ADRs also increased with the number of antihypertensive drugs prescribed. ADRs were documented in 10 of 58 patients receiving monotherapy (17.2%), 13 of 34 receiving dual therapy (38.2%), and 5 of 8 receiving triple therapy (62.5%). The association between increasing antihypertensive treatment intensity and ADR occurrence was statistically significant (χ^2=9.82, p=0.007). ADRs were observed in 16 of 46 female patients (34.8%) and 12 of 54 male patients (22.2%); however, the difference according to sex was not statistically significant (continuity-corrected χ^2=1.37, p=0.242) (Table 5).

Table 5: Factors associated with occurrence of ADRs

Variable	ADR present n (%)	ADR absent n (%)	χ^2	p-value
Age <60 years (n=58)	10 (17.2)	48 (82.8)	6.71	0.010
Age ≥60 years (n=42)	18 (42.9)	24 (57.1)		
Male (n=54)	12 (22.2)	42 (77.8)	1.37	0.242
Female (n=46)	16 (34.8)	30 (65.2)		
Monotherapy (n=58)	10 (17.2)	48 (82.8)	9.82	0.007
Two-drug therapy (n=34)	13 (38.2)	21 (61.8)		
Three-drug therapy (n=8)	5 (62.5)	3 (37.5)		

For age and sex, continuity-corrected chi-square tests were used. Pearson chi-square was used for the three-level treatment comparison. Statistical significance was set at p<0.05.

Overall, approximately one in four patients receiving antihypertensive therapy experienced an ADR during the study period. Most reactions were mild to moderate and clinically manageable. Peripheral edema, dizziness, and dry cough constituted the predominant ADR pattern. Older age and treatment with multiple antihypertensive drugs were significantly associated with a higher occurrence of ADRs.

Discussion

The present prospective observational study identified ADRs in 28% of patients receiving antihypertensive therapy, with 34 individual reactions recorded among 100 participants. Most reactions were mild or moderate, and peripheral edema, dizziness, and dry cough were the dominant clinical patterns. These findings reinforce the practical importance of active ADR surveillance in hypertension, where treatment is prolonged and

adverse effects can influence adherence even when the reactions are not severe. Earlier Indian studies have also documented clinically meaningful ADR burdens with antihypertensive medicines, although reported frequencies have varied with study design, duration, case ascertainment, and prescribing patterns [4,5]. Prospective cardiovascular-drug surveillance likewise demonstrates that systematic monitoring detects a substantial spectrum of drug-related harm in routine care [12].

CCBs were the most frequently prescribed drug class in this cohort and peripheral or ankle edema was the leading ADR. This pattern is pharmacologically plausible and consistent with previous evidence. Makani et al. demonstrated a significantly greater incidence of peripheral edema with CCBs than with placebo or other controls, with risk increasing at higher doses and with longer treatment exposure [8]. A later meta-analysis of amlodipine trials also confirmed peripheral edema as a characteristic treatment-related adverse effect [9]. Real-world Indian data similarly show that pedal edema remains an important tolerability concern during CCB therapy [11]. These observations support routine inquiry for lower-limb swelling, particularly when dose escalation is contemplated.

Dry cough accounted for 14.7% of the recorded ADR events and was primarily linked to ACE-inhibitor exposure. This finding is concordant with established class effects. A systematic review and network meta-analysis found that ACE inhibitors were associated with substantially more cough than placebo, ARBs, or CCBs [10]. Recognition of this association is clinically relevant because persistent cough can lead to unnecessary respiratory evaluation or poor adherence when the medication relationship is not considered.

Older age showed a significant association with ADR occurrence; 42.9% of patients aged 60 years or older experienced an ADR compared with 17.2% of younger patients. Rende et al. similarly reported greater vulnerability among elderly patients receiving antihypertensive therapy [6]. Age-related changes in renal function, drug distribution, autonomic responses, and homeostatic reserve can increase susceptibility to dizziness, hypotension, electrolyte disturbance, and other dose-related effects. Although females had numerically more ADRs than males in the present study, the difference was not statistically significant. Previous antihypertensive pharmacovigilance reports have described higher frequencies in women [4-7], indicating that sex-related patterns can differ between cohorts.

A clear treatment-intensity gradient was observed: ADRs occurred in 17.2% of patients on monotherapy, 38.2% on dual therapy, and 62.5% on triple therapy. Similar associations between combination treatment or broader polypharmacy and ADR occurrence have been reported previously [4-7]. Multiple antihypertensive agents can produce additive pharmacodynamic effects and increase the opportunity for intolerance. Nevertheless, combination therapy remains essential for many patients to achieve blood-pressure targets [2,3]. The clinical implication is not to avoid indicated multidrug therapy, but to strengthen medication review, dose titration, patient counselling, and active surveillance, particularly in older adults and patients receiving several agents.

Limitations

This study was conducted at a single tertiary-care institution with a relatively small sample, which limits external generalizability. Follow-up occurred within routine clinical care, so the duration and intensity of observation were not identical for every participant. ADR identification partly depended on patient reporting and clinical recognition, creating a risk of under-detection of mild symptoms. Drug-specific dose-response relationships and multivariable adjustment for comorbidities were not assessed.

Conclusion

Adverse drug reactions were observed in 28% of patients receiving antihypertensive therapy, and most reactions were mild to moderate in severity. Peripheral edema, dizziness, and dry cough were the predominant events, reflecting recognizable adverse-effect profiles of commonly used antihypertensive classes. Older patients and those receiving multiple antihypertensive medicines experienced significantly more ADRs, whereas sex was not significantly associated with ADR occurrence. These findings emphasize the value of structured pharmacovigilance during long-term hypertension treatment. Regular review of symptoms, blood pressure, laboratory parameters, and treatment complexity can support early identification of reactions and timely therapeutic modification. Individualized prescribing and patient counselling should remain integral components of safe antihypertensive care in routine practice.

References

1. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J Hypertens. 2014;32(6):1170-1177. doi:10.1097/HJH.0000000000000146.
2. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. J Hypertens.

2020;38(6):982-1004. doi:10.1097/HJH.0000000000002453.
3. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021-3104. doi:10.1093/eurheartj/ehy339.
4. Hussain A, Aqil M, Alam MS, Khan MR, Kapur P, Pillai KK. A pharmacovigilance study of antihypertensive medicines at a South Delhi hospital. Indian J Pharm Sci. 2009;71(3):338-341. doi:10.4103/0250-474X.56018.
5. Khurshid F, Aqil M, Alam MS, Kapur P, Pillai KK. Monitoring of adverse drug reactions associated with antihypertensive medicines at a university teaching hospital in New Delhi. Daru. 2012;20(1):34. doi:10.1186/2008-2231-20-34.
6. Rende P, Paletta L, Gallelli G, Raffaele G, Natale V, Brissa N, et al. Retrospective evaluation of adverse drug reactions induced by antihypertensive treatment. J Pharmacol Pharmacother. 2013;4(Suppl 1):S47-S50. doi:10.4103/0976-500X.120954.
7. Olowofela AO, Isah AO. A profile of adverse effects of antihypertensive medicines in a tertiary care clinic in Nigeria. Ann Afr Med. 2017;16(3):114-119. doi:10.4103/aam.aam_6_17.
8. Makani H, Bangalore S, Romero J, Htyte N, Berrios RS, Makwana H, et al. Peripheral edema associated with calcium channel blockers: incidence and withdrawal rate-a meta-analysis of randomized trials. J Hypertens. 2011;29(7):1270-1280. doi:10.1097/HJH.0b013e3283472643.
9. Vukadinovic D, Scholz SS, Messerli FH, Weber MA, Williams B, Bohm M, et al. Peripheral edema and headache associated with amlodipine treatment: a meta-analysis of randomized, placebo-controlled trials. J Hypertens. 2019;37(10):2093-2103. doi:10.1097/HJH.0000000000002145.
10. Hu Y, Liang L, Liu S, Kung JY, Banh HL. Angiotensin-converting enzyme inhibitor induced cough compared with placebo, and other antihypertensives: a systematic review and network meta-analysis. J Clin Hypertens (Greenwich). 2023;25(8):661-688. doi:10.1111/jch.14695.
11. Dalal J, Sawhney JP, Jayagopal PB, Hazra PK, Khan MY, Gaurav K, et al. A retrospective, observational, EMR-based real-world evidence study to assess the incidence of pedal edema in essential hypertensive patients on amlodipine or cilnidipine. Int J Hypertens. 2022;2022:6868143. doi:10.1155/2022/6868143.
12. Mohebbi N, Shalviri G, Salarifar M, Salamzadeh J, Gholami K. Adverse drug reactions induced by cardiovascular drugs in cardiovascular care unit patients. Pharmacoepidemiol Drug Saf. 2010;19(9):889-894. doi:10.1002/pds.1916.
13. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-245. doi:10.1038/clpt.1981.154.
14. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-2232.