

DRUG-DRUG INTERACTIONS IN OUTPATIENT HYPERTENSION PRESCRIPTIONS AT PRIMARY HEALTHCARE CENTERS IN A VIETNAMESE PROVINCE: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Hypertension is one of the most prevalent chronic diseases worldwide and in Vietnam, representing a major public health burden due to its association with cardiovascular morbidity and mortality. Patients with hypertension frequently receive multiple medications because of combination therapy and the presence of coexisting comorbidities. Polypharmacy may increase the risk of clinically significant drug-drug interactions (DDIs), which can affect treatment safety, reduce therapeutic effectiveness, and increase healthcare costs. Therefore, identifying and monitoring potential DDIs in hypertensive patients is essential, particularly in primary healthcare settings where long-term treatment is commonly provided. **Objective:** This study aimed to evaluate prescribing patterns and the prevalence of potential drug-drug interactions in outpatient hypertension management at primary healthcare facilities in Chau Thanh district, Dong Thap province, Vietnam, in 2025. **Materials and methods:** A cross-sectional descriptive study was conducted using 600 outpatient prescriptions systematically sampled from 12 commune health stations. Potential DDIs were identified using two electronic databases, DRUGS.COM and MICROMEDEX. Only interactions with concordant classification and moderate or higher severity in both databases were included in the analysis. **Results:** Antihypertensive monotherapy was the most commonly prescribed regimen, accounting for 93% of prescriptions. Calcium channel blockers (CCB) were the most frequently used drug class (61.5%), with amlodipine being the most commonly prescribed (56.3%), followed by angiotensin receptor blockers (ARB) (24.3%), angiotensin-converting enzyme inhibitors (ACEi) (13.8%), and beta-blockers (BB) (0.5%). Moderate interactions were the most common severity level identified in both databases. Clinically relevant DDIs consistently identified across both databases were observed in 31.7% of prescriptions. The most frequent interacting drug pair was enalapril combined with metformin (41%). **Conclusion:** Potential drug-drug interactions are common in outpatient hypertension treatment. Continuous and individualized monitoring of DDIs is essential to optimize medication safety and therapeutic effectiveness at the primary care level.

Keywords: Drug-drug interaction, hypertension, outpatient prescription, primary healthcare centers.

I. INTRODUCTION

Hypertension is a common chronic disease with an increasing prevalence and is a leading cause of cardiovascular complications and mortality today [1]. In Vietnam, hypertension accounts for a high proportion in the community and most patients are managed and monitored for long-term treatment at primary healthcare facilities [2].

Treatment often requires combination therapy and is commonly associated with comorbidities, thereby increasing the risk of drug-drug interactions affecting treatment effectiveness and safety. Most studies on drug-drug interactions in hypertension treatment have been conducted at provincial or central levels, while at commune health stations such as those in Chau Thanh District, Dong Thap Province, where many outpatients are managed, there has been no study evaluating this situation. Based on the above reality, the study “Drug-drug interactions in outpatient hypertension prescriptions at primary healthcare centers in a Vietnamese province: a cross-sectional study” was conducted to contribute practical evidence for safe and rational drug use at the primary healthcare level.

II. MATERIALS AND METHODS

2.1. Participants

- **Study subject:** Prescriptions of outpatients diagnosed with primary hypertension at 12 Commune Health Stations in Chau Thanh District, Dong Thap Province between January 1 and March 1, 2025.

- **Inclusion criteria:** Prescriptions of patients aged 18 years or older, with a confirmed diagnosis of primary hypertension (I10), having outpatient prescriptions with complete information on active ingredients, dosage, and duration of use.

- **Exclusion criteria:** Prescriptions of pregnant women, breastfeeding women, and prescriptions containing drugs with herbal ingredients.

2.2. Research methods

- **Study design:** A cross-sectional descriptive study was conducted

- **Sample size:** Applying the formula based on a single proportion:

$$n = \frac{Z_{\left(1-\frac{\alpha}{2}\right)}^2 \cdot p \cdot (1-p)}{d^2}$$

Where: n = study sample size; $Z_{\left(1-\frac{\alpha}{2}\right)} = 1.96$ (95% confidence level); d = 0.05; p = 0.631

(According to the study of Vuong Thai Qui in 2022, the rate of drug interactions in treatment hypertension is 63.1% [3]).

Therefore, the minimum sample size for the study was 358 samples. In practice, we collected 600 samples from a total of 12 commune health stations.

- **Data Collection Procedures:**

Prescription information is collected including: patient characteristics, comorbidities, number and treatment regimens of drugs, name of active ingredients, drug groups, strength, and duration of use.

Drug interactions were identified using Decision No. 5948 of the Vietnamese Ministry of Health, DRUGS.COM, and MICROMEDEX. Clinically significant interactions were defined as those concurrently reported in both databases (Drugs.com and Micromedex) with a severity level of moderate or major.

- **Statistical Analysis:** Data were analyzed using IBM SPSS Statistics 27.0.

- **Study ethics:** The study was approved by the Biomedical Research Ethics Committee (IRB No. 25.104.SV, 2025).

III. RESULTS

3.1. Characteristics of the study subjects

Table 1. Characteristics of patients in the study sample

Characteristics		Frequency (N)	Percentage (%)
Age	Highest age	99	
	Lowest age	31	
	Mean age	65.12	
Age group	18 - 59 years	176	29.3
	≥ 60 years	424	70.7
Gender	Male	275	45.8
	Female	325	54.2

Females accounted for 54.2% and the ≥ 60 years age group accounted for 70.7%, showing that most subjects in the study sample were female and patients aged 60 years or older.

3.2. Situation of antihypertensive drug use

Table 2. Characteristics of antihypertensive drug use

Pharmacological group	Active ingredient	Frequency (N)	Percentage (%)
Angiotensin-converting enzyme inhibitors (ACEi)	Captopril	21	3.3
	Enalapril	75	11.8
	Lisinopril	2	0.2
	Perindopril	13	2
Calcium channel blockers (CCB)	Amlodipin	359	56.3
	Nifedipin	10	1.6
Angiotensin receptor blockers (ARB)	Irbesartan	4	0.6
	Losartan	151	23.7
Beta-blockers (BB)	Bisoprolol	3	0.5
Total		638	100

The Table shows that calcium channel blockers accounted for the highest proportion, with amlodipine being the most frequently prescribed active ingredient at 56.3%. Angiotensin receptor blockers ranked second, mainly losartan at 23.7%, whereas beta-blockers were used at the lowest proportion.

Table 3. The percentage of hypertension treatment regimens

	Pharmacological group	Frequency (N)	Percentage (%)
Monotherapy	ACEi group	69	11.5
	CCB group	354	59
	ARB group	136	22.7
	BB group	1	0.2
Two-drug combinations	CCB + CCB	5	0.8
	ACEi + CCB	15	2.5
	ACEi + ARB	3	0.4
	CCB + ARB	15	2.5
	ARB + BB	1	0.2
Three-drug combination	ACEi + ARB + BB	1	0.2
Total		600	100

The table shows that monotherapy was the predominant antihypertensive regimen. Among monotherapy regimens, CCBs were used most frequently at 59.0%, whereas BBs accounted for the lowest proportion at 0.2%. Two-drug combinations predominated, with ACEi + CCB and CCB + ARB being the most common combinations, each accounting for 2.5%.

3.3. Drug-drug interactions in patient prescriptions

Table 4. Rate and level of drug interactions according to each database

According to		DRUGS.COM		MICROMEDEX	
		Frequency (N)	Percentage (%)	Frequency (N)	Percentage (%)
No interaction		400	66.7	410	68.3
Interaction	With antihypertensive drugs	177	29.5	163	27.2
	Without antihypertensive drugs	23	3.8	27	4.5
Total		600	100	600	100
Interaction level					
Minor	With antihypertensive drugs	36	13.6	0	0
	Without antihypertensive drugs	6	2.3	3	1.4
Moderate	With antihypertensive drugs	168	63.4	143	66.8
	Without antihypertensive drugs	50	18.9	21	9.8
Major	With antihypertensive drugs	4	1.5	34	15.9
	Without antihypertensive drugs	1	0.3	13	6.1
Total		265	100	214	100

According to DRUGS.COM, the rate of no interaction was 66.7%; interaction was 33.3%, mainly in the group with antihypertensive drugs (29.5%). Interactions were concentrated at the moderate level and occurred more frequently in the group with antihypertensive drugs. According to MICROMEDEX, the rate of no interaction was 68.3%; interaction was 31.7%, of which the group with antihypertensive drugs accounted for 27.2%. Interactions were mainly at the moderate level and occurred more frequently in the group with antihypertensive drugs.

Table 5. Rate and level of drug interactions according to the consensus of both databases

According to the consensus criteria of the two databases			
		Frequency (N)	Percentage (%)
Clinically significant interactions	With antihypertensive drugs	85	23.6
	Without antihypertensive drugs	29	8.1
Non-clinically significant interactions	With antihypertensive drugs	215	59.7
	Without antihypertensive drugs	31	8.6
Total		360	100

According to the consensus of both databases, interactions were occurred more frequently in the group with antihypertensive drugs including both clinically significant interactions and non-clinically significant interactions.

Table 6. Common interaction pairs containing antihypertensive drugs

Drug-drug interaction pair	Frequency (N)	Percentage (%)
Amlodipin + Methylprednisolon	10	12.0
Enalapril + Metformin	34	41.0

Drug-drug interaction pair	Frequency (N)	Percentage (%)
Losartan + Meloxicam	13	15.7

Table 6 shows that the pair enalapril + metformin accounted for the highest proportion (41.0%).

IV. DISCUSSION

4.1. Characteristics of the study population

The study results show that a prominent characteristic of the study sample was that it was mainly concentrated in older adults and slightly skewed toward females. According to WHO and the Ministry of Health, the prevalence of hypertension increases markedly with age due to the aging process leading to reduced vascular elasticity, increased arterial stiffness, and consequently elevated systolic blood pressure [1,2]. Therefore, the high proportion of participants aged ≥ 60 years in the study sample is consistent with the pathophysiological basis and the real situation in Vietnam. Regarding sex, the proportion of females in the study was higher than that of males (54.2% vs. 45.8%), although the difference was not large. This indicates that the gender distribution in the study sample was relatively balanced. The slightly higher proportion of females may be related to the age characteristics of the sample, as most patients were in the ≥ 60 years age group.

4.2. Situation of antihypertensive drug use

The results showed that the CCB group accounted for the highest proportion, with amlodipin being the most frequently prescribed active ingredient (56.3%). This is consistent with the study by Le Truong Giang at Can Tho City General Hospital (2021-2022), which reported CCB use at 85.3%, mainly amlodipin [4], and with the study by Nguyen Duy Khanh at Vinh Long Provincial Medical Center, where CCBs accounted for 60.5% [5]. This suggests a relatively consistent CCB prescribing pattern across primary healthcare facilities in the Mekong Delta. The findings align with recommendations from the Vietnam National Heart Association and the Ministry of Health, which consider CCBs first-line therapy for hypertension; amlodipin is favored for its long duration, stable effect, minimal metabolic impact, and suitability for elderly patients [6], [7].

Monotherapy predominated over combination therapy (93.4% vs. 6.6%), differing from the study by Le Truong Giang at Can Tho City General Hospital, which prioritized combination therapy (80.6%) [4]. This may be explained by referral practices, as severe hypertension cases are transferred to higher-level hospitals, leaving commune health stations to manage mainly grade 1 hypertension, for which monotherapy remains recommended under Ministry of Health guidelines [6]. The most common combinations were ACEi + CCB and CCB + ARB (both 2.5%), differing from the findings of Nguyen Trong Nhan, where ARB + diuretics were most frequent (4%) and ARB + CCB accounted for 3% [8]. Overall, our results are consistent with recommendations from the Vietnam National Heart Association and the World Health Organization, which prioritize combining CCBs with ACEi or ARB in hypertension management [7], [9].

4.3. Drug interactions in outpatient prescriptions

Based on two databases, the study recorded that the proportion of prescriptions with drug interactions involving antihypertensive drugs (27.2 - 29.5%) was markedly higher than those without antihypertensive drugs (3.8 - 4.5%). This result is similar to the study by

Nguyen Duy Khanh *et al.*, which reported that 82.1% of prescriptions containing antihypertensive drugs had interactions with other drugs, and 37.8% had interactions among antihypertensive drugs themselves [5]. Regarding interaction severity, most cases were recorded at a moderate level in both databases. In the group containing antihypertensive drugs, moderate interactions accounted for the highest proportion (DRUGS.COM: 168 interaction pairs; MICROMEDEX: 143 interaction pairs). This result is similar to the study by Tran Luu Phuc *et al.*, in which DRUGS.COM recorded moderate interactions (1351 pairs), and MICROMEDEX also mainly recorded moderate interactions (346 pairs) [10]. Notably, the significant difference in the proportion of serious interactions between the two databases in this study (MICROMEDEX: 15.9% vs. DRUGS.COM: 1.5%) may reflect inconsistency in classification criteria and data coverage between the sources. A study comparing multiple drug interaction databases showed that the presence of interactions, severity level, mechanism, and management recommendations were not completely consistent across sources [11]. Therefore, each database has its own classification system and cannot completely replace one another in clinical practice.

Among 360 analyzed interaction pairs, 85 (23.6%) were clinically significant and directly involved antihypertensive drugs based on agreement between IBM MICROMEDEX and DRUGS.COM; overall, clinically significant interactions accounted for 31.7% when all pairs were included. These findings highlight the need to monitor drug interactions in outpatient hypertension care, where combination therapy is common. Compared with the study by Perić *et al.* (2022) in Serbia, which reported that up to 86% of patients had at least one potential interaction when screened with Lexicomp, our rate was lower, but this reflects methodological differences rather than lower risk, as Perić included all potential interactions from a single database, whereas our study recorded only clinically significant interactions confirmed by two systems [12]. Another international comparison of IBM MICROMEDEX and DRUGS.COM in metabolic syndrome treatment showed only 37.4% agreement in severity classification, with DRUGS.COM detecting more interactions, underscoring differences in sensitivity [13]. Therefore, our two-source consensus approach enhanced specificity and excluded theoretical alerts; although a single database might yield a higher rate, it could reduce clinical relevance. Therefore, the 23.6% rate reflects strict screening of interactions most likely to affect treatment safety and effectiveness.

V. CONCLUSION

The findings of this study indicate that potential drug-drug interactions remain an important concern in the management of hypertension, particularly among older adults and patients with multiple comorbidities. Strengthening the role of clinical pharmacists in medication review, drug-drug interaction screening, patient counseling, and ongoing medication monitoring may help reduce the risk of adverse drug events and optimize treatment outcomes.

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REFERENCES

1. World Health Organization. Hypertension. 2026. <https://www.who.int/news-room/fact-sheets/detail/hypertension>.
 2. Ministry of Health. Hypertension and Cardiovascular Disease in Older Adults. Ministry of Health. 2026.
 3. Vuong Thai Qui, Do Van Mai, Tran Thi Thu, Tran Do Hung. Survey of Antihypertensive Drug Use at Tam Nong District Health Center, Dong Thap Province. *Journal of Scientific Research and Economic Development, Tay Do University*. 2022. (16), 203-212, <http://115.74.233.203:81/tailieuso/handle/123456789/1397>.
 4. Le Truong Giang, Nguyen Thi Ngoc Van, Le Thanh Tam, Tran Hoang Thuy Phuong. Patterns of Antihypertensive Drug Use and Evaluation of Treatment Outcomes at Can Tho City General Hospital, 2021-2022. *Cantho Journal of Medicine and Pharmacy*. 2022. (51), 221-228, <https://doi.org/10.58490/ctump.2022i51.334>.
 5. Nguyen Duy Khanh, Nguyen Hoang Than, Truong Quoc Ky. Determination of the Prevalence of Drug-Drug Interactions in Antihypertensive Therapy Among Outpatients at Nguyen Van Thu Medical Center, Vung Liem District, Vinh Long Province, 2024. *Vietnam Medical Journal*. 2026. 557(3), 186-191, <https://doi.org/10.51298/vmj.v557i3.16803>.
 6. Ministry of Health. Guidelines for the Diagnosis and Treatment of Hypertension. Ministry of Health. Decision No. 3192/QĐ-BYT dated August 31, 2010. 2026.
 7. Vietnam National Heart Association. Highlights of the 2021 VNHA/VSH Guidelines on Diagnosis and Management of Hypertension in Adults. Vietnam Society of Hypertension. 2026.
 8. Nguyen Trong Nhan, Le Quang Binh, Tran Cong Luan, Vo Thuy Lu Tam, Phung The Dong, *et al.* Patterns of Antihypertensive Drug Use at Thoi Lai District Health Center, Can Tho City. *Journal of Scientific Research and Economic Development, Tay Do University*. 2022. (16), 213-225, <http://115.74.233.203:81/tailieuso/handle/123456789/1398>.
 9. World Health Organization. WHO guideline for the pharmacological treatment of hypertension in adults. 2026.
 10. Tran Luu Phuc, Hoang Thi Thu Huyen, Hoang Thuy Binh, Huynh Thi Nhu Quynh, Le Trung Khoang. Evaluation of Drug-Drug Interactions and Influencing Factors in Hypertension Outpatients at Buon Ma Thuot University of Medicine and Pharmacy Hospital, 2023-2024. *Can Tho University Journal of Science*. 2025. 61(3), 69-76, doi: 10.22144/ctujos.2025.095.
 11. A. Shariff, Belagodu Sridhar S., Abdullah Basha N. F., Bin Taleth Alshemeil S. S. H., Ahmed Aljallaf Alzaabi N. A. th. Assessing Consistency of Drug-Drug Interaction-Related Information Across Various Drug Information Resources. *Cureus*. 2021. 13(3), e13766, doi: 10.7759/cureus.13766.
 12. A. Perić, Udilović A., Dobrić S., Vezmar Kovačević S. The impact of treatment choices on potential drug-drug interactions in hypertensive patients. *British journal of clinical pharmacology*. 2022. 88(5), 2340-2348, doi: 10.1111/bcp.15168.
 13. B. Suriyapakorn, Chairat P., Boonyoprakarn S., *et al.* Comparison of potential drug-drug interactions with metabolic syndrome medications detected by two databases. *PloS one*. 2019.14(11), e0225239, doi: 10.1371/journal.pone.0225239.
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