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A cross-sectional assessment of rational use of antihypertensive medications in central Kayseri

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ABSTRACT

Aim: To evaluate prescriptions issued for patients diagnosed with hypertension in terms of rational drug use and cost-effectiveness.

Methods: This retrospective observational study was conducted using prescriptions issued for patients diagnosed with essential hypertension in the central district of Kayseri, Turkey. Data were obtained from the Medulla Provision System, encompassing prescriptions that included at least one antihypertensive drug and were covered by national health insurance during January 2019. Prescriptions were evaluated based on patient demographics (age and sex), prescribed antihypertensive drugs (pharmacological group and active ingredient), physician specialty, and healthcare institution, presence of comorbidities at treatment initiation and follow-up, and conformity of the chronic disease report to clinical guidelines.

Results: The study included 1,968 prescriptions, with a mean patient age of 63.97 ± 11.88 years. Rational drug use (RDU) was significantly higher in the 18–64 age group (81.6%) compared to those aged ≥80 years (88.9%) ($\chi^2 = 6.123$, $p = 0.039$), and among males (84.8%) versus females (80.8%) ($\chi^2 = 5.123$, $p = 0.024$). Prescriptions from general practitioners showed significantly lower RDU rates compared to those from cardiologists and internists. RDU was observed in 83.6% of patients without asthma using beta-blockers, while only 21.1% of asthmatic patients on beta-blockers met RDU criteria ($\chi^2 = 43.089$, $p < 0.001$). Prescriptions with three active ingredients had the lowest RDU rate (70.9%), compared to those with one (85.0%) or two (88.3%) ingredients ($\chi^2 = 70.976$, $p < 0.001$). The median treatment cost was significantly lower in the RDU group (10.72 USD) than in the non-RDU group (11.76 USD) ($z = 4.076$, $p < 0.001$). Although not statistically significant ($p = 0.081$), the highest RDU rate was observed in prescriptions containing generic imported drugs (26.0%). Cost analysis showed that original imported drugs had the highest unit cost (2.85 USD), while generic imported drugs had the lowest (1.90 USD) ($p < 0.001$).

Conclusion: This study demonstrated that adherence to rational drug use principles in the treatment of hypertension, aligned with current clinical guidelines, results in safer and more cost-effective therapeutic outcomes. Rational prescribing was associated with lower drug counts per prescription and reduced treatment expenditures. However, the widespread use of beta-blockers, particularly outside of their recommended indications, and the preference for original branded products indicate areas for improvement. To enhance rational prescribing practices, awareness must be increased at all levels of the healthcare system, and policy-driven targets should be developed accordingly.

Keywords: Rational drug use, hypertension, antihypertensive treatment approaches, pharmacoeconomics, cost-effectiveness.

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1. Introduction

The treatment of hypertension (HT) is based on two main components: lifestyle modifications and pharmacological therapy. Although lifestyle changes undoubtedly reduce cardiovascular risk and blood pressure levels, the majority of patients still require medication to achieve adequate control [1]. Rational drug use (RDU), defined as the selection of the most appropriate medication for an individual's clinical condition, at the correct dose, duration, and at the lowest possible cost, holds a significant place in the management of hypertension as well [2].

With an aging population, most patients requiring antihypertensive treatment also present with comorbidities [3]. From a pharmacoeconomic perspective, several studies have shown that patients with uncontrolled blood pressure incur higher medication costs compared to those whose hypertension is under control [4, 5].

Irrational drug use (IRDU), as documented both globally and in Turkey, remains a significant contributor to avoidable healthcare expenditures. Suboptimal prescribing practices—such as non-adherence to clinical guidelines, inappropriate drug combinations, and the excessive use of brand-name medications—can substantially elevate treatment costs without yielding proportional clinical benefits.

This issue is particularly critical in the management of chronic conditions like hypertension, where long-term pharmacotherapy is essential. In such contexts, irrational prescribing not only compromises patient outcomes but also imposes a considerable burden on national healthcare systems. Therefore, the evaluation and reduction of IRDU are essential steps toward improving therapeutic effectiveness and ensuring economic sustainability in healthcare delivery [6-8].

Although the data analyzed in this study were collected in early 2019, the patterns observed still offer valuable insights into prescribing behavior prior to recent global and national healthcare shifts. To maintain contextual relevance, the Discussion section has been updated to reflect current literature up to 2025.

This study focused on patients diagnosed with essential hypertension and examined the prescribing patterns of various antihypertensive drug classes, including beta-blockers, ACE inhibitors, ARBs, calcium channel blockers, and diuretics. In light of these concerns, the study compared rational and irrational antihypertensive prescribing patterns in terms of their economic impact. The analysis included the calculation of the number of prescriptions and medication boxes prescribed across these pharmacological groups and active substances. Furthermore, the prescribing trends of physicians from different specialties were evaluated to identify patterns of irrational drug use. Both unit prices and total medication costs were analyzed to highlight the financial implications of prescribing decisions. The findings aim to support the development of more cost-effective and evidence-based healthcare policies in Turkey, particularly in the management of hypertension, a condition with high prevalence and chronic treatment demands.

2. Materials and methods

Ethical approval was obtained from the Erciyes University Non-Interventional Clinical Research Ethics Committee (Approval No: 2020/25). Based on a 95% confidence interval and a 3% margin of error, with an alpha level of 0.05 and beta of 0.20, a total of 6,227 prescriptions were screened to obtain 1,968 prescriptions containing antihypertensive medications. This retrospective cross-sectional study analyzed prescriptions containing antihypertensive medications for patients

diagnosed with essential hypertension (HT), issued at primary healthcare institutions and filled by community pharmacies in central Kayseri, Turkey. The data were collected over one month from 31 volunteer pharmacies covering all districts of the city. The study population consisted of prescriptions including essential HT diagnosis codes. The sample comprised prescriptions obtained from pharmacies whose pharmacists agreed to participate voluntarily.

Prescriptions covered by the Social Security Institution (SGK) were retrieved from the Medulla Provision System. Only prescriptions with essential hypertension diagnoses and at least one antihypertensive drug were included. Patients under the age of 18 were excluded due to their frequent use of pulmonary hypertension medications. Additionally, prescriptions containing acetylsalicylic acid (n=230) were excluded, as this medication is not classified as an antihypertensive drug despite reimbursement under the essential HT diagnosis.

The collected data included: patient age and sex, prescribed medications, physician specialty and healthcare institution, specialty of the physician issuing the chronic disease report, accompanying comorbidities at the start and during treatment, and the active substances listed in the prescription report. For cost calculations, only medications with antihypertensive effects were considered. Drug costs were calculated based on the amounts paid by SGK as listed in their reimbursement database. Commercial drug names were not disclosed in compliance with personal data protection laws; evaluations were based on active substances.

All personal identifiers related to patients, prescribers, and healthcare institutions were excluded from the analysis. Patients who were using acetylsalicylic acid (ASA) or had ASA included in any part of their antihypertensive treatment regimen, as well as those who were pregnant or had diagnoses related to pregnancy-induced hypertension, such as preeclampsia or eclampsia, were excluded from the study. Patients were anonymized using a coding system. Costs were calculated using SGK's reimbursement model, which involves a reference pricing system where drugs within the same therapeutic equivalence group are reimbursed at a common price. The maximum reimbursement is determined by adding 10% to the unit price of the cheapest drug in the group. If patients choose a more expensive alternative, they are responsible for the price difference.

Prescriptions were evaluated for RDU based on the 2018 European Society of Cardiology (ESC) Guidelines for Hypertension Management. Inappropriate prescribing—such as contraindicated drugs considering patient history, age, sex, and comorbidities—or use of clinically unsuitable drug combinations was considered IRDU. To enhance international comparability, all cost values expressed in Turkish Lira (TL) were also converted into US Dollars (USD) using the average exchange rate during the study period (1 USD = 5.3659 TL).

2.1. Statistical analysis

Data were compiled using Microsoft Excel and analyzed with IBM SPSS Statistics (v26, IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as counts (n), percentages (%), medians (M), and minimum–maximum values. The normality of numerical variables was assessed using the Shapiro–Wilk test. The Mann–Whitney U test was used to compare differences between two independent groups. The Pearson chi-square test and Fisher's exact test were used to analyze associations between categorical variables. For multiple-response categorical data, the multiple-response chi-square test was employed. For comparisons involving three or more independent groups, the

Kruskal–Wallis test was used due to the non-normal distribution of the data. A p-value of <0.05 was considered statistically significant.

3. Results

The distribution of active substances included in the initial and updated chronic disease reports, as well as those listed in the prescriptions, is presented in Table 1. At the initiation of treatment, the most frequently prescribed drug group was fixed-dose combinations of angiotensin receptor blockers (ARBs) and diuretics (DUs), followed by beta-blockers (BBs). In the updated reports, however, beta-blockers emerged as the most commonly used group, again followed by ARB+DU combinations. When comparing the initial and current reports of patients with hypertension, an increase was observed in all antihypertensive drug classes except angiotensin-converting enzyme inhibitors (ACEIs). The most notable increase was seen in fixed-dose combination preparations containing ARB + calcium channel blocker (CCB) + diuretic and ACEI + CCB + diuretic (Table 1). A statistically significant relationship was found between the conformity of antihypertensive treatment reports with clinical guidelines and the level of RDU ($p < 0.001$). Among patients whose treatment reports complied with current clinical guidelines, rational drug use was observed in 35.6% of cases (157 out of 441), compared to only 12.4% (190 out of 1527) among those whose reports did not conform to the guidelines. The chi-square test revealed a significant association ($\chi^2 = 126.37$, $p < 0.001$), and the Phi correlation coefficient ($\Phi = 0.253$) indicated a moderate positive relationship (Table 2).

Table 1. Distribution of antihypertensive drugs (from treatment initiation report to current report)

Antihypertensive drugs	**Initial Report (n, %)**	**Updated Report (n, %)**	**Prescription (n, %)**
Beta-blockers (BB)	631 (22.87%)	737 (23.84%)	592 (23.43%)
ACE inhibitors (ACEI)	242 (8.77%)	194 (6.27%)	168 (6.65%)
Angiotensin receptor blockers (ARB)	125 (4.53%)	160 (5.17%)	174 (6.89%)
Calcium channel blockers (CCB)	389 (14.10%)	466 (15.07%)	355 (14.05%)
Diuretics (DU)	152 (5.51%)	122 (3.94%)	122 (4.83%)
Alpha-blockers (AB)	22 (0.80%)	32 (1.03%)	25 (0.99%)
Methyldopa (MD)	41 (1.49%)	31 (1.00%)	46 (1.82%)
BB + DU	410 (15.41%)	531 (17.17%)	474 (18.61%)
ACEI + DU	280 (10.15%)	315 (10.19%)	314 (12.43%)
ARB + DU	669 (24.25%)	708 (22.90%)	599 (23.70%)
ACEI + CCB	93 (3.37%)	112 (3.62%)	89 (3.52%)
ARB + CCB	80 (2.90%)	85 (2.75%)	68 (2.69%)
ACEI + CCB + DU	0 (0.00%)	61 (1.97%)	51 (2.02%)
ARB + CCB + DU	33 (1.20%)	60 (1.94%)	50 (1.98%)
DU + DU	3 (0.11%)	0 (0.00%)	33 (1.31%)
Total	2759	3092	2527

Table 2. Association between report conformity and rational drug use.

Report Conformity	Rational Drug Use, n (%)	Irrational Drug Use, n (%)	Total (n)	χ^2	p-value
Guideline-based	157 (35.6%)	284 (64.4%)	441		
Not Guideline-based	190 (12.4%)	1337 (87.6%)	1527	126.37	<0.001
Total	347 (17.3%)	1621 (82.7%)	1968		

Phi coefficient (Φ) = 0.253, p < 0.001. Statistical test: Chi-square (χ^2), two-tailed.

Table 3. Costs of antihypertensive drugs by pharmacological groups (1 USD 5.3659 TL).

Antihypertensive Drugs	Number of Boxes (n, %)	Total Cost (USD) (n, %)	Unit Cost (USD) (n, %)
Beta-blockers (BB)	2347 (28.10%)	5,070.10 (21.73%)	2.16 (4.87%)
ACE inhibitors (ACEI)	512 (6.13%)	974.11 (4.18%)	1.90 (4.29%)
Angiotensin receptor blockers (ARB)	413 (4.94%)	1,258.12 (5.39%)	3.05 (6.86%)
Calcium channel blockers (CCB)	763 (9.13%)	2,823.01 (12.10%)	3.70 (8.33%)
Diuretics (DU)	327 (3.91%)	728.14 (3.12%)	2.23 (5.01%)
Alpha-blockers (AB)	79 (0.95%)	246.70 (1.06%)	3.12 (7.04%)
Methyldopa (MD)	1 (0.01%)	1.99 (0.01%)	1.99 (4.48%)
BB + DU	2200 (26.34%)	7,123.76 (30.54%)	3.24 (7.30%)
ACEI + DU	894 (10.70%)	2,030.77 (8.71%)	2.27 (5.12%)
ARB + DU	173 (2.07%)	437.48 (1.88%)	2.53 (5.70%)
ACEI + CCB	290 (3.47%)	1,493.24 (6.40%)	5.15 (11.60%)
ARB + CCB	230 (2.75%)	819.11 (3.51%)	3.56 (8.02%)
ACEI + CCB + DU	17 (0.20%)	71.69 (0.31%)	4.22 (9.50%)
ARB + CCB + DU	22 (0.26%)	69.48 (0.30%)	3.16 (7.12%)
DU + DU	85 (1.02%)	179.90 (0.77%)	2.12 (4.77%)
Total	**8353**	23,327.59	44.39

The total and average unit costs of antihypertensive drugs by pharmacological group, along with their frequency and percentage distributions, are presented in Table 3. For all cost analyses, values in TL were recalculated and presented in USD based on the average exchange rate in January 2019 (1 USD = 5.3659 TL), which was the data collection period. Among the prescriptions with a diagnosis of hypertension, beta-blockers (BBs) were the most frequently prescribed drug group, accounting for 28.10% of total box usage and representing a cost of 5,071.28 USD (21.73%). However, the group with the highest total cost was fixed-dose combinations of beta-blockers and diuretics (BB + DU), with a total expenditure of 7,122.41 USD (30.54%). Methyldopa (MD) was the least prescribed antihypertensive agent, with a total cost of only 1.99 USD (0.01%) and minimal box usage (0.01%). Fixed-dose combinations containing three active substances, such as ACEI + CCB + DU or ARB + CCB + DU, remained the least preferred options, collectively accounting for a small portion of prescriptions and costs

(each representing less than 2% of total expenditures). The total cost of antihypertensive drugs across all prescriptions was 23,336.89 USD. Of this, fixed-dose combination products (i.e., single-tablet formulations) accounted for approximately 45.23% of the total expenditure, with a combined cost of 12,226.88 USD. In contrast, single active substance preparations were used in 54.77% of prescriptions, amounting to 11,110.01 USD (Table 3.).

The distribution of RDU across age groups showed a statistically significant difference (χ^2=6.123; p=0.039). In the 18–64 age group, 823 individuals (81.6%) used medications rationally, while 185 (18.4%) did not. In the 65–79 age group, 630 individuals (81.7%) used medications rationally compared to 141 (18.3%) who did not. Among patients aged 80 years and older, 168 (88.9%) practiced rational drug use, whereas only 21 (11.1%) did not. When analyzed by sex, 983 women (80.8%) used medications rationally, while 233 (19.2%) did not. In contrast, 638 men (84.8%) adhered to rational drug use principles, compared to 114 (15.2%) who did not. The difference between sexes was also statistically significant (χ^2=5.123; p=0.024).

The frequency of use and cost of monotherapy antihypertensive drugs were also evaluated in this study. Among beta-blockers (BB), metoprolol was the most frequently prescribed active substance, accounting for 52% of prescriptions, with a total cost of 3,139.17 USD. Other frequently used agents in this group included nebivolol (19%, 788.24 USD), carvedilol (14%, 686.48 USD), and bisoprolol (8%, 328.85 USD). Within the group of angiotensin-converting enzyme inhibitors (ACEIs), ramipril was the most prescribed medication, representing 48% of prescriptions and costing 447.15 USD in total. This was followed by perindopril (25%, 271.85 USD), captopril (9%, 25.73 USD), lisinopril (5%, 36.74 USD), and other ACEIs in smaller proportions. In prescriptions containing angiotensin receptor blockers (ARBs), candesartan was the most commonly preferred agent, with a usage rate of 28% and a total cost of 331.64 USD, followed by losartan (23%, 269.36 USD), valsartan (20%, 276.24 USD), and Olmesartan (20%, 255.17 USD). Among calcium channel blockers (CCBs), amlodipine was the most frequently prescribed drug, accounting for 47% of prescriptions within the CCB group, with a total cost of 934.67 USD. Other common agents in this group were lercanidipine (18%, 460.40 USD), diltiazem (14%, 442.28 USD), and benidipine (11%, 535.94 USD). In the diuretic (DU) group, indapamide was the most preferred medication (44%, 371.02 USD), followed by hydrochlorothiazide (28%, 199.58 USD) and furosemide (28%, 148.24 USD). In the evaluation of dual combination therapies, the most frequently prescribed beta-blocker + diuretic (BB + DU) combination was nebivolol + hydrochlorothiazide (55%, 245.20 USD), followed by atenolol + chlorthalidone (45%, 192.28 USD). Among ACEI + DU combinations, ramipril + HCT was the most common (33%, 698.18 USD), followed by perindopril + indapamide (27%, 515.96 USD), lisinopril + HCT (23%, 252.06 USD), and zofenopril + HCT (10%, 319.74 USD). Less frequent combinations included cilazapril + HCT (3%, 128.34 USD), benazepril + HCT (2%, 66.63 USD), quinapril + HCT (1%, 26.67 USD), and fosinopril + HCT (1%, 23.19 USD). In ARB + DU combinations, candesartan + HCT was the most frequently used (26%, 1,963.01 USD), followed by valsartan + HCT (23%, 1,687.21 USD), irbesartan + HCT (17%, 1,126.66 USD), losartan + HCT (15%, 957.18 USD), olmesartan + HCT (11%, 755.54 USD), and telmisartan + HCT (8%, 634.15 USD). In ACEI + calcium channel blocker (CCB) combinations, perindopril + amlodipine

was the most preferred (55%, 458.83 USD), followed by verapamil + trandolapril (23%, 664.61 USD), enalapril + lercanidipine (20%, 353.87 USD), and lisinopril + amlodipine (2%, 15.93 USD). Finally, within ARB + CCB combinations, olmesartan + amlodipine was the overwhelmingly dominant option (97%, 795.07 USD). Less commonly prescribed combinations included valsartan + amlodipine (2%, 13.22 USD) and candesartan + amlodipine (1%, 10.81 USD).

The top five most frequently prescribed antihypertensive active substances and their corresponding average unit costs are presented in Figure 1. The most commonly used agent was metoprolol, a beta-blocker (BB), followed by amlodipine from the calcium channel blocker (CCB) class; candesartan + hydrochlorothiazide (HCT) and valsartan + HCT, both representing ARB + diuretic (DU) fixed-dose combinations; and nebivolol, another beta-blocker. All values and agents are now clearly labeled in the revised version of Figure 1.

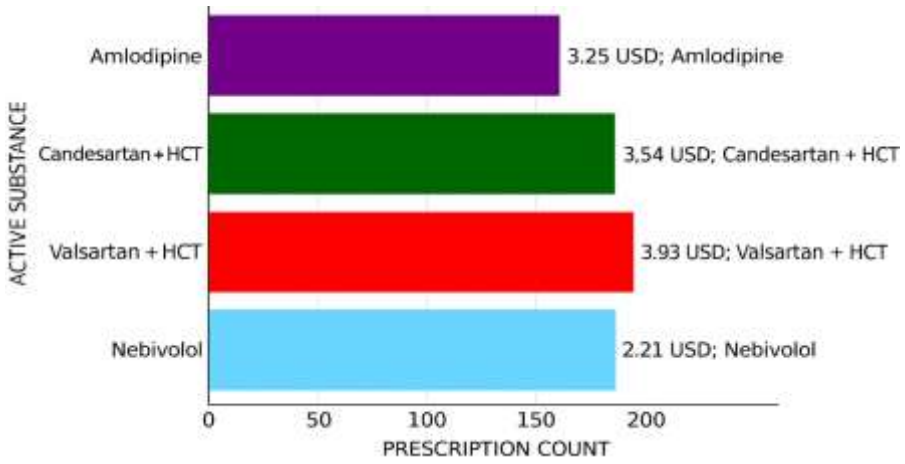

Figure 1. Top five most frequently used active substances in antihypertensive treatment (January 1–31, 2019). *HCT: Hydrochlorothiazide. The average exchange rate in January 2019 was 1 USD = 5.3659 TL.*

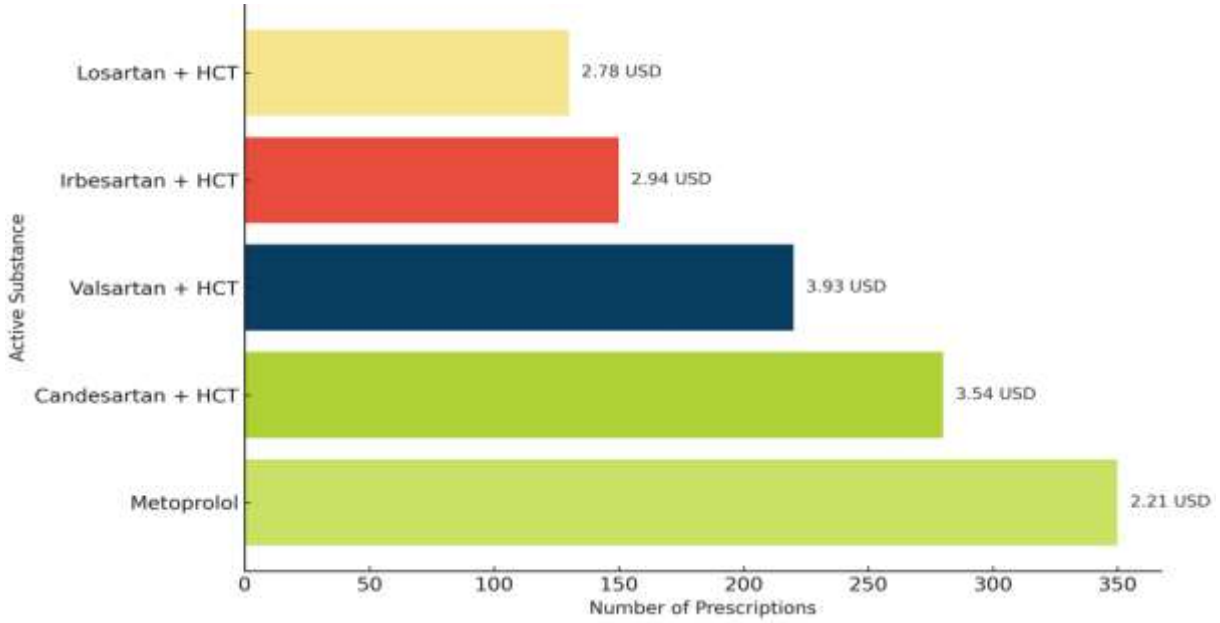

Figure 2. Top five active substances in antihypertensive treatment based on total cost (January 1–31, 2019). *HCT: Hydrochlorothiazide. The average exchange rate in January 2019 was 1 USD = 5.3659 TL.*

From a cost perspective, metoprolol, a beta-blocker (BB), was the active substance with the highest total expenditure. It was followed by fixed-dose combinations of candesartan + HCT, valsartan + HCT, irbesartan + HCT, and losartan + HCT. The average unit costs per box for these five active substances are presented in Figure 2. Among them, metoprolol had the lowest unit cost but was also the most frequently prescribed (Figure 2.).

The prescription of blood pressure–raising medications by physicians is presented in Table 4. The frequency of prescribing such medications varied significantly across physician specialties (χ^2=80.289; p<0.001).

The proportion of cardiologists (2.4%) and internal medicine specialists (9.0%) prescribing drugs known to elevate blood pressure was relatively low. In contrast, 25.0% of general practitioners and 24.0% of family medicine specialists were found to prescribe these medications. The corresponding rate among other specialties was 22.7% (Table 4.).

The distribution of non-steroidal anti-inflammatory drug (NSAID) prescribing by physician specialty is presented in Table 5. The use of NSAIDs differed significantly across specialties (χ^2=71.933; p<0.001). Among general practitioners, 22.1% prescribed NSAIDs, while 22.0% of family medicine specialists also issued such prescriptions. The rate among physicians from other specialties was 20.5%. In contrast, NSAID prescribing rates were much lower among internal medicine specialists (7.3%) and cardiologists (1.9%) (Table 5).

Of the 1968 prescriptions evaluated, a total of 1696 (86.2%) was classified as irrational. The most common reasons for irrational drug use included: inappropriate combination therapy (37.7%), prescribing without clinical indication (26.1%), non-guideline preferred drug selection (17.8%), and duplicate pharmacological agents (13.9%) (Table 6.).

Table 4. Use of blood pressure (BP)–elevating medications by physician specialty.

Physician Specialty	**Use of BP-Elevating Drugs (n, %)**			
	No	**Yes**	**χ^2**	***p-value***
General Practitioner	935 (75.0%)	311 (25.0%)	80.289	**<0.001**
Family Medicine Specialist	173 (74.6%)	59 (25.4%)		
Cardiologist	207 (97.6%)	5 (2.4%)		
Internal Medicine Specialist	213 (90.6%)	21 (9.4%)		
Other Physicians	34 (77.3%)	10 (22.7%)		

Table 5. The distribution of non-steroidal anti-inflammatory drug (NSAID) prescribing by physician specialty.

Physician Specialty	**NSAID Prescribing (n, %)**			
	No	**Yes**	**χ^2**	***p-value***
General Practitioner	971 (77.9%)	275 (22.1%)	71.933	**<0,001**
Family Medicine Specialist	181 (78.0%)	51 (22.0%)		
Cardiologist	208 (98.1%)	4 (1.9%)		
Internal Medicine Specialist	217 (92.7%)	17 (7.3%)		
Other Physicians	35 (79.5%)	9 (20.5%)		

Table 6. Classification of irrational drug use.

Reason for irrational drug use	n	%
Inappropriate combination therapy	640	37.7
Prescribing without clinical indication	443	26.1
Non-guideline preferred drug selection	302	17.8
Duplicate pharmacological agents	236	13.9
Others	75	4.4
Total	1696	100

The cost analysis according to the type of drug production is presented in Table 7. Statistically significant differences were observed among the groups in terms of both unit cost (H = 192.898; $p < 0.001$) and total cost (H = 214.126; $p < 0.001$). The lowest median unit cost was found in generic imported drugs, calculated as 1.90 USD (min–max: 1.35–1.90), whereas the highest was in original imported drugs, at 2.85 USD (min–max: 1.23–8.21). In terms of total cost, generic imported drugs again had the lowest median value at 5.70 USD (min–max: 1.35–17.09), while original imported drugs had the highest, with a median cost of 12.58 USD (min–max: 1.90–31.48). Original domestic drugs showed moderate cost levels, with a median unit cost of 2.66 USD (min–max: 0.85–12.44) and a median total cost of 7.98 USD (min–max: 0.85–49.74). Similarly, generic domestic drugs had a median unit cost of 2.79 USD (min–max: 1.19–9.31) and a total cost of 8.22 USD (min–max: 1.21–22.84) (Table 7.).

4. Discussion

In this study, the rational use of antihypertensive drugs and the associated treatment costs were evaluated in prescriptions issued for patients diagnosed with essential hypertension in Kayseri city center. The findings revealed significant variations in RDU based on age group, gender, physician specialty, presence of comorbidities, number of active substances, and medication production type. Notably, younger patients (aged 18–64) and female patients were more likely to receive rational prescriptions. Furthermore, prescriptions written by cardiologists and internal medicine specialists had significantly lower rates of blood pressure–elevating drugs and NSAIDs, indicating greater adherence to clinical guidelines. In contrast, general practitioners were more likely to prescribe potentially inappropriate medications, suggesting the need for targeted educational interventions.

A national study conducted between 2003 and 2012 on a representative adult sample in Turkey (n=5,437) reported a hypertension prevalence of 32.3% in women and 28.4% in men [9]. In our

Table 7. The cost analysis according to the type of drug production.1 USD = 5.365 TL.

Cost	Groups Median (min-max)				Test Statistics	
	Generic domestic	Generic imported	Original domestic	Original imported	H	p-value
Unit Cost (USD)	2.79 (1.19–9.31) [a]	1.90 (1.35–1.90) [b]	2.66 (0.85–12.44) [c]	2.85 (1.23–8.21) [d]	192.898	<0.001
Total Cost (USD)	8.22 (1.21–22.84) [a]	5.70 (1.35–17.09) [b]	7.98 (0.85–49.74) [c]	12.58 (1.90–31.48) [c]	214.126	<0.001

H: Kruskal–Wallis Test. Superscript letters (a, b, c, d) indicate groups with statistically different values. Groups sharing the same letter do not differ significantly.

study, the average unit cost of original imported antihypertensive drugs was found to be higher than that of original domestically manufactured drugs, consistent with previous research showing that imported medications generally have higher market prices compared to locally manufactured alternatives [10]. Another notable finding was that the average cost of generic imported drugs was lower than that of original imported drugs, highlighting the potential economic benefit of preferring generic formulations. This aligns with the existing literature, which consistently demonstrates that the use of generic drugs contributes to greater cost-effectiveness in pharmacotherapy [11, 12]. Interestingly, the average unit cost of original domestic drugs was lower than that of generic domestic drugs in our analysis, suggesting that some domestically produced generics may be priced higher than their original counterparts. This finding warrants further investigation into pricing strategies and market dynamics in the generic pharmaceutical sector.

In the present study, the majority of patients receiving antihypertensive treatment were managed with two medications, followed by those treated with three drugs, monotherapy, and four or more drugs. Notably, rational drug use (RDU) was more prevalent among prescriptions containing monotherapy or dual therapy, compared to those with three or more active substances. The TURKSAHA study, which evaluated prescribing patterns of antihypertensive drugs in a large cohort (n=12,897), reported that 75.7% of patients were treated with monotherapy, 19.7% with two drugs, 4.1% with three drugs, and 0.5% with four or more drugs. The corresponding blood pressure control rates were 26.3%, 25.9%, 24.5%, and 26.2%, respectively [13]. Similarly, another study revealed that 48.94% of patients received monotherapy, while 51.05% were on combination therapy [14]. Although the distribution of dual therapy in our findings aligns with prior studies, monotherapy appeared to be less frequent, with an increasing proportion of patients receiving two or more agents. The relatively high prevalence of triple or quadruple therapy may reflect a rising incidence of resistant hypertension, which could be attributed to poor blood pressure control or the presence of comorbid conditions [14].

In our study, RDU rates did not significantly differ between patients whose antihypertensive therapy was modified and those whose initial treatment regimen remained unchanged. This suggests that treatment changes—often prompted by inadequate blood pressure control, adverse effects, or comorbidities—do not necessarily impact adherence to rational prescribing principles [1]. However, considering the high proportion of patients requiring multiple medication changes, the potential increase in the prevalence of resistant hypertension should be carefully examined. Current clinical guidelines emphasize the need for comprehensive research to better understand factors contributing to poor medication adherence, which may lead to suboptimal treatment outcomes. Furthermore, the importance of avoiding prescriptions that do not align with up-to-date clinical recommendations is strongly emphasized, as these may compromise treatment efficacy and patient safety [15].

In this study, both antihypertensive drug use and RDU were more prevalent in the 18–64 age group. Particularly among patients in this age group who had comorbidities at the time of evaluation, RDU rates were found to be higher. As age increases and comorbidities become more common, physicians in primary care settings appear to be more likely to prescribe antihypertensive medications in accordance with current clinical guidelines. Previous studies have

shown that the prevalence of antihypertensive medication use increases with age, with a marked rise observed particularly in individuals over the age of 60 [16]. Across all age groups, the most frequently prescribed drug classes are calcium channel blockers (CCBs) and angiotensin receptor blockers (ARBs). Notably, CCB use increases with age, whereas ACEI use tends to decline [17].

In our study, the most commonly prescribed drug groups among patients receiving antihypertensive treatment were ARB + diuretic (DU) combinations and beta-blockers (BBs), respectively. Previous studies conducted in Turkey have reported a growing trend in the use of ARBs and ARB + DU combinations in the treatment of hypertension [18]. ARBs are known to be both clinically effective and cost-effective in hypertension management [19, 20]. In our findings, candesartan was the most frequently prescribed ARB, followed by losartan. Supporting this, a pharmacoeconomic analysis identified losartan as the most appropriate ARB across multiple treatment steps, offering the lowest daily treatment cost and demonstrating dose-dependent improvements in response rates [21]. Consistent with the literature, our study confirms that treatment costs vary considerably across different drug classes, reinforcing the importance of drug selection based not only on efficacy but also on economic considerations.

In this study, the most frequently used active substances were metoprolol, amlodipine, candesartan + HCT, valsartan + HCT, and nebivolol, in that order. Previous research has also reported that the ARB + HCT combination is the most commonly preferred drug group in the treatment of hypertension [22]. Our findings are in line with these observations, further highlighting the widespread clinical acceptance of ARB-based combination therapies in real-world prescribing practices.

In this study, ARB + diuretic (DU) and beta-blocker (BB) use were found to be more common among female patients, while BB and ARB + DU combinations were more frequently prescribed to male patients. The use of alpha-blockers (ABs) was low in both sexes. A study by Tenes et al. investigated the reasons behind physicians' preference for prescribing BBs to hypertensive men and DUs to hypertensive women, and found that physicians believed BBs were more effective in lowering blood pressure in men, while DUs were more effective in women [23]. This suggests a non–evidence-based prescribing behavior, possibly influenced by the higher risk of coronary heart disease in men, leading physicians to favor BBs in male patients. Despite sex-based differences in hypertension characteristics and responses to treatment, current hypertension guidelines do not recommend sex-specific pharmacological approaches [24, 25]. Consistent with the literature, our findings also indicate gender-based variations in antihypertensive drug utilization, particularly in medication class preferences among women and men [23, 26]. These findings underscore the need for further research to clarify the rationale behind sex-based prescribing patterns and to evaluate their long-term clinical implications in hypertension management.

In this study, cardiology specialists exhibited higher rates of RDU and were also less likely to prescribe medications known to elevate blood pressure. Consistent with previous research conducted in primary healthcare settings, our findings also demonstrated higher rates of NSAID prescribing in non-specialist practices [27, 28]. According to the Turkish Pharmaceutical Market Surveillance Report, analgesics accounted for 13.49% of all drugs reimbursed by the Social Security Institution in 2019, ranking third among all drug categories

[27, 29]. NSAIDs can contribute to increased blood pressure and reduced efficacy of antihypertensive therapy due to sodium and water retention and inhibition of prostaglandin synthesis, which leads to reduced vasodilation [30, 31]. These findings highlight the importance of appropriate NSAID prescribing, particularly in hypertensive patients, and reinforce the need for guideline-based decision-making in all healthcare settings.

In this study, 36 individuals with coexisting asthma were found to be prescribed beta-blockers (BBs). Among these, metoprolol was the most frequently used BB, accounting for 42% of prescriptions. Although β1-selective (cardioselective) beta-blockers may reduce the risk of bronchospastic adverse effects, the use of BBs in patients with pulmonary conditions—particularly chronic obstructive pulmonary disease (COPD) and asthma—requires caution. This is because BBs can potentially counteract the bronchodilator effects mediated by β2 receptors, thereby exacerbating respiratory symptoms [32]. Recent studies have emphasized the evolving trends in antihypertensive prescribing following the COVID-19 pandemic and policy shifts in national formularies. While our study reflects pre-pandemic prescribing habits, it offers a comparative baseline. Similar findings or shifts have also been reported in more recent studies, supporting the continued relevance of our observations [33, 34].

One of the main limitations of this study is that the data were restricted to a single province—Kayseri—which may hinder the generalizability of the findings to the national level. Extrapolating results from a single-center study to represent broader populations is challenging; therefore, multicenter studies are warranted to validate and expand upon these findings. One limitation of our study is the use of prescription data from January 2019. While this allows for pre-pandemic analysis, the findings may not fully reflect more recent prescribing patterns. Additionally, the absence of systolic/diastolic blood pressure values in the Medulla Pharmacy Provision System prevented the assessment of hypertension staging, blood pressure control status, medication adherence, and treatment compliance among patients receiving antihypertensive therapy based on current clinical guidelines.

4.1. Conclusion: This study highlights the importance of RDU in the management of hypertension and its implications for public health and healthcare expenditures. The findings suggest that adherence to current clinical guidelines improves RDU rates and reduces treatment costs, particularly when generic alternatives are utilized. Significant differences were observed in prescribing patterns across physician specialties, age groups, and drug types, underlining the need for targeted educational initiatives and guideline-based prescribing.

Given the regional limitations of the study and the absence of blood pressure monitoring data in the national database, future multicenter and prospective studies are needed to provide a more comprehensive evaluation of treatment efficacy, medication adherence, and long-term outcomes. Overall, integrating pharmacoeconomic perspectives into healthcare policies and encouraging rational prescribing practices are essential steps toward optimizing the management of chronic diseases such as hypertension. Further studies using updated datasets are recommended to validate our results and assess how evolving clinical guidelines and market dynamics influence antihypertensive prescribing and pharmacoeconomic.

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Open Access Statement

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