

Currents in Pharmaceutical Research (CPR)

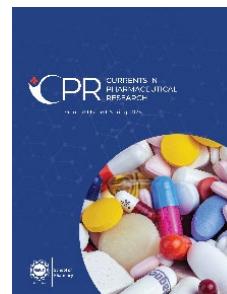
Volume 3 Issue 2, Fall 2025

ISSN(P): 3007-3235, ISSN(E): 3007-3243

Homepage: <https://journals.umt.edu.pk/index.php/cpr>



Article QR



Title: **Cost-Effectiveness Analysis of Antihypertensive Medications Prescribed to Primary Hypertension Patients at District Headquarters Hospital, Kohat**

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DOI: <https://doi.org/10.32350/cpr.32.03>

History: Received: May 20, 2025, Revised: July 05, 2025, Accepted: August 10, 2025, Published: September 29, 2025

Citation: Shaheen M, Sadozai SK, Ullah R, et al. Cost-Effectiveness Analysis of Antihypertensive Medications Prescribed to Primary Hypertension Patients at District Headquarters Hospital, Kohat. *Curr Pharma Res.* 2025;3(2):37–55. <https://doi.org/10.32350/cpr.32.03>

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Conflict of Interest: Author(s) declared no conflict of interest



UMT

A publication of
The School of Pharmacy
University of Management and Technology, Lahore, Pakistan

Cost-Effectiveness Analysis of Antihypertensive Medications Prescribed to Primary Hypertension Patients at District Headquarters Hospital, Kohat

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ABSTRACT

Hypertension, a major risk factor for cardiovascular diseases (CVDs), contributes to 9.3 million deaths annually. In low- and middle-income countries (LMICs) like Pakistan, cost-effective treatment is critical due to limited healthcare resources. This study aimed to evaluate the cost-effectiveness of antihypertensive medications prescribed to patients with primary hypertension at the District Headquarters (DHQ) Hospital, KDA, Kohat in the Khyber Pakhtunkhwa province of Pakistan. A cross-sectional retrospective study was conducted over a period of six months, involving 320 patients (55.31% male, 44.69% female) aged 18-60 years. Prescription patterns and costs of antihypertensive medications (monotherapy and combination therapy) were analyzed using hospital records. The total cost of prescribed antihypertensive medications was PKR 261,153.00, with monotherapy accounting for PKR 208170.00 and combination therapy accounting for PKR 52983.00. Among monotherapies, calcium channel blockers (CCBs) were the most frequently prescribed (107 prescriptions) and accounted for the highest cost (PKR 132114.00, 50.58%), followed by angiotensin receptor blockers (ARBs) (PKR 37238.00, 14.25%). In contrast, diuretics were the most cost-effective option, costing only PKR 25.2 per unit dose. For combination therapy, amlodipine + hydrochlorothiazide combination was the most prescribed, while losartan + amlodipine combination incurred the highest cost. Monotherapy was prescribed in 67.18% of cases, with most patients showing a positive response before transitioning to combination therapy. CCBs and diuretics were found to be more cost-effective, whereas ACE inhibitors were among the most expensive options. CCBs were the most frequently prescribed in

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monotherapy, while the combination of amlodipine and atenolol was commonly used in multidrug regimens. The current study highlights the importance of considering patients' socioeconomic status when initiating pharmacologic treatment. Cost-effective prescribing is crucial in the resource-limited settings of Pakistan, where balancing clinical efficacy and affordability is essential. The findings support WHO recommendations for the rational use of combination therapy and emphasize the use of low-cost medications to optimize treatment outcomes in low- and middle-income countries.

Keywords: antihypertensive drugs, cost-effectiveness, combination therapy, drug utilization, monotherapy, pharmacoeconomics

1.INTRODUCTION

Hypertension, often termed as the “silent killer,” is a leading global risk factor for cardiovascular diseases (CVDs), stroke, and renal failure, contributing to approximately 9.3 million deaths annually, worldwide [1, 2]. Currently, more than 1.13 billion individuals worldwide suffer high blood pressure. The prevalence of hypertension has doubled since 1990, with the vast majority of new patients in low-and-middle income countries (LMICs) [3]. According to a recent cross-sectional study, 17.5% of people in middle-income nations have hypertension. The current study used a pooled data set from 1.1 million people in 44 LMICs [4]. In LMICs, including Pakistan, the burden of hypertension has increased significantly due to urbanization, sedentary lifestyle, dietary shifts, and limited healthcare access [5, 6]. According to the Pakistan Demographic and Health Survey, the prevalence of hypertension among adults has reached alarming levels, with many individuals either undiagnosed or inadequately treated [7, 8].

In resource-constrained settings such as that of Pakistan, where the majority of the population pays out-of-pocket for healthcare, the cost of antihypertensive therapy plays a crucial role in patient adherence and treatment outcomes [9].

Various classes of antihypertensive drugs, such as calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, and diuretics are available in the market, with significant variations in cost, prescribing patterns, and patient response [10, 11]. While clinical guidelines provide

direction regarding pharmacological treatment, real-world prescribing practices often diverge due to physician preferences, drug availability, and patient affordability [12, 13]. Studies show that thiazide diuretics and certain generic formulations offer high cost-effectiveness, yet they remain underutilized [14].

Cost-effectiveness analysis is crucial in hypertension treatment [3, 13]. A study on salt substitution and combination therapy of antihypertensive drug treatment in Chinese prehypertensive adults evaluated the cost-effectiveness of these interventions [15]. Additionally, a cost-effectiveness analysis conducted by a non-physician-led, community-based blood pressure intervention in rural China demonstrated the benefits of such programs [15]. Previous research in Pakistan and other LMICs emphasized the importance of pharmacoeconomic evaluations in chronic disease management. For instance, a study conducted at a tertiary care hospital in Karachi highlighted discrepancies between clinical guidelines and actual prescribing patterns, with more frequent use of costlier agents, such as ARBs and CCBs [15]. Similarly, an Indian study demonstrated that fixed-dose combinations, though more expensive, improved adherence and outcomes, highlighting the trade-off between cost and therapeutic effectiveness [16].

In this context, the current study was designed to evaluate the cost-effectiveness of antihypertensive medications prescribed to patients with primary hypertension at the District Headquarter (DHQ) Hospital, KDA, Kohat in the Khyber Pakhtunkhwa province of Pakistan. This was achieved by analyzing drug utilization patterns and associated treatment costs. The study hypothesized that cost-effective antihypertensive prescribing practices, aligned with clinical guidelines, would optimize treatment outcomes in resource-limited settings such as Pakistan.

2. METHODOLOGY

2.1. Study Design

This retrospective cross-sectional investigation assessed the cost-effectiveness of antihypertensive medications prescribed to patients diagnosed with primary hypertension, following established drug utilization research methodologies [17, 18]. The study was carried out in the medical and cardiology units of District Headquarter Teaching Hospital KDA, located in Kohat, Khyber Pakhtunkhwa, Pakistan.

2.2. Study Setting and Data Collection

The study was based on a retrospective drug utilization review (DUR) of medical records and prescriptions retrieved. A structured data collection form, adapted from a previously validated tool with necessary modifications, was employed to extract relevant information. Data included patient demographics, diagnosis, prescribed antihypertensive medications (generic/proprietary names), dosing regimens, frequency, and cost per unit dose [19]. The form was pilot tested on 20 medical records and reviewed by two pharmacy faculty members with expertise in pharmacoconomics and drug utilization research to ensure its accuracy and relevance for collecting prescription and cost data.

2.3. Sample Size and Sampling Technique

The sample size was calculated using the WHO sample size calculator with a 95% confidence interval and a 5% margin of error. A total of 320 medication orders were selected through a simple random sampling method from hospital records.

2.4. Inclusion and Exclusion Criteria

The study included primary hypertensive patients aged between 18 and 60 years who were admitted to the medical or cardiology wards. These patients were prescribed either monotherapy or combination therapy of antihypertensive medications. Patients admitted to specialty wards, such as emergency, perioperative, oncology, neurology, or transplant units were excluded. Additionally, outpatients, individuals managed in sub-acute care settings (e.g., rehabilitation or observation units), pregnant or lactating women, and those with comorbid conditions such as diabetes, malignancies, renal diseases, or post-transplant status were also excluded from the study.

2.5. Ethical Considerations

The study was approved by the Institutional Research and Ethics Committee of Kohat University of Science and Technology (Ref No. KUST/Ethical Committee/1423). Patient consent was not required, as the study involved retrospective analysis of anonymized medical records, in accordance with ICH-GCP guidelines published in 2012. Patient confidentiality was maintained throughout the study.

2.6. Statistical Analysis

Descriptive statistics were applied using SPSS (Statistical Package for the Social Sciences) [20]. Frequencies and percentages were calculated for categorical variables (e.g., gender, age group, drug types). Cost-related variables, such as cost per unit dose and total therapy cost per patient, were also summarized. Associations between variables (e.g., gender, number of drugs, and cost of therapy) were analyzed, with statistical significance set at $p < 0.05$.

3. RESULTS AND DISCUSSION

3.1. Demographics

A total of 320 hypertensive patients were included in this study. Among these, 177 were male (55.31%) and 143 were female (44.69%) (Table 1), indicating a slightly higher prevalence of hypertension in males, consistent with other Pakistani and South Asian studies which noted male predominance in hypertensive cohorts [17, 21]. Age distribution showed that the highest number of hypertensive patients were in the age group 41-50 years (46.25%), followed by those aged 51-60 years (36.56%), and 18-40 years (17.18%). These findings suggest that hypertension is more prevalent in middle-age individuals. This aligns with the findings of Fatima et al. [22] as well as the WHO data, which indicate increased hypertension incidence after 40 years of age. The associations between variables were analyzed using chi-square test for gender and therapy type (monotherapy vs. combination) and t-test for gender and cost of therapy. No significant association was found between gender and therapy type ($\chi^2 = 1.24$, $p = 0.27$). Similarly, the mean cost of therapy did not differ significantly between males and females ($p = 0.45$), indicating no gender-based differences in prescribing patterns or costs.

Table 1. Patient Demographics

Demographics		Number	Percentage
Gender	Male	177	55.31%
	Female	143	44.69%
Age of Patient	18-40 years	55	17.18%
	41-50 years	148	46.25%
	51-60 years	117	36.56%
Total		320	100%

3.2. Prescribing Pattern: Monotherapy vs Combination Therapy

Out of the 320 prescriptions analyzed, 215 (67.18%) were for monotherapy and 105 (32.82%) were for fixed-dose combination (FDC) therapy, showing a clear preference for monotherapy among prescribers. This trend is consistent with the JNC 8 and ESC/ESH 2018 guidelines, which recommend starting with monotherapy in Stage I hypertension or in elderly patients, especially if comorbidities are absent. As hypertension prevalence continues to rise globally, appropriate therapeutic strategies become increasingly important [22]. The predominance of monotherapy in this cohort suggests an initial attempt at control with a single agent, with escalation to combination therapy in case of an inadequate response. This stepwise approach aligns with international guidelines.

3.3. Monotherapy Trends

Amlodipine emerged as the most commonly prescribed antihypertensive monotherapy drug with 98 prescriptions (45.58%), followed by losartan with 25 prescriptions (11.63%), and atenolol with 18 prescription (8.37%) (Table 2). This preference for amlodipine may stem from its proven efficacy, once-daily dosing, and a favorable side effects profile. Similar results reported CCBs, particularly amlodipine, as the first-line therapy in primary hypertension due to their superior blood pressure-lowering effect and tolerability [23, 24].

ARBs, such as losartan and telmisartan, were prescribed to a lesser extent in monotherapy, likely due to cost and accessibility issues. Diuretics and ACE inhibitors were also utilized but to a lesser extent, perhaps due to the electrolyte imbalance risks and dry cough associated with ACEIs [25].

Table 2. Prevalence of Monotherapy among Prescribed Antihypertensive Medications

Sr. No.	Monotherapy	Prescription Frequency (<i>f</i>)	Prescription %
1.	Amlodipine	98	45.58%
2.	Losartan	25	11.63%
3.	Atenolol	18	8.37%
4.	Telmisartan	14	6.51%
5.	Frusemide	9	4.19%
6.	Nifedipine	9	4.19%
7.	Ramipril	9	4.19%

Sr. No.	Monotherapy	Prescription Frequency (f)	Prescription %
8.	Enalapril	8	3.72%
9.	Prazosin	8	3.72%
10	Torsemide	6	2.79%
11	Olmesartan	6	2.79%
12	Clonidine	5	2.33%
	Sub-total	215	100%

3.4. Combination Therapy Trends

Among the 105 fixed-dose combinations prescribed, the most frequently used combination was amlodipine + atenolol, accounting for 21 prescriptions (20.00%). This was followed by frusemide + spironolactone, prescribed in 17 cases (16.19%), and losartan + hydrochlorothiazide with 15 prescriptions (14.29%), as shown in Table 3.

The combination of amlodipine (CCB) with atenolol (β -blocker) is rational and synergistic, since it improves both blood pressure and heart rate control [24]. The second most common combination, namely frusemide + spironolactone, is commonly used in volume-overloaded patients, especially those with resistant hypertension or concomitant heart failure [26].

The third most common combination, namely losartan + hydrochlorothiazide, is a well-established combination supported by ACC/AHA and NICE guidelines, which advocate using ARBs with thiazide diuretics for better control and compliance. Similar prescribing patterns were documented in studies by Akhtar et al. for Rawalpindi [27] and Karunarathna et al. for India [28].

Table 3. Prevalence and Proportion of Drugs Administered as Combination Therapy

Sr. No.	Drugs Combination	Prescription Frequency (f)	Prescription %
1.	Amlodipine + Atenolol	21	20.00%
2.	Frusemide + Spironolactone	17	16.19%
3.	Hydrochlorothiazide + Losartan	15	14.29%
4.	Amlodipine + Losartan	13	12.38%
5.	Hydrochlorothiazide + Amlodipine	12	11.43%

Sr. No.	Drugs Combination	Prescription Frequency (f)	Prescription %
6.	Hydrochlorothiazide + Enalapril	11	10.48%
7.	Hydrochlorothiazide + Telmisartan	7	6.67%
8.	Amiloride + Frusemide	5	4.76%
9.	Telmisartan + Amlodipine	4	3.81%
	Sub-total	105	100%

3.5. Cost Analysis of Antihypertensive Therapy

The total cost of antihypertensive prescriptions amounted to PKR 261,153.00, with monotherapy costing PKR 208170.00 and combination therapies costing PKR 52983.00, as shown in tables 4 and 5. Contrary to the common assumption that monotherapy is less costly, the data reveals a higher expenditure on monotherapy, primarily due to the larger number of prescriptions.

Amlodipine was the most commonly prescribed medication in monotherapy, accounting for 98 prescriptions, which greatly increased the total cost of CCBs to PKR 126,714.00. It's interesting to note that atenolol costed PKR 19,638.00, which is a significantly higher per unit dose, even though it was prescribed only 18 times. This is further supported by the data in Table 6, which shows that β -blockers costed an average of PKR 109.1 per unit dose, which is a noteworthy amount considering how little they are used.

Among the various drug classes, CCBs incurred the highest total cost at PKR 132,114.00, representing 50.14% of the total drug expenditure and 34.28% of all prescriptions. This was followed by ARBs with a total cost of PKR 37,238.00 (14.23%), and fixed-dose combinations contributing PKR 52,983.00 (19.29%) to the overall cost. Despite a reasonable number of prescriptions, diuretics proved to be the most cost-effective, with the lowest average cost per unit dose of just PKR 25.2.

Despite incurring the highest total cost, CCBs proved to be clinically and financially beneficial, which explains why they were frequently used to treat hypertension. Their average unit dose cost was a reasonable PKR 123.47. However, despite having a high overall cost, ARBs had a moderate average cost per unit dose of PKR 82.8, which put them in the middle of the cost-effective range among monotherapy choices. Centrally acting

antihypertensives (CAA) and alpha-adrenergic blockers (AABs) were also analyzed for their cost-effectiveness, as shown in Table 4.

Table 4. Utilization and Cost of Antihypertensive Drugs Prescribed as Monotherapy: Daily Dose and Prescription Count

Pharmacological Drug Classes	Drugs	Recommended Daily Dose Range (mg)	Prescription Frequency (f)	Drug Cost (PKR)
β-Blockers	Atenolol	25-50	18	19638.0
	Sub-total		18	19638.0
Diuretics	Furosemide	40	9	1980.0
	Torsemide	10-20	6	1800
	Sub-total		15	3780.0
CCBs	Amlodipine	5-10	98	126714.0
	Nifedipine	20-40	9	5400
	Sub-total		107	132114.0
ARBs	Losartan	25-100	25	16038.0
	Telmisartan	40-80	14	14000
	Olmesartan	20	6	7200
	Sub-total		45	37238.0
ACEIs	Enalapril	2.5-5	8	4000.0
	Ramipril	1.25-5	9	5400.0
	Sub-total		17	9400.0
CAAs	Clonidine	0.1	5	2000.0
	Sub-total		5	2000.0
AABs	Prazosin	5	8	4000.0
	Sub-total		8	4000.0
Total			215	208170.00

CCBs: Calcium channel blockers, ARBs: Angiotensin receptor blockers, ACEIs: Angiotensin converting enzyme inhibitors, CAA: calcium channel blockers, AABs: Alpha adrenergic blockers, PKR: Pakistani rupee

Among the combinations, amlodipine + atenolol had the highest number of prescriptions (21) and incurred the total cost of 12600 PKR. Moreover, losartan + amlodipine was the most expensive combination, costing a total of 13000 PKR, despite having 13 prescriptions. Other combinations, such as frusemide + amiloride, telmisartan + amlodipine, and hydrochlorothiazide + enalapril, had fewer prescriptions but still contributed significantly to the overall cost, with prices ranging from 440 PKR to 526 PKR. The most economical combination was frusemide +

spironolactone, accounting for PKR 2550.00. It was the second most prescribed combination with 17 prescriptions. The total number of prescriptions for these combinations amounted to 105, with a total cost of 52983.0 PKR.

The data suggests that while some combinations, such as amlodipine + atenolol, are more frequently prescribed, others, such as losartan + amlodipine, may be preferred for their efficacy despite higher costs. The total expenditure on these combinations highlights the importance of considering cost-effectiveness in prescribing practices. It is also evident that combination therapies play a crucial role in managing hypertension [29], although their cost can vary significantly. These findings indicate the need for a balanced approach to ensure that patients receive both effective and cost-efficient treatments.

Table 5. Utilization and Cost of Antihypertensive Drugs Prescribed in Combination: Daily Dose and Prescription Count

Fixed Dose Combinations	Recommended Daily Dose Range (mg)	Prescription Frequency (f)	Drug Cost (PKR)
Amlodipine + Atenolol	5/25–5/50	21	12600.0
Furosemide + Spironolactone	20/50	17	2550.0
Losartan + Hydrochlorothiazide	25/12.5–50/12.5	15	10500.0
Losartan + Amlodipine	25/5–50/5	13	13000.0
Amlodipine + Hydrochlorothiazide	5/12.5	12	7200.0
Hydrochlorothiazide + Enalapril	12.5/5	11	643.0
Telmisartan + Hydrochlorothiazide	40/12.5	7	3150.0
Furosemide + Amiloride	40/5	5	1100.0
Telmisartan + Amlodipine	40/5	4	2240.0
Sub-Total		105	52983.0

The average cost per unit dose prescription for various classes of antihypertensive drugs, as well as their total cost and percentage distribution across prescriptions, revealed that among the drug classes CCBs incurred the highest total cost (132114.00 PKR). This accounted for 50.58% of the

total drug cost, while the drug was prescribed in 107 cases, representing 34.28% of the total prescriptions. The average cost per unit dose prescription for CCBs was 123.47 PKR, the highest among the classes.

β -Blockers had a total cost of 19638.0 PKR, making up 7.51% of the total drug cost, and were prescribed 18 times (5.71% of the total prescriptions), with an average cost of 109.1 PKR per unit dose. Diuretics, while accounting for a smaller portion of total costs (1.44%), had the lowest average cost per prescription at 25.2 PKR. Angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) incurred moderate total costs, with ARBs contributing 14.25% to the overall cost at an average cost per unit dose of 82.8 PKR. Whereas, ACEIs contributed 3.59% to the overall cost, with an average cost of 55.3 PKR.

Fixed-dose combinations, which represented 20.28% of the total cost, had a relatively low average cost of 50.4 PKR per unit dose. The lowest costs were observed in centrally acting antihypertensive agents (CAAs) and alpha-adrenergic blockers (AABs), with average costs per unit dose of 40.0 PKR and 50.0 PKR, respectively.

CCBs were the most frequently prescribed and accounted for the largest share of the total drug cost. However, diuretics and CAAs were more cost-effective. The data highlights the need for careful cost management in prescribing practices, particularly given the wide variation in costs across different anti-hypertensive drug classes.

Table 6. Comparative Evaluation of Unit Dose Costs among Antihypertensive Medications

Pharmacological Drug Classes	Overall Medication Cost	Overall Medication Expenditure (%)	Number of Prescriptions	Prescription %age	Average Cost/Unit Dose Prescription
Beta Blocker	19638.0	7.51%	18	5.71%	109.1
Diuretics	3780.0	1.44%	15	5%	25.2
CCBs	132114.0	50.58%	107	34.28%	123.47
ARBs	37238.0	14.25%	45	14.06%	82.8
ACEIs	9400.0	3.59%	17	6.07%	55.3
CAAs	2000.0	0.76%	5	1.78%	40.0
AABs	4000.0	1.53%	8	2.84%	50.0
Fixed dose combinations	52983.0	20.28%	105	32.81%	50.4
Total	261,153.00	100%	320	100%	

3.6. Cost Efficiency and Clinical Justification

Despite being costlier on average, combination therapies (especially ARB + HCTZ and CCB + β -blocker) offer improved compliance, fewer adverse effects, and better control in patients with co-existing conditions, justifying their use. Similar pharmacoeconomic outcomes were observed in a study by Sharma et al. [30], which concluded that FDCs improve cost-effectiveness when long-term control and compliance are considered [31].

Previous studies similarly reported cost disparities among antihypertensive drugs. Fixed-dose combinations, although generally more expensive than monotherapy, may ultimately reduce total healthcare costs by improving adherence and clinical outcomes [31, 32]. However, deviation from guideline-recommended regimens, such as underutilization of cost-effective thiazide diuretics, may increase treatment costs unnecessarily [33].

A systematic review of 26 studies conducted between 2000 and 2018 revealed frequent deviations from internationally recognized hypertension management guidelines, including those issued by the Joint National Committee (JNC) and the Pakistan Hypertension League. Although thiazide diuretics are recommended as first-line agents due to their affordability and cardiovascular benefits, beta-blockers and ACE inhibitors continue to be commonly prescribed, thereby increasing overall treatment expenses [34]. This trend was also evident in the current study, where ARBs and CCBs were found to be frequently used, while diuretics were less commonly prescribed.

Brand prescribing over generics further contributes to the economic burden on patients. Educational and behavioral interventions have been shown to improve blood pressure outcomes [35]. For instance, a randomized controlled trial in six major cities of Pakistan demonstrated that combining home health education with general practitioner training significantly improved hypertension control [36]. These findings advocate for integrated, community-based interventions to improve adherence, reduce costs, and enhance overall management.

The current study highlights the urgent need for cost-effective antihypertensive prescribing in low-income countries like Pakistan. There is a clear need for policy reforms promoting the use of affordable, evidence-based therapies. WHO recommendations support the judicious use of combination therapy and emphasize the importance of using cost-effective

medications to optimize health outcomes [37]. The increased cost burden observed in this study can be attributed to the frequent use of ARBs, CCBs, beta-blockers, and FDCs, as well as the underutilization of more affordable options, such as thiazide diuretics.

Additionally, drugs like telmisartan and olmesartan, while expensive, offer renal protection and are suitable for diabetic hypertensive patients, adding clinical value beyond hypertension control.

4. CONCLUSION

This study demonstrates a strong preference for monotherapy, with 67.18% of patients receiving a single antihypertensive agent and amlodipine being the most commonly prescribed medication. The study found that combination therapy, though less frequent, was generally rational and in accordance with clinical guidelines. While amlodipine was the most frequently prescribed drug, atenolol and ACE inhibitors were found to have the highest average unit cost. Calcium channel blockers (CCBs) proved to be the most cost-effective in terms of cost-to-prescription ratio. Overall, while rational prescribing based on clinical need and cost-effectiveness was observed, opportunities remain for improvement through better formulary control and targeted physician training. Policy interventions promoting the use of affordable, evidence-based therapies, such as thiazide diuretics, are recommended to optimize hypertension management in resource-limited settings.

4.1. Limitations

This study was limited to a single-center cohort and drug costs were calculated from the available hospital data, which may vary regionally. Furthermore, indirect costs (e.g., hospital visits, investigations) were not included.

Author Contribution

Marvi Shaheen: data curation, investigation, and methodology. **Sajid Khan Sadozai:** conceptualization, formal analysis, validation, writing, review and editing, and project administration. **Rooh Ullah:** software, supervision, visualization. **Sajid Hussain:** data curation, and investigation. **Fawad Ali:** software, supervision, visualization. **Majid Khan Sadozai:** writing original draft, methodology, and project administration. **Farina Kanwal:** project administration and resources. **Naveed Safdar:** data curation, and software.

Conflict of Interest

The authors of the manuscript have no financial or non-financial conflict of interest.

Data Availability

Relevant data generated and analyzed during this study can be obtained from the corresponding author upon request. Access to certain portions of the dataset may be limited in order to maintain patient confidentiality and to comply with institutional guidelines.

Funding Details

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

Generative AI Disclosure Statement

The authors did not use any type of generative artificial intelligence software for this research.

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