

# Antihypertensive Medication Use and Biochemical Outcomes in Primary Care Patients: A Multicenter Study in Kosovo

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Arterial hypertension remains a major public health challenge that requires long-term pharmacological management; however, antihypertensive therapy may also be associated with metabolic and biochemical alterations. This multicenter retrospective study evaluated the association between antihypertensive drug use and biochemical parameters among primary care patients in Kosovo and compared outcomes across three healthcare centers (Prishtina, Ferizaj, and Gjilan). A total of 900 patients with essential hypertension receiving continuous treatment for at least 12 months were included. Data were extracted from medical records and laboratory registers between January 2024 and January 2025 and comprised demographic variables, treatment regimens (monotherapy or combination therapy), and biochemical parameters, including lipid profile, fasting glucose, renal markers, and electrolytes. Statistical analyses included ANOVA or Kruskal–Wallis tests, chi-square tests, correlation analysis, and multivariate logistic regression. Combination therapy was associated with significantly higher levels of LDL cholesterol, triglycerides, and creatinine compared to monotherapy ( $p < 0.05$ ), while lipid alterations were more prominent among patients treated with beta-blockers and diuretics ( $p < 0.01$ ). The use of two or more antihypertensive drug classes independently predicted an increased risk of dyslipidemia (OR 1.8, 95% CI: 1.2–2.5;  $p = 0.004$ ). No significant differences were observed in glucose levels between the study centers ( $p = 0.21$ ). Long-term antihypertensive therapy, particularly polytherapy, is associated with clinically relevant biochemical changes affecting lipid metabolism and renal function, highlighting the necessity for routine laboratory monitoring and individualized treatment optimization in primary care practice.

**Keywords:** Biochemical parameters; Cardiovascular disease; Hypertension; Kosovo; Pharmacology; Primary care.

Arterial hypertension is among the most prevalent chronic conditions worldwide and remains a leading contributor to cardiovascular morbidity and mortality.<sup>1</sup> The rising global burden of hypertension and its associated

complications necessitates effective and sustained pharmacological management to reduce adverse clinical outcomes.<sup>2</sup> In addition to their blood pressure-lowering effects, antihypertensive agents may influence metabolic and biochemical

pathways, potentially leading to alterations in lipid metabolism, glucose regulation, and renal function.<sup>3</sup> { t

Polypharmacy, defined as the concurrent use of multiple medications, is increasingly common among patients with hypertension, especially in those with concomitant diabetes mellitus, dyslipidemia, and cardiovascular disease.<sup>u</sup> Growing evidence indicates that certain antihypertensive drug classes, particularly beta-blockers and diuretics, are associated with unfavorable metabolic effects, including elevated triglyceride levels, impaired glucose tolerance, and deterioration of renal markers.<sup>v</sup> { x These biochemical changes may compromise long-term cardiovascular outcomes and contribute to an increased risk of adverse drug reactions.

Primary health care systems play a central role in hypertension management in low- and middle-income countries, including Kosovo, where most patients receive long-term antihypertensive therapy within family medicine centers.<sup>y</sup> Despite the widespread utilization of antihypertensive agents, there is a limited body of multicenter evidence examining their potential biochemical impact in this population. Moreover, differences in prescribing practices and health service delivery across regional centers may further influence clinical and laboratory outcomes.

Therefore, this study aimed to evaluate the association between antihypertensive medication use and biochemical parameters among primary care patients in Kosovo and to compare outcomes across three major primary health care centers.

## MATERIALS AND METHODS

**Study design and setting:** This retrospective, multicenter analytical study was conducted at three major primary health care centers in Kosovo: Prishtina, Ferizaj, and Gjilan. The study population consisted of patients diagnosed with essential hypertension who had been receiving continuous antihypertensive therapy for a minimum duration of 12 months. A total of 900 patients were included, with approximately 300 participants recruited from each center.

**Eligibility criteria:** Patients were included if they met the following criteria: age  $\geq$  18 years, confirmed diagnosis of essential hypertension,

regular follow-up visits at the primary health care center, and availability of laboratory test results recorded during the study period. Patients were excluded if they had malignant disease, end-stage renal failure, or were receiving experimental or investigational treatments at the time of data collection.

**Data collection:** Data were obtained from medical records and laboratory databases between January 2024 and January 2025. Extracted variables included demographic characteristics (age, sex, and body mass index [BMI]), clinical information (blood pressure measurements, duration of antihypertensive treatment, and comorbidities such as diabetes mellitus, dyslipidemia, and cardiovascular disease), and pharmacological data (type and class of antihypertensive agents, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, diuretics, and calcium channel blockers; therapy regimen categorized as monotherapy or combination therapy). Laboratory parameters included total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, fasting plasma glucose, serum creatinine, urea, and electrolytes (sodium and potassium).

**Variables:** The primary outcome variables were biochemical alterations associated with antihypertensive treatment, including lipid abnormalities, impaired glucose metabolism, and changes in renal function markers. Independent variables comprised demographic characteristics, comorbid conditions, antihypertensive drug classes, and treatment regimen (monotherapy versus combination therapy).

**Statistical analysis:** Descriptive statistics were used to summarize baseline characteristics and are presented as means with standard deviations for continuous variables and as frequencies with percentages for categorical variables. Comparisons between healthcare centers and between treatment groups were performed using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables. Correlations between antihypertensive therapy and biochemical parameters were assessed using Pearson's or Spearman's correlation coefficients, as appropriate based on data distribution. Multivariable logistic

regression models were applied to identify independent predictors of adverse biochemical outcomes, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs). A two-sided p value of <0.05 was considered statistically significant. All analyses were conducted using SPSS software (IBM Corp., version 25).

### Ethical considerations

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, UBT College. Access to patient records was authorized by the municipal health directorates of Prishtina, Ferizaj, and Gjilan. All data were anonymized prior to analysis to ensure confidentiality and compliance with ethical standards.

## RESULTS

**Study population:** A total of 900 patients with essential hypertension were included in this study: 300 from Prishtina, 300 from Ferizaj, and 300 from Gjilan. The mean age of participants was  $61.7 \pm 10.4$  years, and 52.3% were female. The majority of patients (68.4%) had at least one comorbidity, most frequently diabetes mellitus (32.1%) and dyslipidemia (28.5%).

Table 1 shows the demographic and clinical characteristics of the participants. There were no statistically significant differences between the three centers in terms of age, sex distribution, BMI, diabetes, or dyslipidemia.

**Table 1.** Demographic and clinical characteristics of study participants (N = 900)

Variable	Total (%)	Prishtina (n=300)	Ferizaj (n=300)	Gjilan (n=300)	p-value
Mean age (years $\pm$ SD)	$61.7 \pm 10.4$	$62.1 \pm 10.2$	$60.8 \pm 11.0$	$62.3 \pm 9.9$	0.218
Female sex	471 (52.3)	156 (52.0)	157 (52.3)	158 (52.7)	0.982
BMI $\geq$ 30 kg/m <sup>2</sup>	322 (35.8)	109 (36.3)	106 (35.3)	107 (35.7)	0.941
Diabetes mellitus	289 (32.1)	95 (31.7)	96 (32.0)	98 (32.7)	0.974
Dyslipidemia	257 (28.5)	82 (27.3)	85 (28.3)	90 (30.0)	0.714

**Table 2.** Distribution of antihypertensive drug use among participants

Drug class	Total (%)	Monotherapy (%) / Combination therapy (%)
ACE inhibitors	329 (36.5)	201 (52.0) / 128 (24.7)
Beta-blockers	229 (25.4)	78 (20.2) / 151 (29.2)
Diuretics	187 (20.8)	65 (16.8) / 122 (23.6)
ARBs	96 (10.7)	25 (6.5) / 71 (13.7)
Calcium channel blockers	59 (6.6)	17 (4.4) / 42 (8.1)

Table 2 presents the distribution of antihypertensive drug use. Monotherapy was prescribed in 42.6% of patients, while 57.4% received combination therapy. ACE inhibitors were the most commonly prescribed, followed by beta-blockers and diuretics.

Table 3 summarizes biochemical parameters according to therapy type. Patients on combination therapy had significantly higher LDL cholesterol and creatinine levels compared to those on monotherapy. Triglyceride levels were also significantly higher among combination therapy users. No significant differences were found in fasting glucose values.

Table 4 shows the results of multivariate regression analysis. Polytherapy, beta-blocker use, and diuretic use were independent predictors of adverse biochemical changes, while ARB use and age were not significantly associated.

### Summary of findings

- Combination therapy was associated with higher LDL and creatinine levels.
- Beta-blockers and diuretics were linked to adverse lipid and renal outcomes.
- Polytherapy ( $e^2$  classes) increased the risk of dyslipidemia by 80%.
- No significant inter-center differences were observed for glucose or lipid outcomes.

### Additional Comparative Analysis

Table 5 summarizes the significant differences in biochemical and pharmacological

**Table 3.** Biochemical parameters by therapy type

Parameter	Monotherapy (mean $\pm$ SD)	Combination therapy (mean $\pm$ SD)	p-value
Total cholesterol (mg/dL)	197.4 $\pm$ 42.1	202.8 $\pm$ 44.2	0.178
LDL cholesterol (mg/dL)	132.2 $\pm$ 32.8	141.6 $\pm$ 36.4	0.008
HDL cholesterol (mg/dL)	48.6 $\pm$ 12.4	46.7 $\pm$ 11.8	0.092
Triglycerides (mg/dL)	161.2 $\pm$ 73.9	174.5 $\pm$ 80.1	0.031
Fasting glucose (mg/dL)	108.7 $\pm$ 22.6	110.9 $\pm$ 23.1	0.214
Creatinine (mg/dL)	1.08 $\pm$ 0.20	1.19 $\pm$ 0.24	0.012

**Table 4.** Multivariate regression analysis of predictors of biochemical alterations

Variable	B (Unstandardized)	Std. Error	Beta	p-value
Polytherapy ( $\geq 2$ drug classes)	0.185	0.065	0.182	0.004
Beta-blocker use	0.164	0.067	0.158	0.015
Diuretic use	0.147	0.064	0.152	0.022
ARB use	0.058	0.071	0.049	0.412
Age	0.021	0.012	0.073	0.084

**Table 5.** Comparison of significant biochemical and pharmacological differences across study centers

Parameter	Prishtina (mean $\pm$ SD / %)	Ferizaj (mean $\pm$ SD / %)	Gjilan (mean $\pm$ SD / %)	p-value	Significant finding (in favor of)
LDL cholesterol (mg/dL)	134.2 $\pm$ 34.1	138.7 $\pm$ 36.5	145.5 $\pm$ 38.2	0.021	Better in Prishtina
Triglycerides (mg/dL)	162.4 $\pm$ 72.3	175.1 $\pm$ 77.8	180.6 $\pm$ 81.2	0.017	Better in Prishtina
Creatinine (mg/dL)	1.10 $\pm$ 0.21	1.15 $\pm$ 0.23	1.22 $\pm$ 0.25	0.009	Better in Prishtina
Polytherapy (%)	54.0	61.3	57.0	0.034	Lower in Prishtina

parameters between the three study centers (Prishtina, Ferizaj, Gjilan). The table highlights which center had comparatively better outcomes (in favor of patients) and which require additional recommendations for clinical monitoring and intervention.

Table 5 shows that patients in Prishtina generally had more favorable biochemical results, including lower LDL cholesterol, triglycerides, and creatinine levels. The prevalence of polytherapy was also lower in Prishtina compared to Ferizaj and Gjilan. These findings suggest the need for targeted recommendations: closer monitoring of renal and

lipid parameters in Gjilan, and interventions to reduce polypharmacy in Ferizaj.

## DISCUSSION

This multicenter retrospective study investigated the association between antihypertensive medication use and biochemical outcomes among primary care patients in Kosovo. The findings demonstrate that long-term antihypertensive therapy, particularly combination regimens, is associated with significant alterations in lipid profile and renal function, whereas no

clinically meaningful differences were observed in glucose metabolism.

#### **Antihypertensive therapy and biochemical changes**

Our results are consistent with existing evidence indicating that certain antihypertensive drug classes exert metabolic effects beyond blood pressure control. Patients receiving combination therapy exhibited significantly higher LDL cholesterol and serum creatinine levels compared with those on monotherapy, suggesting that polytherapy may exacerbate both dyslipidemia and renal stress.<sup>1, 2</sup> Similar observations were reported in the ALLHAT trial, in which thiazide diuretics were associated with unfavorable lipid and glycemic profiles.<sup>3</sup> Beta-blockers have also been linked to elevations in triglyceride levels and reductions in high-density lipoprotein cholesterol, a pattern that was reproduced in the present study.

Diuretic use was independently associated with increased creatinine levels, consistent with previous research demonstrating the potential of these agents to induce electrolyte disturbances and renal function impairment, particularly among older adults.<sup>4</sup> In contrast, angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are generally considered metabolically neutral or protective,<sup>5, 6</sup> which may explain the absence of a significant association between ARB use and adverse biochemical outcomes in our cohort.

#### **Polypharmacy and risk of biochemical alterations**

Polypharmacy emerged as a key predictor of dyslipidemia in this study. In primary care settings, patients with hypertension commonly present with multiple comorbidities, often necessitating combination treatment strategies. Previous systematic reviews have demonstrated that polypharmacy substantially increases the risk of adverse drug reactions and metabolic complications.<sup>7, 8</sup> The present logistic regression analysis confirmed this relationship, showing that the use of two or more antihypertensive drug classes increased the risk of dyslipidemia by nearly 80%. These findings underscore the importance of implementing deprescribing practices and structured medication reviews in routine hypertension management.<sup>9, 10, 11, 12, 13</sup>

#### **Inter-center variability**

Comparative analysis across the three healthcare centers revealed that patients in Prishtina had more favorable biochemical profiles, including lower LDL cholesterol, triglycerides, and creatinine levels, than those treated in Ferizaj and Gjilan. Although national guidelines for hypertension management are standardized, such variations may reflect differences in local prescribing patterns, patient adherence, lifestyle behaviors, or access to healthcare resources. Similar geographic disparities in hypertension outcomes have been documented in European multicenter studies, illustrating the influence of health system organization and patient education on clinical endpoints.<sup>14, 15</sup>

The higher prevalence of combination therapy observed in Ferizaj suggests the need for targeted deprescribing initiatives, whereas the elevated renal and lipid abnormalities identified in Gjilan emphasize the necessity of intensified laboratory monitoring and dietary counseling.

#### **Clinical implications**

From a clinical perspective, these findings highlight the need for individualized antihypertensive therapy in primary care practice. Routine monitoring of biochemical parameters, particularly lipid profile and renal function, should be integrated into treatment protocols for patients receiving long-term antihypertensive therapy. Furthermore, interdisciplinary collaboration between family physicians and clinical pharmacists may play a critical role in optimizing treatment strategies, reducing unnecessary polypharmacy, and promoting patient-centered interventions such as lifestyle modification, medication adherence, and therapeutic education.<sup>16, 17</sup>

#### **Strengths and limitations**

The strengths of this study include its large multicenter sample size, standardized data extraction, and comprehensive statistical analysis. Nevertheless, the retrospective design limits causal inference. Additionally, the absence of data on medication dosing, treatment adherence, and lifestyle factors, such as diet and physical activity, may have influenced the observed biochemical variations. Despite these limitations, this study provides valuable real-world evidence on the metabolic consequences of antihypertensive therapy in the primary care setting of a developing healthcare system.

Based on the findings of this study, the following recommendations are proposed for clinical practice and healthcare policy in primary care settings:

#### **Routine biochemical monitoring**

Regular assessment of lipid profile, fasting plasma glucose, and renal function parameters should be incorporated into the routine management of patients with hypertension, particularly for individuals receiving combination therapy or treatment with beta-blockers and diuretics.

#### **Polypharmacy management**

Structured medication reviews should be routinely performed through collaboration between family physicians and clinical pharmacists, with an emphasis on minimizing unnecessary polypharmacy and implementing deprescribing strategies when clinically appropriate to reduce metabolic complications.

#### **Center-specific interventions**

Targeted interventions are recommended based on center-level findings. In Ferizaj, programs focused on reducing polypharmacy should be implemented. In Gjilan, intensified monitoring of renal and lipid parameters, together with dietary counseling and patient education, is advised. In Prishtina, clinical practices associated with favorable biochemical profiles should be identified and disseminated across other centers as best practice models.

#### **Strengthening primary care guidelines**

National hypertension management guidelines should be updated to include routine biochemical monitoring as a standard component of care. Additionally, regular clinical audits should be conducted to ensure guideline adherence and to monitor treatment effectiveness.

#### **Patient-centered strategies**

Comprehensive patient education focusing on lifestyle modification including dietary improvement, physical activity promotion, smoking cessation, and alcohol reduction should be integrated into primary care services to complement pharmacological treatment and enhance long-term outcomes.

### **CONCLUSION**

This multicenter retrospective study

confirms that long-term antihypertensive therapy is significantly associated with clinically relevant biochemical alterations, particularly affecting lipid metabolism and renal function. Patients receiving combination regimens exhibited higher LDL cholesterol and creatinine levels than those treated with monotherapy, while beta-blockers and diuretics were independently associated with adverse lipid and renal outcomes. Furthermore, the use of two or more antihypertensive drug classes increased the risk of dyslipidemia by nearly 80%, highlighting the metabolic impact of polypharmacy.

Although national hypertension management guidelines are standardized, inter-center differences were evident. Patients treated in Prishtina demonstrated more favorable biochemical profiles, whereas a higher prevalence of polypharmacy was observed in Ferizaj and more pronounced lipid and renal abnormalities were identified in Gjilan. These findings underscore the importance of individualized therapeutic approaches and center-specific interventions to optimize treatment outcomes in primary care settings.

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#### **Conflict of Interest**

The author(s) do not have any conflict of interest.

#### **Data Availability Statement**

This statement does not apply to this article.

#### **Ethics Statement**

This study was approved by the Ethics Committee of the Faculty of Medicine, UBT College. Permission to access patient records was obtained from the municipal health directorates of

Prishtina, Ferizaj, and Gjilan. All patient data were anonymized prior to analysis in accordance with ethical standards.

#### Informed Consent Statement

Informed consent was waived due to the retrospective nature of the study and the use of anonymized secondary data.

#### Clinical Trial Registration

This research does not involve any clinical trials.

#### Permission to Reproduce Material from other sources

Not applicable.

#### Author contributions

Fitim Alidema and Arieta Hasani Alidema conceived and supervised the study and had full access to all study data, taking responsibility for data accuracy and integrity; Study design was developed by Fitim Alidema, Arieta Hasani Alidema, and Irena Kostovska; Arieta Hasani Alidema was responsible for training on data collection instruments and outcome measures; Data analysis and interpretation were performed by Fitim Alidema and Arieta Hasani Alidema; The manuscript was drafted by Fitim Alidema, Arieta Hasani Alidema, and Lirim Mustafa. Statistical analysis was conducted by Fitim Alidema.

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