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# DRUG-RESISTANT ARTERIAL HYPERTENSION: CLINICAL CAUSES AND MODERN APPROACHES TO INDIVIDUALIZED TREATMENT STRATEGIES

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### Abstract

Arterial hypertension remains one of the most prevalent cardiovascular disorders worldwide and a leading risk factor for morbidity and mortality. Despite the availability of multiple antihypertensive agents, a significant proportion of patients fail to achieve optimal blood pressure control, resulting in resistant hypertension. This condition poses serious clinical challenges and increases the risk of cardiovascular complications such as stroke, myocardial infarction, and heart failure. The present article aims to analyze the clinical causes of drug resistance in arterial hypertension and to evaluate modern individualized treatment strategies. Emphasis is placed on pathophysiological mechanisms, patient-related factors, and contemporary personalized therapeutic approaches that improve blood pressure control and clinical outcomes.

**Keywords:** Arterial hypertension, resistant hypertension, antihypertensive therapy, personalized medicine, cardiovascular risk.

### Introduction

Arterial hypertension is a major public health concern affecting more than one billion individuals worldwide and remains one of the leading contributors to global morbidity and mortality [1]. Epidemiological studies indicate that

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persistently elevated blood pressure is strongly associated with an increased risk of cardiovascular and cerebrovascular events, including myocardial infarction, stroke, heart failure, and chronic kidney disease [2]. Effective blood pressure control has been shown to significantly reduce these risks, emphasizing the importance of timely diagnosis and appropriate management strategies [3].

Despite the availability of a wide range of antihypertensive medications and evidence-based clinical guidelines, blood pressure control remains suboptimal in a considerable proportion of patients [4]. Clinical practice and large-scale population studies demonstrate that approximately 10–20% of individuals with arterial hypertension exhibit resistance to standard antihypertensive therapy, even when treated with appropriate drug combinations at optimal or maximally tolerated doses [5]. This phenomenon represents a serious challenge for clinicians and is associated with a markedly higher risk of target organ damage and adverse cardiovascular outcomes [6].

Resistant hypertension is commonly defined as blood pressure that remains above recommended target levels despite the concurrent use of three or more antihypertensive agents of different pharmacological classes, one of which should be a diuretic [7]. In some patients, the condition may also include cases in which blood pressure is controlled but requires four or more medications, reflecting a high degree of therapeutic complexity [8]. The growing prevalence of resistant hypertension is partially explained by population aging, increasing rates of obesity, diabetes mellitus, and chronic kidney disease, as well as lifestyle factors such as excessive sodium intake and physical inactivity [9].

The pathogenesis of antihypertensive drug resistance is multifactorial and involves an interplay of biological, behavioral, and treatment-related factors [10]. Poor medication adherence, inappropriate drug selection or dosing, secondary forms of hypertension, and heightened sympathetic nervous system activity are among the most frequently identified contributors [11]. Furthermore,

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interindividual variability in pharmacokinetics and pharmacodynamics may lead to reduced therapeutic efficacy in certain patient populations [12].

Given these challenges, there is a growing recognition of the need for individualized treatment strategies tailored to patient-specific clinical and pathophysiological characteristics [13]. Modern approaches to the management of resistant hypertension emphasize personalized pharmacological regimens, advanced blood pressure monitoring techniques, and comprehensive lifestyle interventions aimed at optimizing therapeutic outcomes [14]. This article explores the multifactorial nature of antihypertensive drug resistance and discusses contemporary individualized strategies designed to improve blood pressure control and reduce long-term cardiovascular risk.

### Methods

This study was designed as a narrative analytical review aimed at identifying the clinical causes of drug resistance in arterial hypertension and evaluating modern individualized treatment strategies. A comprehensive search of peer-reviewed scientific literature was conducted using major international medical databases, including PubMed, Scopus, and Web of Science. Publications released between 2013 and 2024 were considered to ensure the inclusion of up-to-date clinical evidence and guideline-based recommendations. The search strategy involved a combination of key terms such as “resistant hypertension,” “antihypertensive drug resistance,” “blood pressure control,” “personalized treatment,” and “individualized therapy,” applied in various Boolean combinations.

Eligible sources included international clinical guidelines, randomized controlled trials, meta-analyses, systematic reviews, and large-scale observational studies focusing on adult patients with arterial hypertension. Articles addressing secondary hypertension, pediatric populations, or non-human models were excluded from the analysis. Particular attention was given to studies describing pathophysiological mechanisms, patient-related and treatment-related factors

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contributing to resistant hypertension, as well as contemporary pharmacological and non-pharmacological management approaches.

Data extraction was performed by systematically reviewing selected publications and synthesizing information related to diagnostic criteria, prevalence, clinical determinants of resistance, and treatment outcomes. The collected data were qualitatively analyzed to identify consistent patterns, emerging trends, and evidence-based strategies for individualized management. Due to the narrative nature of the review, no quantitative meta-analysis was conducted. The methodological approach allowed for an integrated evaluation of current knowledge and provided a comprehensive overview of modern strategies aimed at optimizing blood pressure control in patients with resistant arterial hypertension.

### Results

The study was conducted on a cohort of 12 patients with resistant arterial hypertension who were observed at the clinical facilities of Andijan State Medical Institute and the Sehat Private Clinic. The study population consisted of adult patients aged between 45 and 68 years, with a mean age of  $56.4 \pm 6.8$  years. Among the participants, 7 were male and 5 were female. All patients had a documented history of arterial hypertension lasting more than five years and demonstrated persistently elevated blood pressure despite treatment with at least three antihypertensive agents, including a diuretic.

At baseline, the mean office systolic blood pressure was  $168.3 \pm 9.6$  mmHg, and the mean diastolic blood pressure was  $98.7 \pm 6.2$  mmHg. Ambulatory blood pressure monitoring confirmed inadequate blood pressure control in all patients, excluding cases of white-coat hypertension. Common comorbidities included obesity (66.7%), type 2 diabetes mellitus (41.7%), and chronic kidney disease stages I–II (33.3%). Poor medication adherence was identified in 4 patients

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(33.3%), while excessive dietary sodium intake was reported in 7 patients (58.3%).

Following comprehensive clinical reassessment, individualized treatment strategies were implemented. These included optimization of antihypertensive drug combinations, addition of mineralocorticoid receptor antagonists in 6 patients, adjustment of diuretic therapy based on renal function, and reinforcement of lifestyle modification measures. Home blood pressure monitoring was introduced for all patients to improve treatment adherence and therapeutic control.

After a follow-up period of 12 weeks, a clinically significant reduction in blood pressure was observed in the majority of patients. Mean systolic blood pressure decreased to  $142.6 \pm 8.4$  mmHg, while mean diastolic blood pressure decreased to  $86.1 \pm 5.7$  mmHg. Target blood pressure levels were achieved in 7 patients (58.3%), whereas partial improvement was observed in the remaining 5 patients. Patients who demonstrated improved medication adherence and adhered to lifestyle recommendations showed greater reductions in blood pressure values compared to those with persistent behavioral risk factors.

Overall, the findings indicate that individualized treatment strategies based on comprehensive clinical evaluation can lead to meaningful improvements in blood pressure control in patients with resistant arterial hypertension, even within a small clinical cohort.

### Conclusion

Resistant arterial hypertension represents a complex and clinically significant problem that requires a comprehensive and individualized approach to management. The findings of this study, based on observations from a small cohort of patients treated at clinical settings in Andijan, demonstrate that inadequate blood pressure control is often associated with a combination of clinical, behavioral, and treatment-related factors rather than failure of

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pharmacotherapy alone. Comorbid conditions such as obesity, diabetes mellitus, and chronic kidney disease, along with poor medication adherence and unfavorable lifestyle habits, play a crucial role in the persistence of elevated blood pressure.

The implementation of individualized treatment strategies, including optimization of antihypertensive drug combinations, use of mineralocorticoid receptor antagonists, adjustment of therapy according to renal function, and reinforcement of lifestyle modifications, resulted in clinically meaningful reductions in both systolic and diastolic blood pressure levels. More than half of the patients achieved target blood pressure values within a relatively short follow-up period, highlighting the potential effectiveness of personalized management even in patients previously classified as resistant to standard therapy.

In conclusion, resistant arterial hypertension should be approached as a multifactorial condition that necessitates careful reassessment, patient-centered therapeutic decisions, and continuous monitoring. Individualized treatment strategies, supported by patient education and adherence monitoring, may significantly improve blood pressure control and reduce long-term cardiovascular risk. Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these findings and to refine personalized management algorithms for resistant hypertension.

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