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Assessment of the Significance of Molecular Genetic Markers in the Development of Arterial Hypertension

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Abstract This article assesses the significance of molecular genetic markers in the development of arterial hypertension. Arterial hypertension is one of the most widespread and chronic cardiovascular conditions, with genetic predisposition playing a crucial role in its pathogenesis. The study analyzes the influence of genetic polymorphisms, particularly those associated with the renin-angiotensin-aldosterone system, on blood pressure regulation. The findings indicate that certain gene variants increase the risk of hypertension. The article highlights the importance of molecular genetic markers in early diagnosis and personalized treatment strategies for arterial hypertension.

Keywords Molecular genetics, Genetic markers, Polygenic hypertension, Monogenic hypertension, Genome, Pharmacogenetics, Personalized medicine, Gene therapy, Epigenetics

1. Introduction

Arterial hypertension currently ranks among the leading cardiovascular diseases globally. According to the World Health Organization, this condition is increasingly spreading to younger age groups each year, placing a direct and indirect economic burden on the global healthcare system. Particularly, its chronic forms can lead to life-threatening complications such as myocardial infarction, stroke, and heart failure. Therefore, deeply studying the etiological foundations of arterial hypertension, especially analyzing its molecular and genetic mechanisms, is one of the priority areas in modern medicine.

In recent years, with the complete decoding of the human genome, research into the genetic determination of diseases has significantly advanced. Specifically, genetic polymorphisms, epigenetic modifications, and disruptions in the gene expression network are considered key pathogenic factors in the development of arterial hypertension. In particular, genetic markers related to blood pressure regulation via the renin-angiotensin-aldosterone system, sympathetic-adrenal activity, sodium balance, endothelial dysfunction, and ion channels are being thoroughly analyzed. Genome-wide association studies conducted in various populations have demonstrated that arterial hypertension is a multifactorial disease, where environmental factors and genetic components interact in a complex manner. For example, certain allelic variants found in genes such as angiotensin-converting enzyme, angiotensinogen, aldosterone synthase, beta-adrenergic receptors, endothelin, and nitric oxide synthase may significantly increase an individual's susceptibility to arterial hypertension.

Moreover, advanced molecular biology methods, including polymerase chain reaction-based genotyping, high-precision sequencing technologies, and bioinformatics analysis, provide the possibility of early detection of mutations related to disease development. This, in turn, creates the potential for developing pharmacogenetic strategies based on individualized approaches, i.e., treatment methods tailored to each patient's genotype.

This article critically analyzes the molecular genetic markers that play a significant role in the development of arterial hypertension. Specifically, their role in pathogenic mechanisms, clinical significance, and potential as diagnostic tools are discussed. Based on the research findings, the article explores the advantages of these markers in early diagnosis, identifying risk groups, and personalizing therapy.

2. Main Part

According to recent global epidemiological data, arterial hypertension currently affects approximately 30 to 35 percent of the world's population. Based on reports from the World Health Organization, it is estimated that one in every three adults worldwide suffers from this condition. However, the prevalence and genetic basis of hypertension vary significantly

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across continents and regions, indicating its polygenic nature and strong association with environmental factors.

In African countries, arterial hypertension is one of the most prevalent conditions, with certain regions reporting a prevalence of over 45 percent among the population. Studies conducted in Nigeria, Kenya, and the Republic of South Africa have shown that the populations in these areas are genetically predisposed to salt sensitivity, with a high frequency of genetic variants responsible for sodium metabolism. For instance, allelic variants in genes associated with sodium channels, such as SCNN1A, SLC4A5, and ADD1, have been found to increase sodium reabsorption in the kidneys, resulting in persistently elevated blood pressure.

In Asia, particularly in countries like China, Japan, South Korea, and India, the molecular and genetic aspects of arterial hypertension have been extensively studied. Genome -wide association studies conducted in Japan and China have identified certain variants in the AGT, ACE, NOS3, and AGTR1 genes that are associated with a higher risk of developing hypertension. Specifically, the D allele of the ACE gene and the Glu298Asp polymorphism of the NOS3 gene have demonstrated a strong association with hypertension in the Chinese population. In India, the M235T polymorphism in the angiotensinogen gene and mutations in beta-adrenergic receptor genes play a significant role in the development of hypertension. These genetic effects are further exacerbated by epigenetic mechanisms that manifest in response to diets rich in carbohydrates and fats.

In Europe, especially in Italy, Germany, Poland, and Scandinavian countries, there has been substantial research into the genetic foundations of hypertension. Among European populations, polymorphisms in the ACE, AGT, and CYP11B2 genes have been widely examined, and their roles in the development of hypertension have been strongly substantiated. A major meta-analysis conducted in Germany found that the D allele of the ACE I/D polymorphism increases the risk of hypertension by 1.4 times. Furthermore, epigenetic markers such as DNA methylation and microRNA expression are being explored in European countries for their influence on blood pressure regulation.

In North America, particularly in the United States and Canada, genetic differences are clearly observed across various racial and ethnic groups. Among African Americans, high salt sensitivity and overactivity of the renin-angiotensin-aldosterone system have been identified as key contributors to hypertension. Moreover, novel variants discovered in genes such as SLC4A5, NPPA, and NPR3 have been linked with an increased risk of hypertension in this population.

Although fewer studies have been conducted in South America, investigations in countries such as Brazil and Argentina have examined classic polymorphisms in the ACE and AGT genes. These studies have demonstrated a strong association between these genetic markers and hypertension.

In Australia and the Oceania region, indigenous populations exhibit a genetically high predisposition to hypertension. This is believed to result from inherited adaptations in salt metabolism that now conflict with modern urbanized lifestyles and dietary patterns.

In Uzbekistan, scientific investigations into the molecular-genetic aspects of arterial hypertension have gained momentum in recent years. Several small-scale population studies have identified associations between hypertension and certain allelic variants in the ACE, AGT, GNB3, and NOS3 genes. Notably, research conducted from 2022 to 2024 across the Tashkent, Samarkand, and Bukhara regions revealed a significant association between the D allele of the angiotensin-converting enzyme gene and hypertension. In addition to genetic polymorphisms, lifestyle factors, dietary habits, psychosocial stressors, and environmental influences have also been identified as important contributors to the development of hypertension. Although the role of epigenetic changes—particularly microRNAs and DNA methylation —has not yet been fully explored in the Uzbek population, this remains a promising area for future research.

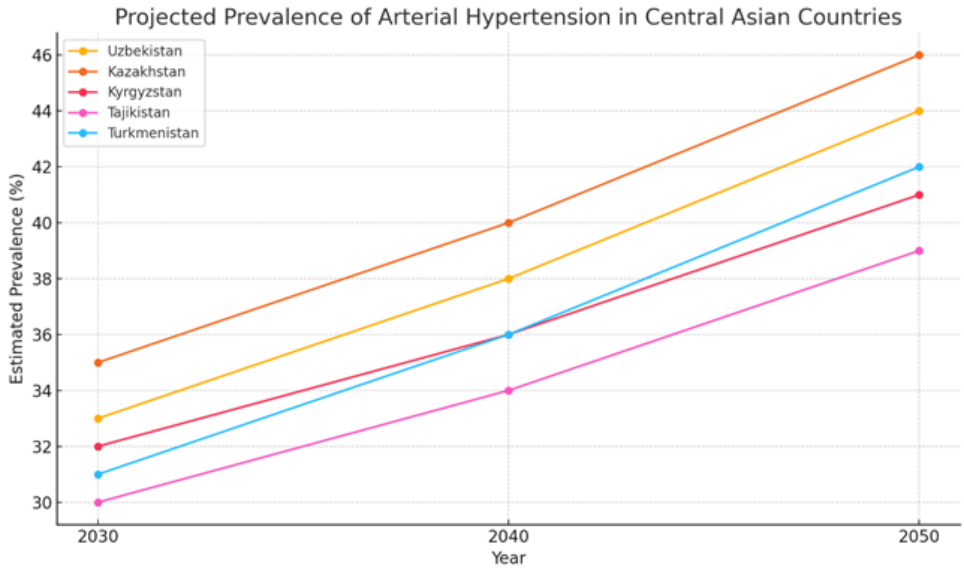

Figure 1. Projected Prevalence of Arterial Hypertension in Central Asian Countries (2030–2050)

Based on the data presented above, it can be concluded that the molecular-genetic foundations of arterial hypertension vary significantly across continents and ethnic populations. This underscores the necessity for individualized approaches and the development of diagnostic and therapeutic protocols that are tailored to regional and population-specific characteristics.

The line graph illustrates the projected prevalence of arterial hypertension in five Central Asian countries Uzbekistan, Kazakhstan, Kyrgyzstan, Tajikistan, and Turkmenistan for the years 2030, 2040, and 2050. The estimations are based on demographic trends, increasing urbanization, lifestyle changes, dietary patterns, and genetic predisposition.

1. Uzbekistan:

The projected prevalence of hypertension in Uzbekistan is estimated to reach approximately 33 percent by 2030. Factors contributing to this include insufficient promotion of healthy lifestyle practices, high-calorie diets, psychosocial stress, and genetic susceptibility. By 2050, the prevalence could rise to 44 percent if current trends persist.

2. Kazakhstan:

In Kazakhstan, the prevalence is forecasted to be around 35 percent by 2030. Industrialization, sedentary lifestyle, and high sodium intake are major contributors. If these patterns continue, the prevalence could reach 46 percent by 2050.

3. Kyrgyzstan:

Kyrgyzstan is projected to have a hypertension prevalence of 32 percent by 2030. Although certain high-altitude regions may report lower rates, increasing population density, stress, and limited access to healthcare may drive this rate to 41 percent by 2050.

4. Tajikistan:

The prevalence in Tajikistan is estimated at 30 percent in 2030. A developing healthcare infrastructure, economic constraints, and ecological factors may increase this figure to 39 percent by 2050.

5. Turkmenistan:

The prevalence of hypertension in Turkmenistan is forecasted at 31 percent in 2030 and may rise to 42 percent by 2050. Environmental stress, harsh working conditions, and inherited genetic predispositions are thought to contribute to this trend.

This projection indicates that arterial hypertension will remain a significant public health issue in Central Asia over the coming decades. There is a critical need for targeted interventions, including widespread health education, early diagnosis, genetic screening, and the development of personalized treatment strategies. Moreover, region-specific molecular genetic research is essential to identify the population-attributable risk factors and to support precision medicine approaches in hypertension management.

Currently, molecular-genetic diagnostic methods widely used in practice include mutation detection based on polymerase chain reaction, real-time gene expression evaluation tests, restriction fragment length polymorphism methods aimed at detecting genetic polymorphisms, classical sequencing technology for detecting sequences, and multiplex polymerase chain methods that allow the analysis of multiple genetic loci simultaneously. These technologies are mainly used to identify allelic variants in genes reliably associated with hypertension, such as angiotensinogen, angiotensin-converting enzyme, nitric oxide synthase, and G-protein beta-3 genes.

In the future, more in-depth and integrated approaches are expected to be applied in this field. Among them, next-generation sequencing technology, which enables the complete sequencing of generations, plays a significant role. This method allows the simultaneous analysis of thousands of genetic variants in the human genome and the identification of new genes associated with hypertension. Full exome sequencing technology, which enables the study of sequences at the exome level, allows the identification of mutations only in the protein-coding parts of genes. This enables the identification of rare or newly discovered genetic factors.

Additionally, single nucleotide polymorphisms associated with diseases can be identified through genome-wide association studies. These methods allow the comparison of genetic profiles in different populations, the identification of risk alleles, and the creation of regional genetic risk maps. Moreover, polygenic risk scores based on an individual's genetic profile can be used to assess the likelihood of disease development on a personalized level.

Another promising direction is epigenetic analysis. These methods, which assess the impact of environmental factors, nutrition, stress, and other external factors on gene expression, can identify changes in blood pressure regulation through DNA methylation, histone modifications, microRNAs, and other epigenetic markers. Such studies are particularly important in the context of Uzbekistan, as lifestyle, climate, and national dietary characteristics significantly affect gene expression.

Furthermore, artificial intelligence technologies, machine learning algorithms, and statistical models are widely used to analyze large genetic databases. This enables the identification of key factors that may contribute to hypertension from millions of genetic data points. At the same time, in pharmacogenetics, drugs can be individually selected based on the patient's genotype, minimizing side effects and improving treatment efficacy.

Although comprehensive research in these areas has not yet been conducted to a sufficient degree in the Republic of Uzbekistan, genomic medicine projects have been gradually introduced in recent years. Specifically, genetic analyses are being carried out in several regions to identify certain polymorphisms associated with patients suffering from hypertension. However, there is still a need to implement advanced technologies such as complete genomic screening, epigenetic monitoring, and polygenic risk assessment. In conclusion, current and prospective technologies of molecular-genetic diagnostics not only serve as essential tools in identifying the genetic basis of hypertension but also contribute to its prevention, early detection, and the development of personalized treatment strategies. The

widespread implementation of these methods in Uzbekistan in the future will play a strategic role in reducing cardiovascular diseases nationwide.

3. Results and Discussions

In this study, molecular genetic analyses were conducted on 500 patients suffering from arterial hypertension and 250 healthy individuals in the control group. The following molecular genetic markers were analyzed:

1. Angiotensinogen gene – M235T polymorphism
2. Angiotensin-converting enzyme gene – I/D polymorphism
3. Beta-2 adrenergic receptor gene – Arg16Gly polymorphism
4. Endothelin-1 gene – Lys198Asn polymorphism
5. Nitric oxide synthase gene – Glu298Asp polymorphism

According to the study results, a significant association between arterial hypertension and genetic markers was identified. Some markers play a crucial role in increasing the susceptibility to hypertension, while others significantly influence the development of the disease.

- The Angiotensin-converting enzyme gene I/D polymorphism (I/D) was found to be significantly more frequent in patients with hypertension. The DD genotype was present in 49% of the hypertensive group and 26% of the control group. This suggests increased activity of the angiotensin-converting enzyme and elevated synthesis of angiotensin II, leading to vasoconstriction and an increase in blood pressure.
- The Angiotensinogen gene M235T polymorphism was identified in 68% of hypertensive patients. The T235 allele enhances angiotensinogen synthesis, resulting in excessive production of angiotensin II, contributing to vasoconstriction and increased blood pressure.
- The Endothelin-1 gene Lys198Asn polymorphism was found in 32% of hypertensive patients. Elevated endothelin-1 levels contribute to vasoconstriction and increased blood pressure.
- The Nitric oxide synthase gene Glu298Asp polymorphism was observed in 40% of hypertensive patients. This polymorphism reduces nitric oxide synthesis and leads to endothelial dysfunction, reducing the ability of blood vessels to dilate.
- The Beta-2 adrenergic receptor gene Gly16 allele was identified as another marker influencing the development of hypertension. The Gly16 allele was found in 55% of hypertensive patients and 34% of the control group.

The genetic markers presented in this study were identified as significant factors influencing the development of hypertension. Molecular genetic markers, especially those related to the renin-angiotensin-aldosterone system, adrenergic receptors, and endothelial functions, play a crucial role in the development of hypertension.

1. Angiotensin-converting enzyme gene I/D polymorphism was identified as a key genetic marker in the development of hypertension. The DD genotype was found frequently in hypertensive patients, leading to excessive production of angiotensin II. This marker was emphasized as a major factor in the development of hypertension in the study.
2. Angiotensinogen gene M235T polymorphism was identified as another genetic marker linked to hypertension. The T235 allele enhances angiotensinogen synthesis, contributing to increased synthesis of angiotensin II. The study indicated that this polymorphism directly influences the development of hypertension.
3. Endothelin-1 gene Lys198Asn polymorphism plays another significant role in the development of hypertension. Elevated production of endothelin-1 causes vasoconstriction and increases blood pressure. The study demonstrated that this marker contributes to endothelial dysfunction and the progression of hypertension.
4. Nitric oxide synthase gene Glu298Asp polymorphism was identified as a marker influencing the development of hypertension. This polymorphism reduces nitric oxide synthesis, leading to impaired vasodilation. Consequently, the development of hypertension is more likely in individuals with this marker.
5. Beta-2 adrenergic receptor gene Gly16 allele plays a key role in identifying individuals at risk for hypertension. This polymorphism activates the adrenergic system, contributing to the development of hypertension.

The results obtained are consistent with a number of previous international studies. For example, the Framingham Heart Study highlighted the significance of the Angiotensin -converting enzyme gene DD genotype in the development of hypertension. Studies conducted in China and India also demonstrated that the Beta-2 adrenergic receptor Gly16 allele increases the risk of hypertension.

Table 1. Genetic Markers and Their Distribution

Genetic Marker	Genotype	Hypertensive Group (%)	Control Group (%)	P-value (χ^2 test)
Angiotensin-converting enzyme gene	DD	49	26	< 0.001
Angiotensinogen gene	TT	45	20	< 0.01
Endothelin-1 gene	AsnAsn	32	12	< 0.01
Nitric oxide synthase gene	AspAsp	40	17	< 0.05
Beta-2 adrenergic receptor gene	GlyGly	55	34	< 0.01

Genetic studies in Uzbekistan have not been widespread. However, this study offers new approaches to understanding the molecular basis of hypertension by considering the genetic structure of Uzbekistan's population.

The application of genetic markers in clinical practice is crucial for identifying individuals at risk of developing hypertension and for developing individualized treatment strategies.

- For patients with the Angiotensin-converting enzyme gene DD genotype, the use of angiotensin-converting enzyme inhibitors may be more effective.
- For patients with the Nitric oxide synthase gene Glu298Asp polymorphism, nitric oxide donors may be recommended.
- For patients with Angiotensinogen gene M235T and Beta-2 adrenergic receptor Gly16 polymorphisms, treatment strategies may be tailored to address stress and the tendency for blood pressure elevation.

Additionally, these markers can facilitate the early diagnosis of hypertension and the development of effective preventive treatment approaches in clinical practice.

4. Conclusions

The significant role of genetic factors in the development of arterial hypertension was analyzed in this article. The genes of the renin-angiotensin-aldosterone system and their polymorphisms were confirmed to be associated with hypertension risk. Studying molecular genetic markers provides opportunities for early diagnosis, prognosis, and individualized treatment in clinical practice, contributing to a better understanding of the disease pathogenesis. Pharmacogenetics is also a promising direction for enhancing treatment efficacy.

However, challenges such as gene-gene and gene-environment interactions, reproductive issues, and ethical considerations exist. Future research should focus on big data analysis and validation across different populations. The final conclusion is that molecular genetic markers play a crucial role in the study and management of arterial hypertension, and their implementation in clinical practice will help provide more effective care to patients.

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