American Journal of Medicine and Medical Sciences 2025, 15(5): 1562-1565
DOI: 10.5923/j.ajmms.20251505.56

Comparative Study of the Frequency of Beta-Adrenoreceptor Gene Polymorphisms in Patients with Essential Arterial Hypertension Associated with Obesity and without It

Umida Iminzhanovna Usmanova[1,*], Umidjon Khusanovich Musashaykhov[1], Kodirjon Tukhtaevich Boboyev[2], Dildora Abdumalikovna Nabieva[3]

[1]Andijan State Medical Institute, Andijan, Uzbekistan
[2]Republican Scientific and Practical Center of Hematology, Ministry of Health of the Republic of Uzbekistan
[3]Tashkent Medical Academy, Uzbekistan

Abstract This study presents a comparative analysis of the frequency of β-adrenoceptor gene polymorphisms − ADRB1 (Gly389Arg and Ser49Gly) and ADRB2 (Arg16Gly and Gln27Gln) − in individuals with essential arterial hypertension (EAH), both with and without obesity, as well as in relatively healthy volunteers. A total of 276 participants were enrolled and divided into main and control groups. The findings indicate a potential association between the Arg389Gly polymorphism of the ADRB1 gene and an increased risk of EAH: the Gly allele and the heterozygous Arg/Gly genotype were significantly more frequent among patients, while the Arg/Arg genotype demonstrated a potential protective effect. In contrast, the Ser49Gly (ADRB1) and Arg16Gly/Gln27Gln (ADRB2) polymorphisms did not show statistically significant differences in allele or genotype frequencies between the study groups. These results suggest a possible role of specific β-adrenoceptor gene polymorphisms in the pathogenesis of EAH and highlight the need for further studies with larger sample sizes and functional analyses of the identified variants.

Keywords Arterial hypertension, Obesity, Polymorphism, β-adrenoceptors, Genetic predisposition

1. Introduction

Contemporary scientific evidence points to a steady rise in the prevalence of essential arterial hypertension (EAH) and obesity, highlighting the critical need for in-depth exploration of their molecular and pathophysiological mechanisms, as well as their impact on cardiovascular system function [3]. Findings from clinical and experimental studies underscore the importance of a detailed examination of the pathogenic pathways through which obesity initiates, exacerbates, and accelerates the progression of EAH, while also contributing to the development and escalation of cardiovascular complications. Currently, obesity is recognized not merely as a modifiable risk factor but as a central component in the pathogenic framework of the cardiovascular continuum. It is characterized by pronounced pro-atherogenic, metabolically disruptive, and pro-inflammatory effects. Visceral adipose tissue functions as an active endocrine organ, secreting a broad array of bioactive molecules, including adipokines and pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). These mediators drive hyperactivation of the sympathetic-adrenal system (SAS) and the renin-angiotensin-aldosterone system (RAAS) [5,6], sustain chronic subclinical inflammation [2,4], induce insulin resistance, impair endothelial function, and reduce nitric oxide (NO) bioavailability. Collectively, these processes promote atherogenesis, elevate blood pressure, and disrupt vasomotor regulation [7]. These mechanisms play a pivotal role in the development of persistent, including treatment-resistant, hypertension, thereby reducing the efficacy of standard antihypertensive therapies and significantly increasing the risk of adverse cardiovascular events [1,8].

* Corresponding author:
doc.umida.usmanova1105@gmail.com (Umida Iminzhanovna Usmanova)
Received: Apr. 16, 2025; Accepted: May 19, 2025; Published: May 30, 2025
Published online at http://journal.sapub.org/ajmms

2. Purpose of the Study

To identify differences in the frequency of Gly389Arg and Ser49Gly polymorphisms of the ADRB1 gene, as well as Arg16Gly and Gln27Gln polymorphisms of the ADRB2 gene, in patients with essential arterial hypertension, stratified by the presence or absence of obesity, with the aim of elucidating

potential genetic factors influencing the development and progression of the disease.

3. Material and Methods of Research

A cohort of 276 participants was enrolled and categorized into two primary groups: the study group (n=171) and the control group (n=105). The study group comprised individuals diagnosed with EAH and those without this condition, further stratified by body mass index (BMI) into subgroups with normal body weight or obesity. This stratification aimed to evaluate the role of obesity in the onset and progression of EAH. The study group was subdivided as follows: Group I (EAH without obesity): Included 57 patients with a mean age of 61.8 ± 1.46 years (range: 37–71 years). Men (n=28) had an average age of 60.6 ± 2.27 years (range: 37–71 years), and women (n=29) had an average age of 63.0 ± 1.60 years (range: 44–73 years); Group II (EAH with obesity): Consisted of 59 patients with a mean age of 61.8 ± 1.98 years (range: 44–80 years). Men (n=22) had an average age of 62.5 ± 2.12 years (range: 46–74 years), and women (n=37) had an average age of 61.4 ± 3.56 years (range: 33–80 years); Group III (obesity without EAH): Comprised 55 patients with a mean age of 44.5 ± 0.00 years (range: 26–62 years). Men (n=12) had an average age of 37.1 ± 0.00 years (range: 26–54 years), and women (n=43) had an average age of 46.6 ± 0.00 years (range: 29–62 years); The control group (n=105) included relatively healthy volunteers, matched for age and sex with the study group, and without a familial predisposition to arterial hypertension.

To investigate the association between specific gene polymorphisms and EAH development, a case-control epidemiological approach was employed, involving comparative analysis of the study and control groups. DNA quantification was performed using a NanoDrop 2000 spectrophotometer (NanoDrop Technologies, USA) at an absorbance ratio of A260/280 nm. All DNA samples exhibited purity within the acceptable range (A260/280 ratio of 1.7–1.8), meeting standard quality criteria.

4. The Results Obtained and Their Discussion

The study of the frequency distribution of allelic and genotypic variants of the Arg389Gly/Ser49Gly polymorphism of the ADRB1 gene revealed statistically significant differences between the main group of patients and the control group. The obtained results suggest that this polymorphism may play a significant role in shaping the genetic profile of predisposition to the disease. The data presented in Table 1 enable an assessment of the potential association of this polymorphism with the development of the disease.

In the analysis of the Arg389Gly polymorphism, the evaluation of allelic frequencies revealed that the Arg allele was significantly more prevalent in the healthy population (82.4%) compared to patients, where its frequency was only 71.6% ($\chi^2 = 8.2$; $p = 0.01$). Conversely, the Gly allele frequency was significantly higher in the main patient group (28.4%) compared to the control group (17.6%; $\chi^2 = 8.2$; $p = 0.01$). These findings suggest a potential association of the Gly allele with increased susceptibility to the pathological process. Statistical assessment of odds ratios (OR) supported this hypothesis: carriage of the Arg allele was associated with a reduced likelihood of disease development (OR = 0.5; 95% CI: 0.35–0.82), whereas the presence of the Gly allele increased this risk (OR = 1.9; 95% CI: 1.21–2.82).

Table 1. Differences in the Frequency of Allelic and Genotypic Variants of the Arg389Gly/Ser49Gly Polymorphism in the ADRB1 Gene Among Examined Patient Groups and Healthy Individuals (n = 276)

Alleles and Genotypes of Arg389Gly	Number of examined alleles and genotypes				χ2	p	OR	95%CI
	Main group		Control group					
	n	%	n	%				
Arg	245	71,6	173	82,4	8,2	0,01	0,5	0,35 - 0,82
Gly	97	28,4	37	17,6	8,2	0,01	1,9	1,21 - 2,82
Arg/Arg	86	50,3	72	68,6	8,9	0,01	0,5	0,28 - 0,77
Arg/Gly	73	42,7	29	27,6	6,3	0,03	2,0	1,16 - 3,29
Gly/Gly	12	7,0	4	3,8	1,2	0,30	1,9	0,61 - 5,97
Alleles and Genotypes of Ser49Gly	**Number of examined alleles and genotypes**				**χ2**	**p**	**OR**	**95%CI**
	Main group		**Control group**					
	n	**%**	**n**	**%**				
Ser	278	81,3	179	85,2	1,4	0,30	0,8	0,47 - 1,2
Gly	64	18,7	31	14,8	1,4	0,30	1,3	0,83 - 2,12
Ser/Ser	110	64,3	76	72,4	1,9	0,20	0,7	0,41 - 1,17
Ser/Gly	58	33,9	27	25,7	2,1	0,20	1,5	0,87 - 2,54
Gly/Gly	3	1,8	2	1,9	0,0	0,95	0,9	0,15 - 5,59

The analysis of genotype distribution also revealed significant patterns. The homozygous Arg/Arg genotype was predominantly observed in the control group (68.6%), whereas its frequency was significantly lower among patients (50.3%), suggesting a potential protective effect ($\chi^2 = 8.9$; $p = 0.01$; OR = 0.5; 95% CI: 0.28–0.77). In contrast, the heterozygous Arg/Gly genotype was significantly more frequent in the main patient group (42.7%) compared to the control group (27.6%), supporting its potential association with increased disease susceptibility ($\chi^2 = 6.3$; $p = 0.03$; OR = 2.0; 95% CI: 1.16–3.29). The Gly/Gly genotype was less common (7.0% in patients versus 3.8% in healthy individuals), but the lack of statistically significant differences ($\chi^2 = 1.2$; $p = 0.30$; OR = 1.9; 95% CI: 0.61–5.97) precludes definitive conclusions about its role, possibly due to the limited sample size (Table 1).

In the analysis of the Ser49Gly polymorphism, the evaluation of allelic frequencies did not reveal statistically significant differences between the patient and control groups. The Ser allele, associated with the wild-type form of the β1-adrenoceptor, was identified in 81.3% of patients in the main group and 85.2% of healthy individuals ($\chi^2 = 1.4$; $p = 0.30$; OR = 0.8; 95% CI: 0.47–1.2). Conversely, the Gly allele, which may hypothetically alter the receptor's conformational properties and sensitivity to agonists, was observed in 18.7% of patients and 14.8% of the control group ($\chi^2 = 1.4$; $p = 0.30$; OR = 1.3; 95% CI: 0.83–2.12). The absence of significant differences between the groups suggests a low likelihood of this polymorphism substantially influencing disease predisposition (Table 1).

The analysis of genotypic frequencies also revealed no statistically significant differences between the groups. The homozygous Ser/Ser variant, corresponding to normal functional activity of the receptor, was observed in 64.3% of patients in the main group and 72.4% of control subjects ($\chi^2 = 1.9$; $p = 0.20$; OR = 0.7; 95% CI: 0.41–1.17). These findings do not support the hypothesis of a protective role for this genotype in the development of the disease. The heterozygous Ser/Gly variant, which may potentially alter the sensitivity of the β1-adrenoceptor, was identified in 33.9% of patients in the main group compared to 25.7% in healthy individuals ($\chi^2 = 2.1$; $p = 0.20$; OR = 1.5; 95% CI: 0.87–2.54). Although there was a trend toward higher prevalence of this genotype among patients, the difference did not reach statistical significance, precluding definitive conclusions about its pathogenic relevance. The rare homozygous Gly/Gly variant, which could theoretically have the most pronounced effect on modulating the receptor's functional properties, was detected in only 1.8% of patients and 1.9% of control group participants ($\chi^2 = 0.0$; $p = 0.95$; OR = 0.9; 95% CI: 0.15–5.59), indicating no significant association between this genotype and the studied pathology (Table 1).

The study results did not identify a significant association between the Ser49Gly polymorphism of the ADRB1 gene and predisposition to the investigated disease. Despite a slightly higher frequency of the Gly allele and the heterozygous Ser/Gly variant among patients in the main group, the differences between groups did not reach statistical significance. This may suggest either a limited contribution of this polymorphism to the development of the pathology or the need to consider additional factors, such as other genetic markers or the influence of environmental factors.

This study involved a comprehensive analysis of polymorphic variants of the ADRB2 gene to investigate their potential association with the development of EAH, both in the presence and absence of obesity. The assessment of allelic and genotypic frequency distributions of this gene enhanced the understanding of the molecular-genetic mechanisms underlying predisposition to this pathology and facilitated the evaluation of its probable influence on the disease's pathogenic processes.

Table 2. Differences in the frequency of allelic and genotypic variants of the Arg16Gly/Gln27Gln polymorphism in the ADRB2 gene among the studied groups of patients and healthy individuals (n = 276).

Alleles and Genotypes of Arg16Gly	**Number of examined alleles and genotypes**				**χ2**	**p**	**OR**	**95%CI**
	Main group		**Control group**					
	n	**%**	**n**	**%**				
Arg	208	60,8	125	59,5	0,1	0,80	1,1	0,74 - 1,5
Gly	134	39,2	85	40,5	0,1	0,80	0,9	0,67 - 1,35
Arg/Arg	69	40,4	38	36,2	0,5	0,50	1,2	0,72 - 1,97
Arg/Gly	70	40,9	49	46,7	0,9	0,40	0,8	0,49 - 1,29
Gly/Gly	32	18,7	18	17,1	0,1	0,80	1,1	0,59 - 2,1
Alleles and Genotypes of Gln27Gln	**Number of examined alleles and genotypes**				**χ2**	**p**	**OR**	**95%CI**
	Main group		**Control group**					
	n	**%**	**n**	**%**				
Gln	261	76,3	161	76,7	0,0	0,95	1,0	0,65 - 1,47
Glu	81	23,7	49	23,3	0,0	0,95	1,0	0,68 - 1,53
Gln/Gln	99	57,9	61	58,1	0,0	0,98	1,0	0,61 - 1,62
Gln/Glu	63	36,8	39	37,1	0,0	0,98	1,0	0,6 - 1,63
Glu/Glu	9	5,3	5	4,8	0,0	0,90	1,1	0,36 - 3,41

The summarized results of the study are presented in Table 2. These data illustrate the distribution patterns of allelic and genotypic variants of the Arg16Gly/Gln27Gln polymorphism of the ADRB2 gene among patients with EAH, with and without obesity, as well as in the control group.

Based on the data presented in Table 2, a detailed comparative analysis was conducted to assess the frequency distribution of allelic and genotypic variants of the Arg16 Gly/Gln27Gln polymorphism in the ADRB2 gene among patients in the main group and individuals in the control group. This analysis aimed to evaluate the potential association of this genetic marker with predisposition to the disease.

The investigation of allelic frequencies for the Arg16Gly polymorphism revealed that the Arg allele was predominant in both patients with the pathology (60.8%) and the control group (59.5%). However, the observed differences were not statistically significant ($\chi^2 = 0.1$; $p = 0.80$). The odds ratio calculation (OR = 1.1; 95% CI: 0.74–1.5) did not demonstrate a significant influence of this allele on the risk of disease development. A similar trend was observed for the Gly allele, with frequencies of 39.2% in the main group and 40.5% in the control group ($\chi^2 = 0.1$; $p = 0.80$; OR = 0.9; 95% CI: 0.67–1.35), indicating no significant association with the pathological process.

Analysis of genotypic distribution showed that the homozygous Arg/Arg variant was present in 40.4% of patients with the disease and 36.2% of healthy individuals, with no statistically significant differences between groups ($\chi^2 = 0.5$; $p = 0.50$; OR = 1.2; 95% CI: 0.72–1.97). The heterozygous Arg/Gly genotype was recorded in 40.9% of patients in the main group and 46.7% of control subjects ($\chi^2 = 0.9$; $p = 0.40$; OR = 0.8; 95% CI: 0.49–1.29), suggesting no definitive role in disease predisposition. The homozygous Gly/Gly variant was observed in 18.7% of the main group and 17.1% of the control group ($\chi^2 = 0.1$; $p = 0.80$; OR = 1.1; 95% CI: 0.59–2.1), further confirming the lack of a significant association with the studied disease (Table 2).

For the Gln27Gln polymorphism, the analysis of allelic distribution similarly revealed no statistically significant differences between the main and control groups. The Gln allele was observed in 76.3% of patients with the pathology and 76.7% of healthy individuals ($\chi^2 = 0.0$; $p = 0.95$; OR = 1.0; 95% CI: 0.65–1.47), while the Glu allele had frequencies of 23.7% and 23.3%, respectively ($\chi^2 = 0.0$; $p = 0.95$; OR = 1.0; 95% CI: 0.68–1.53), indicating no association with disease predisposition.

Genotypic distribution analysis also showed no significant differences between groups. The homozygous Gln/Gln variant was recorded in 57.9% of patients in the main group and 58.1% of healthy individuals ($\chi^2 = 0.0$; $p = 0.98$; OR = 1.0; 95% CI: 0.61–1.62). The heterozygous Gln/Glu genotype was detected in 36.8% of patients with the disease and 37.1% of control subjects ($\chi^2 = 0.0$; $p = 0.98$; OR = 1.0; 95% CI: 0.6–1.63), while the homozygous Glu/Glu variant was observed in 5.3% and 4.8% of cases, respectively ($\chi^2 = 0.0$; $p = 0.90$; OR = 1.1; 95% CI: 0.36–3.41) (Table 2).

5. Conclusions

The obtained results support a potential association between the Arg389Gly polymorphism of the ADRB1 gene and predisposition to the studied pathology. The increased frequency of the Gly allele and Arg/Gly genotype among patients suggests their potential role in disease development, whereas the Arg/Arg genotype may confer a protective effect. Further studies involving larger cohorts and functional analyses of this polymorphism are needed to elucidate its mechanisms of influence on pathogenesis and potential clinical implications.

The study findings indicate that the Arg16Gly/Gln27Gln polymorphism of the ADRB2 gene does not significantly influence the risk of disease development, as the frequencies of its allelic and genotypic variants showed no significant differences between the main and control groups. These data suggest the absence of a substantial link between this genetic marker and the pathogenesis of the investigated pathology.

REFERENCES

[1] Agababyan I.R., Yusupova Z.K. Opportunities for effective control of arterial hypertension in individuals with excess body weight // Research Focus. – 2023. – Vol. 2, No. 6. – Pp. 269–274.

[2] Druzhilov M.A., Kuznetsova T.Yu. Visceral obesity as a risk factor for arterial hypertension // Russian Journal of Cardiology. – 2019. – Vol. 24, No. 4. – Pp. 7–12.

[3] Chazova I.E., Aksenova A.V., Oshchepkova E.V. Characteristics of arterial hypertension in men and women (according to the National Registry of Arterial Hypertension) // Therapeutic Archive. – 2019. – Vol. 91, No. 1.

[4] Chumakova G.A., Kuznetsova T.Yu., Druzhilov M.A. The multifaceted nature of arterial hypertension in obesity // Russian Journal of Cardiology. – 2023. – Vol. 28, No. 4. – P. 5360.

[5] Chumakova G.A., Kuznetsova T.Yu., Druzhilov M.A., Veselovskaya N.G. Obesity-induced arterial hypertension: key pathophysiological mechanisms of development // Arterial Hypertension. – 2021. – Vol. 27, No. 3. – Pp. 260–268.

[6] Hall J.E., do Carmo J.M., da Silva A.A., Wang Z., Hall M.E. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms // Circulation Research. – 2015. – Vol. 116, No. 6. – Pp. 991–1006.

[7] Sletten A.C., Peterson L.R., Schaffer J.E. Manifestations and mechanisms of myocardial lipotoxicity in obesity // Journal of Internal Medicine. – 2018. – Vol. 284, No. 5. – Pp. 478–491.

[8] Tadic M., Cuspidi C. Obesity and resistant hypertension: Never ending story // Journal of Clinical Hypertension. – 2019. – Vol. 21, No. 10. – Pp. 1516–1518.