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Prevalence Of The Ppargc1a Gene Gly482ser Polymorphism In Women With Obesity

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Abstract
In recent years, according to leading scientists, a hereditary predisposition to obesity has been identified. Various mutations that significantly affect energy metabolism and adipose tissue proliferation can lead to the development of obesity, but in most patients they are not detected. This article presents the results of research on proving the prevalence of the PPARGC1A gene polymorphism in Uzbek women of childbearing age with obesity and creating the necessary conditions for determining the potential goals of drug therapy and developing personalized effective approaches to the diagnosis, treatment, and prevention of obesity.
Key words: women of childbearing age, metabolic healthy obesity, metabolic complicated obesity, gene polymorphism

Relevance of the study. In recent years, many studies have studied the correlation of genes that cause the development of excess body weight and obesity with various symptoms of metabolic syndrome [6,9,12,13]. Obesity is a heterogeneous disease where genetic factors, environmental influences, and their interactions play a significant role [3, 4, 10, 11]. One such genetic factor is the Gly482Ser polymorphism of the PPARGC1A gene, which contributes to increased body fat, higher BMI, hyperinsulinemia, and the development of insulin resistance (IR) [1, 2, 7, 8]. Due to conflicting results in studies regarding the prevalence of this gene polymorphism, it is difficult to reach a single conclusion on its frequency. Such discrepancies may be attributed to the genomic characteristics of different ethnic and racial groups, their lifestyles, gender differences, and geographic conditions. Therefore, studying the distribution of these gene polymorphisms among Uzbek women diagnosed with obesity opens new perspectives for the prevention of obesity and its associated pathological conditions.
The aim of the study is to study the prevalence of Gly482Ser polymorphism of the PPARGC1A gene in women of Uzbek ethnicity who have been diagnosed with healthy and metabolically complicated obesity.
Materials and methods. In 2019-2022, 224 Uzbek women of childbearing age were involved in the study. Criteria for inclusion in the study group: Women of childbearing age, BMI≥30 kg/m^2, W/R>80 cm, arterial hypertension (AG) Phase I-II, insulin resistance (IR) and absence of clinical signs of kidney damage were defined. Anthropometric indicators of women have been determined and classified into 2 groups according to the above examinations and metabolic syndrome criteria (WHO, 2016; International diabetic Federation, 2009), Group 1 was made up of 133 women with 42.0±0.5-year-old metabolic complication obesity (MCO); Group 2 was made up of 91 women with 41.7±0.7-year-old metabolic healthy obesity (MHO). The control group (CG) consisted of 45 healthy average aged women aged 43.2±0.8 [3.4.5].
Results and their analysis. The prevalence was 33.1, 39.8, and 27.1%, respectively, when GLYGLYy, GlySer, and SerSer genotypes of the PPARGC1A Gene met Gly482Ser polymorphism in the observed MCO Group. In contrast, CG had genotypes of Gly482Ser polymorphism in the form of 53.3% - GlyGly, 35.6% - GlySer, and 11.1% - SerSer. In this group, the Gly allele of Gly482Ser polymorphism was found in 53.0%, the Ser allele in 47.0%, while in the control group the Gly allele was found in 71.1%, and the Ser allele in 28.9%. In the MCO Group, the Gly allele of the Gly482Ser polymorphism of the PPARGC1A gene was found to have an incidence of 1,128, and the CG was 2,462, meaning that healthy individuals had a 2.2-fold reliable incidence of this allele compared to the group found to be obese.

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This result indicates that the Gly allele possesses significant protective properties against the development of MCO ($\chi^2 = 8.3$; OR = 0.5; 95% CI: 0.274–0.767; p = 0.004). The frequency of the Ser allele was 0.887 in this group compared to 0.406 in the control group (CG), demonstrating that this allele is significantly 2.2 times more prevalent in the MCO group than in the CG. This finding suggests that the Ser allele has a significant risk-enhancing (aggressive) effect on the development of this syndrome ($\chi^2 = 9.3$; OR = 2.2; 95% CI: 1.303–3.654; p = 0.003). The frequency of the GlyGly genotype as a risk factor for obesity was 0.494 in the MCO group, while in the control group, this figure was 1.143, indicating that this genotype is 2.3 times more prevalent in healthy individuals than in the MCO group. This result demonstrates that the GlyGly genotype has a statistically significant protective effect against the development of this syndrome ($\chi^2 = 5.7$; OR = 0.4; 95% CI: 0.217–0.861; p = 0.017). The frequency of the GlySer genotype as a risk factor for the development of the disease was 0.662 in the MCO group and 0.552 in the control group. Although this genotype was 1.2 times more prevalent in women with MCO compared to healthy individuals, this difference was not statistically significant ($\chi^2 = 0.3$; OR = 1.2; 95% CI: 0.595–2.423; p = 0.6). The frequency of the SerSer genotype as a risk factor for disease development was 0.371 in patients with MCO and 0.125 in the control group. Thus, this genotype was 3.0 times more prevalent in MCO patients than in healthy individuals, which is statistically significant. This result indicates that the SerSer genotype possesses a significant risk-enhancing (aggressive) property regarding the development of MCO ($\chi^2 = 5.4$; OR = 3.0; 95% CI: 1.086–8.114; p = 0.021).

In the MHO group, the prevalence of GlyGly, GlySer, and SerSer genotypes of the PPARGC1A gene Gly482Ser polymorphism was 46.2%, 37.4%, and 16.4%, respectively. The Gly allele of the PPARGC1A gene Gly482Ser polymorphism was found in 64.8% of women in the MHO group; its frequency in this group was 1.857, compared to 1.972 in the control group. It was determined that the probability of this allele occurring in the control group was 1.1 times higher than in the MHO group, but this difference was not statistically significant ($\chi^2 = 0.8$; OR = 0.9; p = 0.36).

In this group, the prevalence of the Ser allele was 35.2%, with a frequency of 0.538 compared to 0.408 in the control group. This indicates that the probability of this allele occurring in the MHO group was 1.3 times higher than in the control group; however, this difference was not statistically significant ($\chi^2 = 0.83$; OR = 1.3; p = 0.4). The frequency of the GlyGly genotype as a risk factor for the development of obesity was 0.852 in the MHO group, compared to 1.128 in the control group. This indicates that this genotype is 1.3 times more likely to occur in healthy individuals than in the MHO group; however, this finding was not statistically significant ($\chi^2 = 1.0$; OR = 0.8; p = 0.32). In this group, the frequency of the GlySer genotype as a risk factor for the development of obesity was 0.587, while in the control group, it was 0.538. No significant difference was found in the prevalence of this genotype between the groups ($\chi^2 = 0.09$; OR = 1.1; p = 0.77). The frequency of the SerSer genotype as a risk factor for the development of obesity was 0.205 in the MHO group and 0.124 in the control group. It was noted that this genotype may occur 1.7 times more frequently in the MHO group than in healthy individuals. This result suggests that the SerSer genotype may have pathogenetic significance in the development of obesity ($\chi^2 = 1.5$; OR = 1.7; p = 0.22). Based on the results obtained, it was determined that the risk of occurrence for the Gly allele and GlyGly genotype of the PPARGC1A gene Gly482Ser polymorphism was 1.1 and 1.3 times higher in the control group compared to the MHO group, respectively. Conversely, the risk of occurrence for the Ser allele and SerSer genotype was 1.3 and 1.7 times higher in the MHO group than in the control group, respectively. These findings suggest that the former allele and genotype possess protective properties against increased BMI, while the latter allele and genotype exhibit aggressive (risk-enhancing) characteristics.

Conclusion. According to the results obtained, the prevalence of the GlyGly, GlySer, and SerSer genotypes of the PPARGC1A gene Gly482Ser polymorphism in the MCO group was 33.1%, 39.8%, and 27.1%, respectively. In the control group, the genotypes were distributed as follows: 53.3% for GlyGly, 35.6% for GlySer, and 11.1% for SerSer. In the MCO group, the Gly allele was found in 53.0% of cases and the Ser allele in 47.0%, whereas in the control group, the Gly allele was identified in 71.1% and the Ser allele in 28.9% of cases. In the MHO group, the prevalence of these genotypes was 46.2%, 37.4%, and 16.4%, respectively. In the MCO group, the frequency of the Gly allele of the PPARGC1A Gly482Ser polymorphism was 1.128, while in the control group it was 2.462, indicating that this allele was significantly 2.2 times more prevalent in healthy individuals than in the obese group. This result suggests that the Gly allele possesses a

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