ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 9| Issue: 7| July 2023|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2023: 8.224 || ISI Value: 1.188

MOLECULAR AND GENETIC BASIS OF PROGNOSTICS OF METABOLIC SYNDROME

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ABSTRACT

In the course of the study, in 183 patients with MS and MI, the associative relationship A/G polymorphism of the PPARD lane in the formation of pathology data was analyzed. In the studied groups, the actual distribution of polymorphism/G polymorphism of the PARK lane genotypes corresponded to those expected at the Hardy-Weinberg equilibrium (HWE) (p<0.05).

KEY WORDS: ***metabolic syndrome, obesity, insulin, allele, genetic A/G polymorphism of the PPARD gene, genotype.***

1. INTRODUCTION

According to WHO experts, "... we are facing a new pandemic of the XXI century, covering industrialized countries. This could prove to be a demographic disaster for developing countries. The prevalence of metabolic syndrome is 2 times higher than the prevalence of diabetes mellitus, and its growth rate is expected to increase by 50% in the next 25 years" [3].

As is known, metabolic syndrome increases the risk of developing type 2 diabetes mellitus, atherosclerosis, arterial hypertension and other diseases [1]. To date, epidemiological indicators, for all their importance, still do not fully reveal the relevance of the MS problem. It is important for the clinician not only as a widespread pathology, but above all as a life-threatening condition. Of course, this syndrome plays a significant role in accelerating the development and progression of diseases associated with atherosclerosis and occupying, according to WHO experts, the first place among the causes of mortality of the population of industrially developed countries of the world [6].

In recent years, there has been an idea that metabolic syndrome (MS) is a common risk factor (FR) for the development of both coronary heart disease (CHD) and type 2 diabetes mellitus [2,5]. Cardiovascular diseases are the main cause of death in the world and account for 30% of total mortality, or 17.5 million deaths per year. Mortality rates from CVD are steadily increasing from year to year all over the world [4].

2. PURPOSE OF THE STUDY

To study the associative relationship of the A/G polymorphism of the PPARD gene in the development of MS and MI.

3. MATERIAL AND METHODS OF RESEARCH

The peripheral blood of 183 patients with MS and MI (the main group) and 155 conditionally healthy donors (the control group) served as the material for molecular genetic research. The main group was divided into 3 subgroups: among them patients with MS + IM-64; MS without IM-61 and with IM without MS-58. In the main study group of patients, the median age was 60.4±0.7 years. Testing of A/G polymorphism in the PPARD gene was carried out on a Rotor-Gene Q device (Quagen, Germany), using a commercial test kit of Syntol LLC (Russia). Statistical processing of the results was performed using the standard OpenEpi V.9.2 application software package. Molecular genetic studies were carried out in the Department of Molecular Medicine and Cellular Technologies of the RSSPMC of Hematology of the Republic of Uzbekistan.

The frequency distribution of alleles and genotypes in the studied genes was checked for compliance with the Hardy-Weinberg equilibrium.

4. THE RESULTS OBTAINED AND THEIR DISCUSSION

As shown in Table 1, in patients with MI without MS, the degree of difference in the frequency of detection of A major and G minor type alleles was OR=0.9 at $\chi 2$=0.1 and p=0.9 and OR=1.1 at $\chi 2$=0.1 and p=0.9 compared to the reference (see Table 1).

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Table 1. Associative relationship between polymorphism of the PPARD gene in patient IM without MS and control groups.

Alleles and genotypes	Number of alleles and genotypes examined				χ^2	p	OR	95%CI
	IM without MS		Control group					
	n	%	n	%				
A	92	79,3	249	80,3	0,1	0,90	0,9	0,55 - 1,59
G	24	20,7	61	19,7	0,1	0,90	1,1	0,63 - 1,81
A/A	37	63,8	101	65,2	0,0	0,90	0,9	0,5 - 1,77
A/G	18	31,0	47	30,3	0,0	0,95	1,0	0,54 - 1,99
G/G	3	5,2	7	4,5	0,0	0,90	1,2	0,29 - 4,61

The distribution of genotypes according to the A/G polymorphism of the PPARD gene within the groups showed that in the main group of patients with MI without MS, the wild homozygous genotype A/A was 63.8%, the heterozygous genotype A/G was 31.0%, and the mutant homozygous genotype G/G was 5.2%.

The obtained results of statistical treatments showed that in terms of indicators, the control group differed slightly from the main group of patients with MI without MS. That is, it was found that in the group of patients with MI without MS, the homozygous genotype A/A is almost 1 times less common, the heterozygous genotype A/G is 1 times more common, and the mutant genotype G/G is 1.2 times more common.

Further, differences in the frequency of occurrence of alleles and genotypes of A/G polymorphism of the PPARD gene between the main group of patients were investigated.

It was revealed that 77.3% of all examined patients with MS+MI were carriers of the wild allele A of the A/G polymorphism of the PPARD gene associated with the risk of developing cardiovascular diseases, whereas this allele was detected in 79.3% of patients with MI without MS. Among patients with MS+MI and in patients with MI without metabolic syndrome, there were no significant differences in the frequency of carrying the T allele (at $\chi2<0.1$, $p>0.8$, 95%CI:0.48-1.64, OR=0.9) (see Table 2).

And the unfavorable G allele of the A/G polymorphism of the PPARD gene was slightly higher in patients with MS+MI compared to the 3rd group of patients with MI without MS revealed (at $\chi2<0.1$, $p>0.8$, 95%CI:0.61–2.07, OR=1.1) (see Table 2).

Table 2. Associative relationship between polymorphism of the PPARD gene in patient MS + IM and IM without MS.

Alleles and genotypes	Number of alleles and genotypes examined				χ^2	p	OR	95%CI
	MS + IM		IM without MS					
	n	%	n	%				
A	99	77,3	92	79,3	0,1	0,80	0,9	0,48 - 1,64
G	29	22,7	24	20,7	0,1	0,80	1,1	0,61 - 2,07
A/A	39	60,9	37	63,8	0,1	0,80	0,9	0,42 - 1,84
A/G	21	32,8	18	31,0	0,0	0,90	1,1	0,51 - 2,33
G/G	4	6,3	3	5,2	0,1	0,80	1,2	0,26 - 5,69

In group 1 of the studied patients with MS+MI, the frequency of occurrence of wild genotype A/A was 60.9%, and in patients with MI without MS 63.8%, the difference does not reach the level of statistical reliability (at $\chi2<0.1$, $p>0.8$, 95%CI: 0.42-1.84, OR=0.9) (see table 2).

When comparing the frequency of occurrence of the heterozygous A/G genotype of the A/G polymorphism of the PPARD gene in the group with MS+MI and MI without it, the heterozygous A/G genotype was found by 1.1 times insignificantly often in patients with MS+MI compared with MI without MS (32.8% vs. 31.0% at $\chi2<0.0$, $p>0.9$, 95%CI:0.5 -2.33, OR=1.1) (see Table 2).

According to the data obtained, in MS+MI, the unfavorable haplotype G/G of the A/G polymorphism of the PPARD gene occurs in 6.3% of patients.

It should be noted that only 5.2% of patients with MI without MS have a carrier of the mutant haplotype G/G polymorphism A/G of the PPARD gene. From Table 2, it can be concluded that the differences in the frequency of occurrence of G/G polymorphism A/G of the PPARD gene were not statistically significant (see Table 2).

In the comparison groups of MS without MI and IM without MS, two equivalent comparable values of the occurrence of alleles and genotypes of the polymorphic marker A/G of the PPARD gene were determined (see Table 3).

However, the calculation of the frequency of identification of alleles and genotypes above the indicated marker showed that the difference in the frequency of distribution of alleles and genotypes between the 2nd group of patients with MS without MI compared with patients with MI without MS was not significant ($\chi2<3.84$, $p>0.05$) (see Table 3).

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Table 3. Associative relationship between polymorphism of the PPARD gene in patient MS without IM and IM without MS.

Alleles and genotypes	Number of alleles and genotypes examined				χ^2	p	OR	95%CI
	MS without IM		IM without MS					
	n	%	n	%				
A	96	78,7	92	79,3	0,0	0,95	1,0	0,52 - 1,8
G	26	21,3	24	20,7	0,0	0,95	1,0	0,56 - 1,94
A/A	38	62,3	37	63,8	0,0	0,90	0,9	0,45 - 1,97
A/G	20	32,8	18	31,0	0,0	0,90	1,1	0,5 - 2,34
G/G	3	4,9	3	5,2	0,0	0,95	1,0	0,18 - 4,9

5. CONCLUSION

Thus, the distribution of frequencies of genotypes and alleles by polymorphism A/G of the PPARG gene is the same in all the compared subgroups. There were no statistically significant differences in the frequency distribution of genotypes and alleles for this polymorphism between the main group of patients with MS+MI and MS without MI and MI without MS.

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