EVALUATION OF THE EFFICACY OF ASSISTED REPRODUCTIVE TECHNOLOGIES IN POLYCYSTIC OVARIAN SYNDROME

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Annotation: Authors did genetic tests have been carried outgene polymorphism studies CYP17A1(rs743572)106 patients with PCOS. The results of the study showed that the mutant form (AA) of the CYP17A1 rs743572 gene, this risk of PCOS in patients without metabolic syndrome, but this risk is not significant. The CY17A1 polymorphism in patients with PCOS can be said that the GG mutant genotype was statistically significantly more common in the observed patients compared to the control group.

Keywords: polycystic ovary syndrome, reproductive age, metabolic disorders, assisted reproductive technologies.

Relevance: PCOS is an extremely heterogeneous and complex disease. The genetic basis of PCOS varies between families and within families, but is associated with a common pathway [1]. Due to complexity and heterogeneity, a single gene or related genes in the same family have not been described [1,2]. The genetic predisposition to different genes varies among patients from the same family. Recently, intrauterine programming has been suggested as a predisposition factor for PCOS [2]. Genome screening to find a candidate gene in a disease as complex as PCOS is unrealistic. Linkage analysis in such families always gives a negative result [3]. In this disease, case-control studies with large population sizes and genome-wide association studies (GWAS) are useful to look for possible associations. Parental analysis in such diseases is often impractical; however, the known risk of disease can be assessed [3,4].

The CYP11a gene encodes an enzyme required at the intermediate stage of the conversion of cholesterol into progesterone [4]. This is the rate-limiting step in the conversion of cholesterol. Moreover, Gharani et al. reported polymorphs and variations as related factors in a study of 97 women with infertility [5,11]. Two other studies from China and Greece replicated the finding and reported that CYP11a is an association factor with PCOS. Later, a large UK study did not replicate the results [6,9].

The conversion of pregnenolone and progesterone to 17-hydroxypregnenolone and 17-hydroxyprogesterone is catalyzed by an enzyme (P450c17α) encoded by CYP17 [7]. Rosenfield et al. reported elevated androgen levels in patients with PCOS.70 Wickenheisser et al. reported an increase in CYP17 expression in theca cells. Carey et al. reported a polymorph in the promoter region associated with PCOS [8,10].

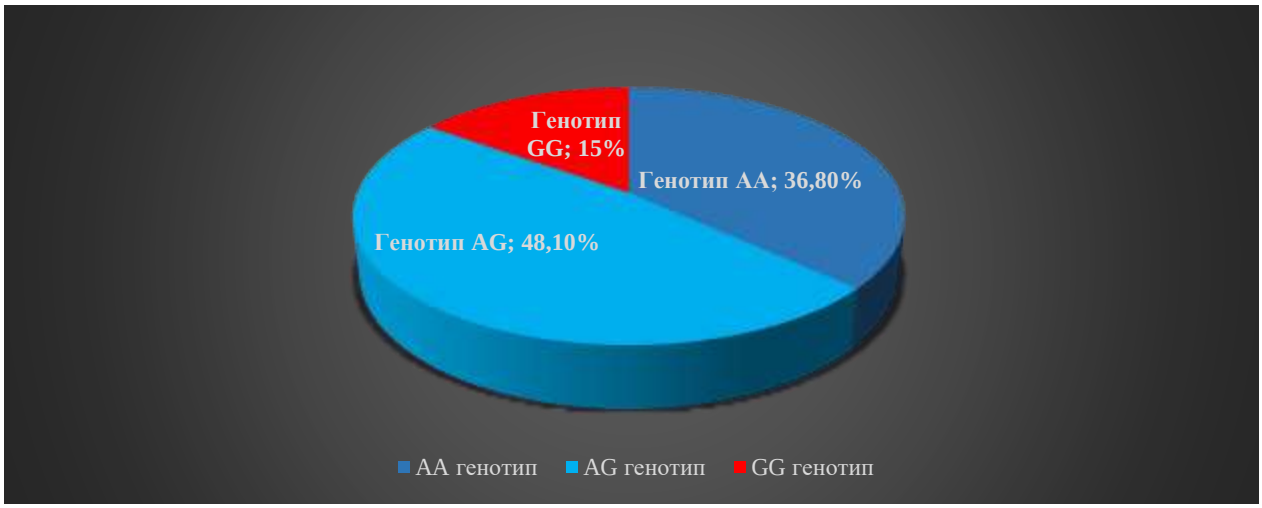
The CYP19 gene responsible for the p450 aromatase required for estrogen production is located on chromosome number 15q21.2.73 Lower aromatase activity has been reported in both obese and lean women with PCOS [9,12].

Purpose of the study: The study of the features of allelic variants of gene polymorphism in women with PCOS.

Material and research methods: all 106 observed patients underwent a genetic study of gene

polymorphismCYP17A1(rs743572).All 106 patients were divided into 2 groups: the first group - patients with metabolic syndrome (n=60) (MS+), the second group - patients with PCOS without metabolic syndrome (n=46) (MS-). The control group consisted of 52 healthy volunteers with no history of predisposition to PCOS.

Results and discussions: In the process of studying the distribution in patients with PCOS, AA homozygous or wild type of the allelic genotype of the CYP17A1 gene was 36.8%, AG heterozygous genotype in 48.1% of patients, GG homozygous mutant genotype was found in 15.1% of patients (Fig. 1.) .



Rice. 1. Distribution of polymorphic variants of the CYP17A1 gene in patients with PCOS.

During the study, polymorphism of the homozygous normal or wild AA genotype of the CYP17A1 gene was observed in 45.0% of patients with MS+, compared with the MS-group where this percentage was 26.1%, in the third observation group this percentage was 40.4%. In addition, among MS+ patients with PCOS, the rate of mutant homozygous GG genotype of the CYP17A1 gene polymorphism was low and amounted to 11.7% in the first group, 19.6% in the second group and 13.5% in the control group. Also, the difference in the occurrence of the heterozygous genotype (genotype AG) in the first and second groups was 9%, and patients of the second group (54.3%) prevailed in this indicator, the difference between the indicators of the first and control groups was only 3.2%, where the first group (Fig. 2).

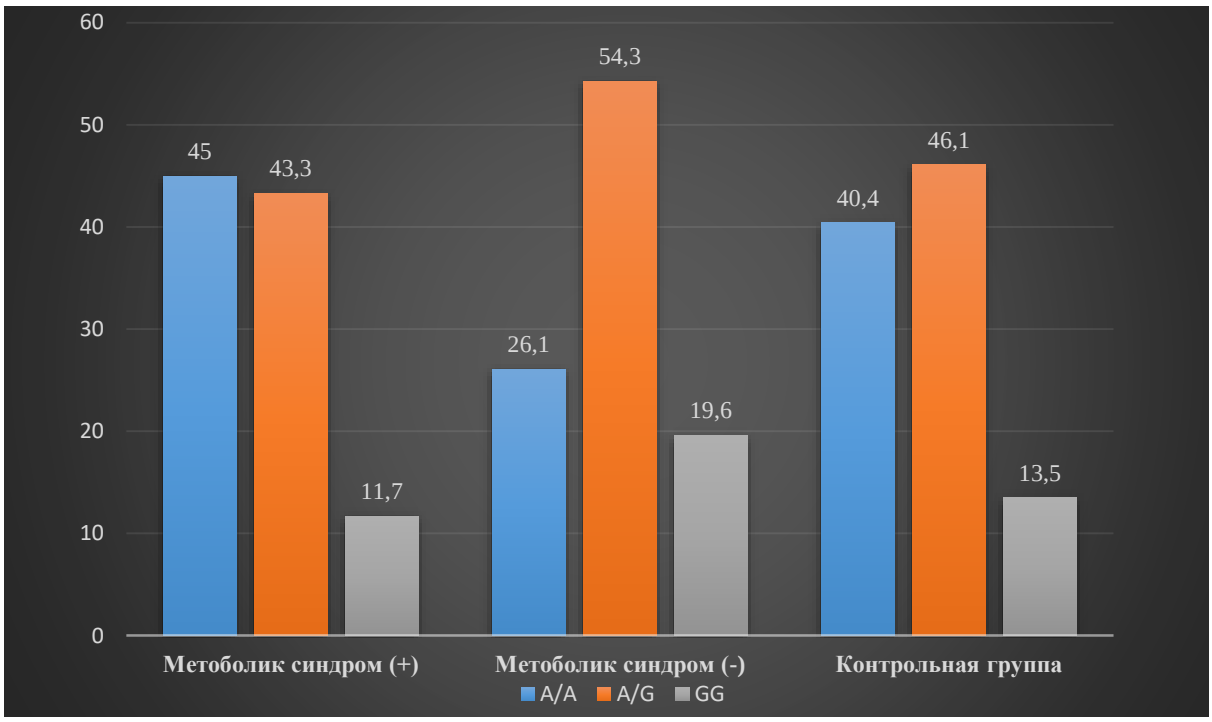


Fig. 2 Level of percentage occurrence of CYP17A1 gene polymorphism among MS+ and MS- patients with PCOS

According to the level of occurrence of allelic variants of the CYP17A1 gene, the percentage of patients with allelic A in the MS+ group was 66.7% and 55.3% in patients with the MS group. G allele was determined in 40% of patients of the first group and 43% of patients of the second group (Table 1). When we compared the level of occurrence of CYP17A1 gene polymorphism with the control group, it was found that normal - "wild" AA genotypes with a smaller difference were more common in the control group, while heterozygous AA and mutant GG genotypes slightly prevailed in the group of patients with PCOS (OR=1.06; 95%CI 0.55-2.10; p<0.8 for heterozygous genotype and OR=1.14; 95%CI 0.44-2.98; P<0.8 for homozygous genotype) (Table 1).

Table 1

Results of comparison of CYP17A1 gene polymorphism between patients with PCOS and healthy people

Alleles and genotypes	Number of examined alleles and genotypes				Chi2	P	RR	95%CI	OR	95%CI
	Main group (n=106)		Control group (n=52)							
	N	%	N	%						
A	129	60.8	66	63.0	0.2	p<0.7	0.96	0.82 - 1.128	0.9	0.551 - 1.45
G	83	39.2	38	37.0	0.2	p<0.7	1.0	0.88 - 1.213	1.1	0.68 - 1.815
A/A	39	36.8	21	40.4	0.2	p<0.7	0.9	0.75 - 1.196	0.86	0.435 - 1.69
A/G	51	48.1	24	46.1	0.05	p<0.8	1.06	0.85 - 1.328	1.1	0.55 - 2.10

G/G	16	15.1	7	13.5	0.075	p<0.8	1.04	0.77 - 1.40	1.14	0.44 - 2.98

Interestingly, when dividing patients with PCOS into two groups with the presence of metabolic syndrome disease, it was found that in the MC+ group, the wild variant (AA genotype) of the CYP17A1 gene is even higher than in the control group (45.0% and 40.4%, respectively).), the heterozygous variant (genotype AG) is almost equal (43.3 and 46.1%, respectively), and the mutant variant was more common in the control group. Therefore, we can conclude that the importance of developing PCOS in MS+ patients with the mutant form of the genotype - GG does not matter (chi2=0.08; OR=0.85; 95% CI:0.27 - 2.60; p=0.77). (Table 2).

table 2

The results of genotyping of CYP17A1 gene polymorphism in patients with PCOS MS+, as well as in healthy people are presented.

Alleles and genotypes	Number of examined alleles and genotypes				Chi2	P	RR	95%CI	OR N	95%CI %
	PCOS with metabolic syndrome (n=60)		Control group (n=52)							
	n	%	N	%						
A	80	66.7	66	63.0	0.25	p=0.61	1.06	0.88 - 1.38	1.15	0.66 - 1.99
G	40	33.3	38	37.0	0.25	p=0.61	0.9	0.72 - 1.21	0.87	0.50 - 1.50
A/A	27	45.0	21	40.4	0.24	p=0.62	1.1	0.77 - 1.54	1.2	0.57 - 2.56
A/G	26	43.3	24	46.1	0.09	p=0.76	0.95	0.67 - 1.34	0.9	0.42 - 1.88
G/G	7	11.7	7	13.5	0.08	p=0.77	0.9	0.53 - 1.61	0.85	0.27 - 2.60

The distribution of genotypes in the studied polymorphic loci was checked for compliance with the Hardy-Weinberg equation. The deviation of genotypes from the Hardy-Weinberg equation in the main and control groups was almost not observed. (D=0.00 and D=-0.01, respectively). (Table 4.4).

Table 3

Correspondence of the CYP17 gene polymorphism genotype to the Hardy-Weinberg equation in PCOS patients and in healthy patients.

(chi-squared test, df=1)

Main group (n=106)					
alleles	Allele frequency				
A	0.61				
G	0.39				
Genotypes	Genotype frequency		Xi2	p	df
	observable	expected			

A/A	0.37	0.37	0		
A/G	0.48	0.48	0		
G/G	0.15	0.15	0		
Total	one	one	0.01	0.877	one
Control group					
alleles	Allele frequency				
A	0.63				
G	0.37				
Genotypes	Genotype frequency		Xi2	p	df
	observable	expected			
A/A	0.404	0.4	0.01		
A/G	0.461	0.466	0.05		
G/G	0.135	0.136	0.04		
Total	one	one	0.1	0.721	one

Groups	Ho	He	D*
Main group	0.48	0.48	0.00
Control group	0.461	0.466	-0.01

Note: D = (Ho - He)/He

In this way, the study showedthat the GG mutant genotype was statistically significantly more common in patients than in controls. When dividing PCOS patients, they were divided into groups and compared with the control group, MS+ PCOS patients had a lower level of the genotype of the mutant form (GG) compared to the control group, but in MS-PCOS patients compared to the control group, the mutant gene was determined more. From this it follows that in the development of PCOS in MS-patients, the CYP17A1 gene mutation (rs743572) plays a certain role, while in MS+ patients the development of PCOS is due to factors other than the mutation of the CYP17 gene. But this finding was not significant when measured through xi2, since our results for chi2 were less than 3.84. The normal wild variant played a protective role in the main group (OR=0.9), especially in MC(-) patients (OR=0.65). When it comes to the Hardy Weinberg equation, we found no significant difference between expected and observed outcomes in the main and control group. Estimates of polymorphism prediction efficiency, as already mentioned, showed only 0.6, which means that the prediction efficiency was not reliable in terms of mutant allele and genotype.

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