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To the Results of Detection of the Association of FGB Gene (rs1695) IIe 105 Val Polymorphism Genotypes in Pregnant Women in Uzbekistan

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Pregnancy, Fetoplacental insufficiency, Genetics, "Circulatory system" of the gene.

With the development of a genetic approach to the study of the etiology and pathogenesis of many diseases, including FPI, great importance has been attached to congenital or hereditary disorders in the processes of storage, transmission and realization of genetic information. In a view of the priority of endothelial dysfunction in the FPI genesis , the importance of the vascular system, as the main diagnostic feature of the disease, and findings of previous studies on the genetics of this pathology, namely the existence of polymorphism of the "vascular system" and "endothelial dysfunction" genes in many ways can explain the obvious individual differences in origin and course of the disease.

The aim of our research was to determine the frequency of polymorphisms of hemostasis and fibrinolysis genes: FGB in pregnant women in Uzbekistan.

Research Material and Methods

The object and subject of the study were pregnant women, patients' DNA samples and the FGB gene (rs1695) IIe 105 Val fibrinolysis gene.The study included 50 pregnant women aged from 20 to 45 years who were observed at the base of the clinic of the RSSPMC For Obstetrics and Gynecology under the Ministry of Health of the Republic of Uzbekistan. All the pregnant women have underwent clinical, laboratory, instrumental and functional (ultrasound) studies. The FPI was diagnosed on the basis of clinical, laboratory and functional studies. Molecular genetic examination of biomaterials (DNA) was performed on the Department of Molecular Medicine and Cellular Technologies of the Research Institute of Hematology and Blood Transfusion under the Ministry of Health of the Republic of Uzbekistan.

DNA samples were isolated from peripheral blood lymphocytes in accordance with the modified method. The concentration and purity of the isolated DNA was assessed by measuring the optical density of DNA-containing solutions at a wavelength of 260 and 280 nm against TE on a NanoDrop 2000 spectrophotometer (USA). PAI polymorphism genotype was determined by PCR on programmable thermal cyclers CG-1-96 Corbett Research (Australia) and 2720 Applied Biosystems (USA) using test systems of Liteh LLC (Russia), according to the manufacturer's instructions. The temprature mode was set as follows: 94°C - 4 minutes; 94°C- 30 seconds, 60°C -30 seconds, 72°C - 30 – 35 cycle; 72°C - 7 minutes.

Statistical analysis of the results was carried out using the statistical software package "OpenEpi 2009, Version 2.3". The frequency of variants of alleles and genotypes (f) was calculated by the formula: f=n/2N и f=n/N, where n is the incidence of the variant (allele and genotype) and N is sample size.

Results and Discussion

The results of clinical, instrumental and functional studies of 50 pregnant women showed that fetoplacental insufficiency (FPI) was diagnosed in 40, which accounted for 80% of cases. Information about gene sequences and primer structure was obtained taking into account the original literary source and in GeneBank.

We have studied the distribution of polymorphisms of the IIe 105Val enzyme gene FGB in pregnant women with FPI and the control group without FPI (Table 1).

№	Group	Allele frequency				Genotype distribution frequency					
		A		G		A\A		A/G		G/G	
		n	%	n	%	n	%	n	%	n	%
1.	The main group of pregnant women with FWS n= 40 (80)	70	87.5	10	12.5	30	75.0	10	25.0	0	0.0
2.	Pregnant women without FWS n=10 (20)	17	85	3	15	8	80.0	1	10.0	1	10.0

Table 1: The frequency distribution of alleles and genotypes of IIe 105 Val polymorphism of the FGB gene in groups of pregnant women with FPI and controls (without FPI).
n –the number of patients examined; * n - the number of chromosomes studied.

As can be seen from the table, a comparative analysis of the distribution frequencies of alleles and genotypes of the FGB fibrinolysis gene IIe 105 Val polymorphism among 80 DNA samples in 40 pregnant women revealed the presence of a normal A allele and the G allele in 87.5% and in 12.5% of cases, respectively ($\chi 2$=0.1; P=0.8; OR=1.2; 95%CI 0.306-4.983).

Whereas, in the control group in 10 pregnant women without FPI, the frequency of incidence of the normal allele A of the FGB gene was 85%, whereas the FGB gene IIe 105 Val mutant A allele was 15%, respectively. The frequency distribution of the genotypes of this polymorphism also revealed significant differences between the main and control comparison groups in the total sample (P<0.05).

Thus, A / A genotypes were observed in 30 pregnant women with FPI, which accounted for 75% of cases. Whereas, the A / G genotypes of the FGB gene was found in 10 out of 40 pregnant women with FPI, which amounted to 25.0%, and in the group of pregnant women without FPI it was found in 1 women (10.0%), respectively. The G / G genotype was found in 1 (10.0%) pregnant women without FPI. According to the odds ratio, the risk of developing FPI in the main group in the presence of G / A polymorphism ($\chi 2$=1.0; P=0.3; OR=3.0; 95%CI 0.3- 26.71) is 2.5 times higher compared to the control group of pregnant women without FPI.

Genotypes	Genotype frequency		χ^2	P
	Observed	Expected		
A/A	75,0	76,6	0,013	0.4
A/G	25,0	21,8	0,179	
G/G	0,0	1.56	0,625	
Total	1,00	1,00	0,816	

Table 2: Expected and observed frequencies of distribution of genotypes of IIe FGB gene 105Val polymorphism by RCM in the group of pregnant women with FWS.

As follows from table 2, indicators of the frequency of the distribution of genotypes according to the RCM of FGB gene IIe 105 Val polymorphism in the main group of pregnant women with FPI showed that the observed frequency of A / A genotypes was found in 75.0%, heterozygous A / G genotypes in 25.0% and homozygous - G / G genotypes in 0%, respectively, whereas the expected frequency of A / A and heterozygous A / G genotypes in the group were found in 76.6% and 21.8% of cases, respectively, and G / G - in 1.56%. For the IIe 105Val FGB gene in the group of pregnant women with FWS, the empirical (Hobs) distribution of genotypes corresponds to the theoretically expected (Hexp) in PSC (p>0.05).

Genotypes	Genotype frequency		χ^2	P
	Observed	Expected		
A/A	80	72,3	0,083	0.056
A/G	10	25,5	0,942	
G/G	10	2,25	2,669	
Всего	100,00	100,00	3,695	

Table 3: Expected and observed frequencies of distribution of FGB gene IIe 105 Val polymorphism genotypes by RCM in the group of pregnant women without FWS.

While in the control group of pregnant women without FPI, the observed frequency of A / A genotypes was found in 80% of cases, and the expected frequency of genotypes was 72.3%, whereas the frequency of heterozygous A / G genotypes was found in 10% and 25.5% of cases, and homozygous mutant genotypes G / G were determined in 10 and 2.6%, respectively (Table 3).

For this locus, the empirical (Hobs) distribution of genotypes in the control group almost corresponds to the theoretically expected (Hexp) in RCM (p>0.05). However, there is a tendency to deviate.

Thus, the results of the study showed a tendency to increase of the expected mutant in the main group of pregnant women with placental insufficiency (FPI) against the group without FPI (10% and 2.25% respectively.). The results require further study of this gene in pregnant women.

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