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Evaluation of the detectability of the integrin alpha-2 (platelet platelet glycoprotein Ia/IIa) (ITGA2) gene polymorphism in pregnant women with fetal growth restriction syndrome.

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Resume
The article presents a molecular genetic study of the polymorphism of the integrin alpha-2 (platelet glycoprotein Ia/IIa) (ITGA2) gene in pregnant women with fetal growth restriction syndrome.
Goal. Evaluation of the detectability of the association of the integrin alpha-2 (platelet glycoprotein Ia/IIa) (ITGA2) gene polymorphism in women with the physiological course of pregnancy and fetal growth restriction syndrome in the Uzbek population of the Bukhara region.
Materials and methods. 80 pregnant women were examined at the gestation period from 8-36 weeks: 40 pregnant women with fetal growth restriction syndrome and 40 women with physiological pregnancy.
The results of the study showed that the functionally unfavorable T allele and the association of polymorphism of the genotype C / T polymorphism of the ITGA2-α2 gene is not a significant determinant of an increased risk of developing SORP in Uzbekistan ($\chi 2<3.8$; $P>0.05$).

Key words: fetal growth restriction syndrome, endothelial system gene, ITGA2 gene

Fetal growth restriction syndrome (FGRS) is a cause of perinatal morbidity and mortality, a risk of sudden infant death worldwide, and a public health problem in general [1]. According to the statistics of the World Health Organization, the number of newborns with fetal growth restriction syndrome ranges from 31.1% in Central Asian countries to 6.5% in developed European countries. In the US, SORP occurs in 10–15% of births, with signs of perinatal hypoxia occurring in 30% of children diagnosed with FGRS. In Uzbekistan, this syndrome occurs with a frequency of 3.4-18% of cases according to various authors.

According to the literature data, when studying the etiology and pathogenesis of FGRS, it is necessary to take into account genetic predisposition factors that cause the occurrence of a number of pathological conditions when interacting with environmental factors, characterized by immunological disorders, endocrinopathies, disorders of the endothelial system, in particular with thrombophilia, etc. [1,3,5].

Associations of polymorphisms of genes of factors and components of the hemostasis system play a certain role in the occurrence of FGRS, leading to impaired functional activity. However, the data of different authors are significantly contradictory. Thus, some researchers have established an association between the risk of FGRS and the presence of factor V coagulation in a patient [2,4]; and according

to other authors, there is no relationship between the polymorphism of the genes that determine thrombophilia and the risk of FGRS [5].

Despite the study of some genes associated with the mechanism of development of fetal growth restriction syndrome, this problem dictates the need for further studies, including genetic studies, for the most effective diagnosis and prognosis of the development of this pathology.

The aim of the study was to assess the detectability of the association of polymorphism of the integrin alpha-2 gene (platelet glycoprotein Ia / IIa) (ITGA2) of the hemostasis system in women with a physiological course of pregnancy and fetal growth restriction syndrome in the Uzbek population of the Bukhara region.

Materials and research methods. We examined 80 pregnant women in gestational age from 22-36 weeks: The main group consisted of 40 pregnant women with FGRS (main group), the second subgroup consisted of 40 women with physiological ongoing pregnancy (control group) and timely delivery, observed from early gestational age in antenatal clinics and hospitalized in an obstetric hospital in Bukhara.

Research results. The age of women in the main group ranged from 17 to 36 years and averaged 22.5+1.8 years. The age of patients in the control group ranged from 16 to 38 years, averaging 23.2+1.4 years (p>0.05). In terms of pregnancy parity, both groups were comparable.

Clinical and functional studies of 80 pregnant women showed that 40 had fetal growth restriction syndrome (FGR), which amounted to 50%. According to the severity of SORP, the I degree of severity was diagnosed in 4 (10%), the II degree - in 19 (47.5%) and the III degree of severity - in 13 (32.5%).

In patients of the main group, compared with the control group, a burdened somatic and obstetric-gynecological history was noted. Among extragenital diseases, cardiovascular disease prevailed in 14 (34.2%) observations of the main group and in 11 (28.8%) of the control group. Diseases of the gastrointestinal tract - in 11 (28.5) and 14 (34.3) patients, respectively. Neuroendocrine disorders occurred in 15 (37.1) and 14 (34.3) pregnant women, respectively, in the main and control groups.

The course of this pregnancy, among the complications of pregnancy in women, the threat of termination of pregnancy in the 1st and 2nd trimesters was more often detected (53.6%, p=0.026); gestational arterial hypertension (12.2% p=0.010); development of placental disorders (100.0%, p=0.000).

Molecular genetic study of the C/T polymorphism of the ITGA2-α2 gene in pregnant women revealed the following indicators (Table 1).

Table 1 .

Distribution frequency of genotypes of ITGA2-α2 gene C/T polymorphism (PLAII) in groups of pregnant women with and without FGRS.

Groups		Allele frequency				Frequency distribution of genotypes					
		C		T		C/C		C/T		T/T	
		n*	%	n*	%	n	%	n	%	N	%
1	Control group	77	96.3	3	3.75	37	92,5	3	7,5		

	Pregnant women without FGRS n=40 (80)										
2	Pregnant women with FGRS n=40 (80)	76	95.0	4	5	36	90,0	4	10		

Note: n is the number of examined patients;

As can be seen from Table 1, the distribution of alleles of the C/T polymorphism of the ITGA2-α2 gene in pregnant women with a physiological course revealed the presence of a favorable C allele in 96.3% of cases (77/80), while an unfavorable T allele - in 3.75% % (3), which was significant. And in the group of pregnant women with SORP, the frequency of detection of the favorable allele C was 95% of cases (76/80), and the mutant allele T was 5% (4), respectively.

Analysis of the detectability of the association of polymorphism of the ITGA2-α2 gene genotypes in the control group of pregnant women showed that the association of polymorphism of favorable C/C genotypes was 92.5% of cases (37/40) in 28.6% of cases, heterozygous C/T genotypes - in 7, 5% of cases (3/40), which was 12.3 times lower compared to the indices of C/C genotypes, respectively ($P<0.05$). Whereas in the group of pregnant women with SORP, the incidence of association of polymorphism of favorable C/C genotypes was 90% (36/80), and heterozygous variants of C/T genotypes were detected in 10% of cases (4/80), respectively. The data obtained indicated that the heterozygous C/T variant was 1.3 times higher than in the control group.

An analysis of the obtained molecular genetic results of the study shows that the association of C/T polymorphism of the ITGA2-α2 gene with the risk of developing fetal growth restriction syndrome is unreliable. ($\chi2=0.2$; $P=0.7$;) That is, according to preliminary data, the functionally unfavorable T allele of the C/T polymorphism of the ITGA2-α2 gene is not a significant determinant of an increased risk of developing fetal growth restriction syndrome in the population of Bukhara region. ($P>0.05$).

Table 2.

Expected and observed frequency of distribution of genotypes according to RHV C/T polymorphism of the ITGA2-α2 gene in groups of pregnant women without FGRS:

Genotypes	genotype frequency		χ^2	P
	Observed	Expected		
C/C	92,5	92,64	0,0	0,6
C/T	7,5	7,2	0,004	
T/T	0,0	0,14,4	0,056	
Total	100,0	100,0	0,060	

At the same time, there is a slight tendency towards an increase in the frequency of the T/T genotype of the C/T polymorphism of the ITGA2-α2 gene in the group of pregnant women with ORPS compared with the group of pregnant women without ORPS.

According to Table 2, a non-significant difference between the expected and observed genotype frequencies of the C/T polymorphism of the ITGA2-α2 gene was revealed. The observed genotype frequencies correspond to the theoretically expected ones and are in Hardy-Weinberg equilibrium.

Table 3.
Expected and observed frequency of distribution of genotypes according to RHV C/T polymorphism of the ITGA2-α2 gene in groups of pregnant women with FGRS:

Genotypes	genotype frequency		χ^2	P
	Observed	Expected		
C/C	90,0	90,25	0,0	0,7
C/T	10,0	9,5	0,01	
T/T	0,0	0,254	0,1	
Total	100,00	100,00	0,1	

According to Table 3, it is noted that the index of heterozygous deficiency is not very high (D=-0.1). An insignificant deviation of the observed distribution of genotypes from the C/T polymorphism of the ITGA2-α2 gene expected in RCM was found due to the lack of the observed number of heterozygotes in the main group of patients.

Conclusions:

1. The association of C/T polymorphism of the ITGA2-α2 gene with the risk of developing fetal growth restriction syndrome is not significant. ($\chi2=0.2$; $P=0.7$)
2. Preliminary analysis of molecular genetic studies shows that. that the functionally unfavorable T allele and the association of the C/T genotype polymorphism of the ITGA2-α2 gene polymorphism is not a significant determinant of the increased risk of developing ORPS in Uzbekistan ($\chi2<3.8$; $P>0.05$).

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