

# Assessment of ITGA-2 (C807T) Gene Polymorphism in Pregnant Women with Abdominal Delivery

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**Abstract Background.** New data have shown that the collagen-binding platelet receptor ITGA-2 (C807T) may play an important role in the pathogenesis of intraoperative hemostatic complications. One of the most effective ways to study the genetic mechanisms of platelet aggregation disorders is to identify genes that make a significant contribution to the pathogenesis of the disease. **Aim.** From this perspective, the purpose of this study was to assess the frequency of ITGA-2 (C807T) gene polymorphism in pregnant women with abdominal delivery. **Materials and methods.** Genetic studies were conducted on 80 pregnant women of the main group and 85 women with physiological pregnancy, the polymorphism of the ITGA-2 (C807T) genes was studied. In turn, we divided the 80 pregnant women of the main group into 2 groups. More precisely, in Group I we included 55 pregnant women who underwent a planned cesarean section. Group II included 25 pregnant women who underwent an emergency cesarean section. **Results.** From the above indicators, it became clear that the mutant T allele, in turn, significantly increases the likelihood of bleeding during surgery. The wild S allele plays a protective role. The results of our study were reliable ( $\chi^2=9.0$ ;  $P=0.01$ ). Thus, since the AUC averages 0.7, the mutant C allele of the ITGA-2 gene has relatively high prognostic efficacy in hemostatic disorders and as a marker for predicting their pathophysiology. **Conclusions.** Thus, the ITGA-2 gene polymorphism (C807T) in the mutant T/T genotype had an AUC of more than 60.0, which proves its important role in the risk of developing hemostatic dysfunction.

**Keywords** ITGA-2, Polymorphism (C807T), Cesarean section pregnant women, Hypertension in Pregnancy

## 1. Introduction

The increase in the frequency of cesarean section in recent years, associated with the expansion of indications for surgery, mainly due to relative indications in the interests of the fetus, remains consistently high [1,2,4,5,8,9,10]. In Uzbekistan, this level averages 25% during cesarean section, and reaches 25-30% in perinatal centers, with no signs of decreasing this trend.

Recent studies have shown that polymorphisms of the ITGA-2 (C807T) gene, which encodes the collagen-binding platelet receptor, can play an important role in the development of intraoperative hemostasis disorders [3,6,7,9,10]. One of the main methods for studying the genetic basis of platelet aggregation disorders is to identify genes that significantly influence the pathogenesis of these conditions. Studies of genetic factors of thrombosis indicate that hemostatic cascade proteins are more common in individuals with "unfavorable" alleles [1,10]. In this regard, a decision was made to study the role of these polymorphisms in the population of Uzbekistan's women.

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purpose of this study was to assess the frequency of ITGA-2 (C807T) gene polymorphism in pregnant women with abdominal delivery.

## 2. Material Methods

Genetic studies were conducted among 80 pregnant women who delivered via cesarean section (main group) and 85 women with physiologically progressing pregnancy (control group). ITGA-2 (C807T) gene polymorphisms were analyzed. The main group was divided into two subgroups: the first subgroup included 55 women who underwent planned cesarean section, and the second subgroup included 25 women who underwent emergency cesarean section.

The inclusion criteria were pregnant women

- Women subject to abominate childbirth, as well as
  - Pregnant women with history of obstetric bleeding
- The exclusion criteria were women who were noted:

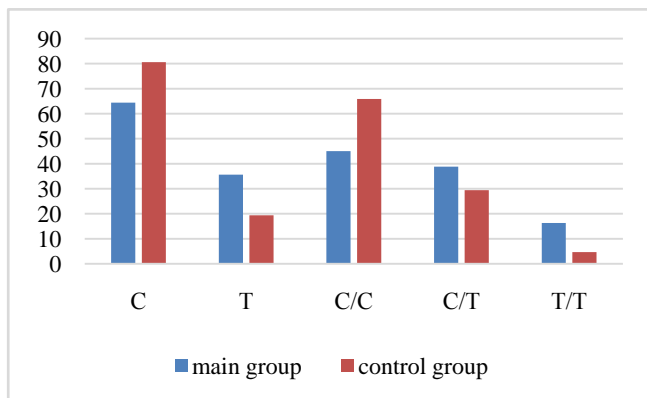
- Severe extragenital pathology
- Hormonal pathology
- Multiple pregnancy
- Infectious pathology
- Endocrine pathology
- Autoimmune pathology

A statistical method was used on a personal computer, which includes data processing using the variation statistics method, calculating the following parameters for each sample: arithmetic mean (M), standard deviation ( $\delta$ ), error of arithmetic mean (m). Comparison of the mean values of the studied indicators was carried out according to Student's criterion (t), if the distributions obeyed the normal law. The difference between two compared quantities was considered significant if the probability of their identity was less than 5% ( $p < 0.05$ ).

### 3. Debate

When studying the distribution of alleles and genotypes of the ITGA-2 (C807T) gene polymorphism among pregnant women who underwent planned and emergency cesarean section, as well as among women with natural childbirth, we identified the following indicators.

In the main group, the mutant homozygous T/T genotype was 16.25%, the heterozygous C/T genotype was 38.75% and the homozygous C/C genotype was 45% (Figure 1).



**Figure 1.** Distribution of alleles and genotypes of the ITGA-2 gene in pregnant women of the main group

We conducted a study of pregnant women in the main group, dividing them into two subgroups, the distribution of which is described above. The results showed that the frequency of the homozygous C/C genotype (wild type) was 47.27% in group I, 40% in group II, and 65.88% in the control group. The heterozygous C/T genotype was detected in 34.55% of women in group I, 48% of women in group II, and 29.41% of women in the control group. Compared to the control group, the homozygous mutant T/T genotype was more common in groups I and II - 18.18% and 12%, respectively, while in the control group its frequency was 4.71% (Figure 1).

The correspondence of the distribution of genotypes of the ITGA-2 (C807T) gene polymorphism to Hardy-Weinberg equilibrium was verified. In the main and control groups, there were practically no deviations of genotypes from the Hardy-Weinberg equilibrium ( $D = -0.16$  and  $D = -0.06$ , respectively).

In the main group, for the ITGA-2 gene, the observed empirical indicator  $H_{obs}$  for the homozygous C/C genotype

was 0.45%, and the theoretical  $H_{exp}$  - 0.41% ( $\chi^2 = 0.244$ ;  $p = 0.165$ ). For C/T and T/T genotypes, the observed empirical  $H_{obs}$  indicators were 0.38% and 0.163%, and the theoretical  $H_{exp}$  - 0.45% and 0.127%, respectively ( $\chi^2 = 0.88$ ;  $p = 0.165$  and  $\chi^2 = 0.798$ ;  $p = 0.165$ ), which did not show a statistically significant decrease.

In the control group, the frequency of C/C, C/T, and T/T genotypes was 0.659/0.649, 0.294/0.313, and 0.047/0.038, respectively ( $\chi^2 = 0.305$ ;  $p = 0.554$ ), indicating a low probability of systematic errors in the study (Table 1).

**Table 1.** Observed and expected distribution indicators of the ITGA-2 (C807T) gene polymorphism genotypes according to Hardy-Weinberg equilibrium in the main and control groups

Main group					
Alleles	Allele frequency				
C	0.64				
T	0.36				
Genotypes	Genotype frequency		$\chi^2$	p.	df
	observed	expected			
S/S	0.45	0.414	0.244		
S/T	0.388	0.459	0.883		
T/T	0.163	0.127	0.798		
Total	1.	1.	1,926	0.165	1.

Control group					
Alleles	Allele frequency				
C	0.81				
T	0.19				
Genotypes	Genotype frequency		$\chi^2$	p.	df
	observed	expected			
S/S	0.659	0.649	0.012		
S/T	0.294	0.313	0.096		
T/T	0.047	0.038	0.198		
Total	1.	1.	0.305	0.554	1.

Note: (\* $H_{exp}$  - Expected indicator, \* $H_{obs}$  - Observed indicator)

Analysis of the data presented in the table shows that in the main group of pregnant women, the observed indicator of the heterozygous genotype of the ITGA-2 (C807T) gene polymorphism was closer to the expected value (0.39/0.46;  $D = -0.16$ ). In the control group, these indicators were 0.29/0.31;  $D = -0.06$ .

In our study, the frequency of alleles of the ITGA-2 gene was distributed as follows: in the main group, the C allele was 64.4%, and the mutant T allele was 35.6%, while in the control group, these indicators were 80.6% and 19.4%, respectively. For the C allele:  $\chi^2 = 10.9$ ;  $p > 0.01$ ;  $RR = 0.8$ ; 95% CI: 0.52-1.22;  $OR = 0.4$ ; 95% CI: 0.27-0.71. For the mutant T allele:  $\chi^2 = 10.9$ ;  $p > 0.01$ ;  $RR = 1.3$ ; 95% CI: 0.71-2.22;  $OR = 2.3$ ; 95% CI: 1.4-3.76. From the perspective of odds ratio (OR), the mutant T allele increases the risk of hemostasiological complications during cesarean section in the pregnant women included in the study ( $OR = 2.3$ ; 95% CI: 1.4-3.76). Results for both alleles were statistically significant

( $\chi^2=4.5$ ;  $p=0.05$ ).

When comparing the distribution of C/C, C/T, and T/T genotypes of the ITGA-2 gene (C807T) in the main and control groups, it was found that the wild C/C genotype was more common in the control group, while the heterozygous (C/T) and mutant (T/T) genotypes prevailed in the main group. The frequency of C/C, C/T, and T/T genotypes in the main group was 45.0%, 38.8%, and 16.3%, respectively, while in the control group it was 65.9%, 29.4%, and 4.7%. For the C/C genotype in the control group:  $\chi^2=7.3$ ;  $p>0.1$ ; RR=0.7; 95% CI: 0.37-1.27; OR=0.4; 95% CI: 0.23-0.79. In the main group, the heterozygous genotype C/T ( $\chi^2=1.6$ ;  $p=0.48$ ; RR=1.3; 95% CI: 0.71-2.44; OR=1.5; 95% CI: 0.8-2.9) and the mutant genotype T/T ( $\chi^2=5.9$ ;  $p=0.08$ ; RR=3.5; 95% CI: 1.85-6.44; OR=3.9; 95% CI: 1.31-11.81) were more common.

#### 4. Conclusions

Analysis of the presented data showed that in our study, the mutant T/T genotype of the ITGA-2 gene (C807T) was associated with a significant increase in the risk of intraoperative hemostatic complications during childbirth and cesarean section (OR=3.9; 95% CI: 1.45-14.01). The C allele and the homozygous C/C genotype of the ITGA-2 (C807T) gene polymorphism do not have a significant effect on the development of intraoperative hemostasiological complications in the Uzbek population, however, the wild type of the C allele likely performs a protective function in relation to such complications. At the same time, intraoperative hemostatic complications were observed in women with the mutant T allele and T/T genotype. For a deeper understanding of the role of genes in unfavorable pregnancy outcomes, it is necessary to expand the sample of families under study and create a database that includes a list of mutations associated with bleeding.

Thus, ITGA-2 (C807T) gene polymorphisms can act as risk factors for intraoperative hemostasiological complications and, as an independent genetic marker, increase the likelihood of bleeding during cesarean section in pregnant women.

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