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GENETIC FACTORS OF HEMOSTASIS DISORDERS IN WOMEN OF REPRODUCTIVE AGE

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ABSTRACT

Background. According to studies, mutations in the genes of the hemostasis system are associated with an increased risk of venous thromboembolism and infertility. However, the diagnosis of thrombophilia is often erroneously established due to overdiagnosis, which can lead to unjustified and potentially harmful prescription of drugs.

The aim of the work is to study the hemostasis system in pregnant women with complicated hemostatic history.

Materials and methods. Data from 59 pregnant and postpartum women who were in Maternity Hospital No. 2 in Andijan were analyzed. Anamnesis, anthropometric parameters, results of genetic testing for polymorphisms of the genes of the hemostasis system and risk factors for coagulopathic disorders were assessed.

Results and discussion. When assessing the body mass index (BMI), it was normal in 49.4% of the postpartum women, and exceeded the norm in 50.6%. Polymorphism G-455A of the FGB gene was almost not detected. Mutation of the ITGA2 gene was detected in 48.1% of cases. Polymorphism of the PAI-1 gene was recorded in 84.8% of cases.

Conclusion. Hereditary disorders of the hemostasis system are a key risk factor for thromboembolic complications. Antithrombotic therapy started before pregnancy reduces the likelihood of obstetric complications and contributes to a favorable pregnancy outcome.

Keywords: thrombophilia, hemostasis, reproductive health, pregnancy complications, genetic polymorphisms.

Introduction.

In recent years, mutations in the genes of the hemostasis system have attracted increased interest from specialists, including obstetricians and gynecologists and hematologists, due to their association with obstetric complications and the risk of venous thromboembolism. The term "thrombophilia" was officially introduced in 1995 by the World Health Organization and the International Society on Thrombosis and Hemostasis, three decades after the first description of hereditary deficiency of antithrombin III by O. Egenberg in 1965 [1].

Classification of hemostasis disorders distinguishes between hereditary and acquired factors. Particular attention is paid to conditions such as diabetes, obesity, immune thrombovasculitis, sepsis and the influence of drugs [2,5]. Numerous studies confirm the existence of physiological hypercoagulability in pregnant women, aimed at preventing massive bleeding during childbirth [1–3,4,8]. Many authors emphasize that the presence of thrombogenic risk factors without clinical manifestations in the form of thrombosis or obstetric complications is not classified as thrombophilia and does not require the administration of drug prophylaxis [1, 6, 8]. However, it has been proven that coagulation disorders significantly increase the risk of complications during pregnancy and childbirth [3, 7, 9].

The aim of the work is to study the hemostasis system in pregnant women with complicated hemostatic history**.**

Materials and methods. The study was conducted at the Maternity Complex №2 in Andijan. It included 59 women in labor with a history of hemostasis disorders in previous births. Inclusion criteria: bleeding in the second stage of labor in the past and signed informed consent to participate in the study.

Anamnesis data and anthropometric parameters (height, body weight) were assessed. At the start of the study, all participants underwent hemostasis tests: hemostasiogram, genetic analysis of the hemostasis system (genetic passport) and general clinical blood test. Polymorphisms of the hemostasis system genes were determined, including coagulation factors I (FGB: -455_G>A), plasminogen activator inhibitor (PAI-1: -675 5G/4G) and platelet integrins (ITGA2: 807_C>T).

Blood was collected in the morning on an empty stomach from a peripheral vein into vacuum systems with an anticoagulant (3.2% sodium citrate) in a ratio of 1:9. To prevent clotting, the blood was immediately mixed. Citrated plasma, poor in platelets, obtained after centrifugation for 15 minutes at 3000 rpm at a temperature of 20–25 °C, was used. All coagulation tests were performed within 2 hours after blood collection using clotting, chromogenic, and immunoturbidimetric methods on an automatic analyzer.

Statistical analysis of the data was performed using Microsoft Office Excel 2010.

Results

The median age of the women was 33.1 years (range 21–44 years). According to WHO recommendations, normal body weight was observed in 39 patients (66.1%), and increased body mass index (BMI) was observed in 20 patients (33.9%). The distribution of pregnant women is presented in Table 1. The participants had a history of 1 to 5 pregnancies, while the number of miscarriages varied from 2 to 5. Hemoglobin levels below 110 g/l were detected in 76.7% of women, and anemia in all cases was due to iron deficiency, which was confirmed by laboratory data.

The results of the analysis of the prevalence of prothrombotic polymorphisms in the examined women are presented in Table 1. FGB gene polymorphisms were almost not detected. ITGA2 gene mutations associated with increased platelet aggregation were detected in 48.1% of cases. A mutation in the PAI-1 gene, which reduces the fibrinolytic activity of the blood and affects trophoblast invasion in early pregnancy, was detected in 84.8% of cases.

It is noteworthy that in women with high BMI, the frequency of these hemostasis system polymorphisms was comparable to the general population, and for some genes, even lower. This indicates an independent effect of metabolic syndrome on increased secretion of coagulation factors and decreased fibrinolytic activity.

Discussion. Data on the association of polymorphisms associated with hereditary thrombophilia with the risk of venous thrombosis or pregnancy complications remain contradictory. This may be due to population specificity, incorrect selection of study participants, limited sample size, or insufficient consideration of unfavorable combinations of allelic variants of different genes [9].

It is important to note that polymorphisms of different genes affect the development of complications of pregnancy and childbirth to varying degrees. Therefore, when assessing the risk of complications, it is necessary to take into account the potential impact of all alleles of the genes under study. In addition, physiological pregnancy itself is a condition that increases the risk of thrombosis. Genetic hemostatic disorders enhance physiological hypercoagulation during pregnancy, which often leads to activation of intravascular thrombosis and adverse pregnancy outcomes [1–3, 8, 9].

Thus, when assessing the thrombogenic risk in a patient, a set of factors reflecting the multigenic nature of thrombophilia should be taken into account. Specialists should pay special attention to women with habitual miscarriage in order to accurately determine the causes, avoid overdiagnosis, carefully analyze comorbid conditions, collect a detailed anamnesis and correctly interpret laboratory data [3, 6].

1. Table 1.

Prevalence of carriage of prothrombotic polymorphisms in the patients

Gene	Polymorphisms	Cases	Total percentage of genetic polymorphisms
FGB:_- 455_G>A	AA	3	4,2
	GA	2	
ITGA2:_807_C>T	CC	4	48,1
	CT	17	
PAI-1:-675_5G>4G	4G/4G	18	84,8
	5G/4G	19	
	5G/5G	11	

Analysis of the carriage of the most common congenital thrombophilias and polymorphisms of the hemostasis system showed high significance for pregnancy and childbirth of the following polymorphisms: the ITGA2 gene, associated with increased platelet aggregation, and the PAI-1 gene, causing a decrease in the fibrinolytic activity of the blood.

Hereditary gene polymorphisms are key risk factors for thromboembolic complications during childbirth. Early antithrombotic therapy, started before pregnancy, helps to reduce obstetric risks and improve birth outcomes.

The high prevalence of iron deficiency anemia and its negative impact on pregnancy and fetal development emphasize the need for timely correction using modern drugs in appropriate doses.

These data emphasize the importance of a thorough study and assessment of the hemostasis system in women with a complicated obstetric history.

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