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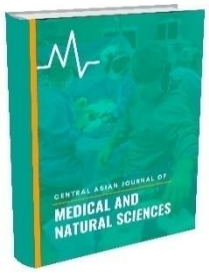

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Assessment of the Role of Genetic Polymorphism of the Hemostatic System Factors of the F3 Gene in the Development of Thrombophilia in Women of the Uzbek Population

1. Khafizova D. B.

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[1] Bukhara State Medical Institute named after Abu Ali ibn Sino

Summary: The article presents the results of molecular genetic studies of the hemostasis gene G/T gene F3 in women with unsuccessful IVF who have thrombophilia in the Uzbek population living. Analysis of molecular genetic studies of the frequency distribution of alleles of the G/T polymorphism of the F3 gene in a sample of women from the main group showed that the functional G allele was determined in 72.7%, and in the group of control individuals without thrombophilia - in 100%, respectively. ($\chi 2$=10.65; p<0.001; OR=0.04; 95%CI 0.00 – 0.73). While the mutant allele "T" in the main group was detected in 49 chromosomes (49/180), which accounted for 37.4% of cases. ($\chi 2$=10.65; p<0.001; OR=22.96; 95%CI 1.38 – 382.75). Clinical molecular genetic studies indicate that patients with identified non-functional genotypes G/T of the F3 gene are at risk of developing severe thrombophilia, which amounted to 38.8% of cases. ($\chi 2$=11.67; p<0.003; OR=19.83; 95% CI1.15 – 341.95). Variants of polymorphisms of hetero-G/T and homozygous genotypes T/T of the F3 gene are significant prognostic criteria for the risk of developing undeveloped pregnancies in women with thrombophilia among women of the Uzbek population.

Key words: thrombophilia, genetics, G/T polymorphism of the F3 gene.

The problem of thrombophilia in obstetric practice is one of the most important health problems throughout the world, including in Uzbekistan. It should be said that thrombophilia is associated not only with the development of venous thromboembolic complications (VTEC), but also with whole problems of obstetric complications - the so-called Great Obstetrical Syndromes. [1-4; 9,10, 14]

The term "thrombophilia" was first coined in 1995 by the World Health Organization (WHO) and the International Society of Thrombosis and Haemostasis (ISTH). [1,3, 5-7,9,10] The process of thrombophilia is characterized by a state of predisposition to the formation of thrombosis, the onset of which begins at an early age in persons with a family history, i.e. congenital types of thrombophilia

associated with profound hereditary deficiency of antithrombin III, factor V Leiden mutation, prothrombin mutation (620210D), decreased levels of proteins C and B. [9,10-14]

The acquired form of thrombophilia was characterized by the carriage of antiphospholipid antibodies (APA) in antiphospholipid syndrome (APS), associated with arterial and venous thrombosis, and fetal loss syndrome. [3,5,16] . In this case, the morphological substrate of most arterial disasters is a damaged (unstable) atherosclerotic plaque with thrombosis of the artery lumen.

Scientific publications express contradictions about the connection between carriage of prothrombogenic mutations and polymorphisms and the risk of phenotypic implementation in the form of thrombosis and/or obstetric complications. A number of studies and meta-analyses note an association with the presence of mutations. [2,3,7-10]. In this case, the associated probability of thrombosis and/or obstetric complications is estimated to range from 10 to 50%. It follows from this that approximately 50-90% of prothrombotic mutations have only a constant uncontrollable risk factor that is not realized phenotypically. Data analysis suggests that such a relationship has its own objectivity and validity; it is recommended to evaluate it in the context of the presence in an individual of not just any one risk factor, but their combinations, which in all cases determine the multigenic origin of thrombophilia.

Studies have established the importance of blood clots in pregnant women and fetal loss syndrome, which is one of the leading causes of death during pregnancy and delivery. On the other hand, women with a history of thrombosis have an increased risk of preeclampsia, as well as miscarriage and stillbirth due to blood clots in the placenta, umbilical cord or blood vessels in the fetus.

In connection with the above, we were interested in assessing the state of hemostasis - the multigene origin of thrombophilia in women with unsuccessful IVF in the Uzbek population, taking into account the assessment of plasma genes - F3 and F7.

The F3 gene encodes coagulation factor III, which is a cell surface glycoprotein. This factor allows cells to initiate coagulation cascades and functions as a high-affinity receptor for coagulation factor VII. The resulting complex provides the catalytic event responsible for the initiation of protease coagulation cascades through specific limited proteolysis. Unlike other cofactors of these protease cascades, which circulate as nonfunctional precursors, this factor is a potent initiator that is fully functional when expressed on cell surfaces, such as monocytes[13-24].

There are 3 different domains of this factor: extracellular, transmembrane and cytoplasmic. Platelets and monocytes have been shown to express this coagulation factor under procoagulant and proinflammatory stimuli, and a major role in HIV-associated coagulopathy has been described. Platelet-dependent coagulation factor III expression in monocytes has been described to be associated with severity and mortality of coronavirus disease 2019 (COVID-19). This protein is the only one in the coagulation pathway for which no congenital deficiency has been described. Alternative splicing results in many transcript variants. [25-42.]

The purpose of our research was to evaluate the detectability of allelic variants and genotypes of the F3 gene polymorphism (G/T) in the development of thrombophilia in women with unsuccessful IVF in the Uzbek population.

Material and research methods. We examined 105 women aged 20 to 39 years. All pregnant women underwent general clinical, instrumental, functional (ultrasound, Doppler), and ELISA studies. Pregnant women were consulted by related specialists. (therapist, neurologist, infectious disease specialist, dermatologist, endocrinologist, etc.) Among the 105 patients, the main group consisted of 90 women with an established diagnosis of thrombophilia and 15 women made up the age-matched

control group. Molecular genetic examination of biomaterials (DNA) was carried out on the basis of the clinical laboratory of Genotechnologies LLC. DNA extraction from all biological blood samples was carried out using the Ribo-prep kit (Interlabservice, Russia).

To identify the genotype polymorphism consisting of the G>T alleles of the F3 gene, allele-specific primers from the manufacturer were selected from DNA samples. To genotype DNA samples using polymerase chain reaction (PCR), 200 DNA samples were examined. For this purpose, the 96-cell automated amplifier "Applied Biosystems Veriti" was optimized according to the following program: initial denaturation once at 180 sec 94°C, 94°C - 10 sec, 64°C - 10 sec, 72°C - 20 sec in the program we did these specified steps 40 times for the polymerase chain reaction to occur. Statistical analysis of the results was carried out using the statistical software package “OpenEpi 2009, Version 2.3”.

Research results. Based on informed consent, the patients underwent molecular genetic studies to determine the occurrence of allelic variants and associations of polymorphisms of genotypes of the F3 gene using PCR. (Table 1.)

Table 1. Frequency of distribution of allelic variants and polymorphism of the F3 gene (G/T) with unsuccessful IVF in women with thrombophilia and the healthy control group.

№	Group	Allele frequency				Genotype distribution frequency					
		G		T		G/G		G/T		T /T	
		N	%	n	%	N	%	n	%	n	%
1.	Main group n=90(180)	83	79,8	21	20,2	48	53,3*	35	38,8	7	7,7
2	Counter. group n=15 (30)	30	100			15	100,0				

N – number of examined patients; *n - number of alleles studied; * - reliability indicator in relation to the control group (P<0.05)

As follows from the table, the frequency of distribution of alleles of the G/T polymorphism of the F3 gene in the sample of women of the main group showed that the functional G allele was determined in 72.7% (133/180), and in the group of control individuals without thrombophilia - in 100% (30 /30) respectively. (χ2=10.65; p<0.001; OR=0.04; 95%CI 0.00 – 0.73). While the mutant allele “T” in the main group was detected in 49 chromosomes (49/180), which accounted for 37.4% of cases. And in the group of control persons in our cases it was not detected. (χ2=10.65; p<0.001; OR=22.96; 95%CI 1.38 – 382.75); The data obtained were statistically significant (p<0.001) with a high odds ratio (OR=22.96), indicating a high association between the mutant allele “T” of the F3 gene polymorphism in thrombophilia in women of the Uzbek population.

The data obtained indicate a significant association of the allelic frequency of the mutant allele T of the F3 gene of the studied polymorphism with thrombophilia in women with unsuccessful IVF.

Analysis of the frequency distribution of genotypic variants of the G/T polymorphism of the F3 gene showed the detection of favorable homozygous G/G variants in 53.3% of cases (48/90), while in the group of control individuals this genotype was 100% (15/15), respectively . (χ2=11.67; p<0.003; OR=0.04; 95%CI0.00 – 0.63) (Table 1) . (P <0.001)

It should be noted that heterozygous genotypes G/T of the F3 gene were detected only in the main group and accounted for 53.3% of cases (48/90). (χ2=11.67; p<0.003; OR=19.83; 95% CI1.15 – 341.95) and mutant homozygous genotypes T/T - in 7 patients, which amounted to 7.7%, respectively. (χ2=11.67; p<0.003; OR=2.78; 95% CI 0.15 – 51.30). Moreover, in the control group, hetero- and

homozygous genotypes with mutant allelic variants were not detected. The data obtained were statistically reliable. (P <0.003).

Thus, the data from our study showed the association of the unfavorable variant allele "T" of the F3 gene polymorphism, leading to the replacement of Gln with Tim amino acid sequence, with the development of the risk of non-developing pregnancies (NP) due to thrombophilia in women with unsuccessful IVF in the Uzbek population. We found that the risk of developing this NB in the presence of a variant T allele polymorphism in the genome is increased by 22.9 times (OR = 19,83).

Table 2. Differences in the frequency of occurrence of alleles and genotypes of the G/T polymorphism of the F3 gene in the main and control groups

Alleles and genotypes	**Frequency of occurrence of alleles and genotypes**		**Statistical difference**
	Main group	***Control***	
Allele G	131	30	χ^2=10.65; p<0.001; OR=22.96; 95%CI 1.38 – 382.75
Allele T	49		
Genotype G/G	48	15	χ^2=11.67; p<0.003; OR=0.04; 95%CI0.00 – 0.63
Genotype G/T	35	0	χ^2=11.67; p<0.003; OR=19.83; 95% CI1.15 – 341.95
Genotype **T/T**	7	0	χ^2=11.67; p<0.003; OR=2.78; 95% CI 0.15 – 51.30

An important step in the study of polymorphic genes potentially associated with the development and pathogenesis of diseases is the analysis of the expected and observed frequency of genotypes of the studied polymorphisms and the correspondence of the frequency distribution to the Hardy-Weinberg equilibrium (HW), which contributes to the assessment of the population risk of genetically determined diseases.

Table 3. Expected and observed frequency of distribution of genotypes for the RCV polymorphism G/T of the F3 gene in the main group with unsuccessful IVF in women with thrombophilia.

Genotypes	genotype frequency		χ^2	P
	Observable	Expected		
G/G	53,3	53,01	0.530	
G/T	38,8	39,6	0.396	
T/T	7,8	7,4	0.074	
Total	100,00	100,00	0,01	0,9

Based on the calculation by the XB equation, in the main group the theoretically expected frequency of the favorable homozygous genotype G/G of the G/T polymorphism of the F3 gene was 53.01%, and of the observed genotype - 53.3%, respectively, which is 0.9 lower than the observed one. Whereas the expected frequency of the heterozygous genotype G/T was 39.6, and the observed one was 38.8%, which was 1.02 times higher than the indicators (P <0.05). It should be noted that in the variants of unfavorable genotypes T/T, the expected frequency was 7.4%, and the observed frequency was 7.8%, which were in unreliable indicators, i.e. were almost no different from each other.

Table 4. Expected and observed frequency of distribution of genotypes for RHB polymorphism G/T of the F3 gene in the control group of women without thrombophilia.

Genotypes	genotype frequency		χ^2	P
	Observable	Expected		
G/G	100,0	60,5	1.0	
G/T	0	34,5	0	1

T/T	0	4,9	0	
Total	100,00	100,00	0	

Whereas in the control group, based on the XB equation, the theoretically expected frequency of the favorable homozygous genotype G/G polymorphism of the F3 gene was 60.5%, and the observed genotype was noted to be 100.0%, respectively, which is 1.6 lower than the observed values. The frequency of the expected heterozygous variant G/A was 34.5% and the homozygous genotype T/T - 4.9% of cases, and the observed ones - 0%, which was 34.5 and 4.9 times higher than the indicators ($P < 0.05$).

Analysis of the results obtained shows that the distribution of all genotypes of the G/T polymorphism of the F3 gene in the main group of women and controls corresponds to RHV, indicating the absence of the influence of systematic or random factors that can change the genetic structure of populations. The study of the genetic structure of this marker revealed a high level of expected heterozygosity in the main and control groups of patients (39.6% and 34.5%, respectively).

Analysis of concomitant pathology in patients with unsuccessful IVF with thrombophilia showed that in patients with favorable genotypes G/G variants of the F3 gene, urinary tract infections (UTI) were detected in 12.2% of cases, blood disease (various degrees of anemia) was detected in 10.4% severity), endocrinopathy (thyroid disease) - 8.7%, respectively. Whereas in patients with heterozygous genotypes G/T, BMI was most often detected - 47.7%, endocrinopathy - 34.4%, ENT disease (chronic tonsillitis) - 34.4%, which is 3.9 and 3.4 times exceeded the indicators of patients with favorable genotypes of the F2 gene. ($P < 0.05$). In our opinion, the data obtained are important in the clinical course of pregnancy in patients with thrombophilia, which requires further study.

In the studies of Musalaeva I.O. (2022) found that intrauterine infection may cause fetal infection and inflammation, which can lead to a severe inflammatory response in the fetus called fetal inflammatory response syndrome.

It should be noted that in patients with mutant allelic variants of the F3 gene with concomitant pathology of the urinary tract, the blood system may be one of the leading provoking factors in the development of non-developing pregnancies with thrombophilia.

Taking into account the correspondence of the observed proportion of genotypes of the G/T polymorphism of the F3 gene in the studied samples to the Hardy-Weinberg equilibrium, our study indicates the connection of the functionally unfavorable allele “T”, leading to the replacement of Gln with Tia. amino acid sequence, with the development of non-developing pregnancies in thrombophilia. At the same time, the risk of developing a secondary pathology in the presence of a variant allele of polymorphism in the genome increases almost 20 times.

We have also shown that the heterozygous genotype of the G/T polymorphism of the F3 gene is a genetic determinant that determines the formation of thrombophilia in non-continuous pregnancies, and its carriage is a predisposition factor to the development of this pathology, increasing its risk by 19 times (OR = 19.8). The identified connection between the functionally unfavorable allele and the heterozygous genotype of the studied polymorphism with the pathogenesis of thrombophilia against the background of non-developing pregnancies may also indicate a high probability of association of this pathology with the variant G/T genotype.

Thus, clinical molecular genetic studies indicate that patients with identified non-functional genotypes G/T of the F3 gene have a risk of developing thrombophilia, which amounted to 38.8% of cases. ($\chi 2=11.67$; $p<0.003$; OR=19.83; 95% CI1.15 – 341.95). Variants of polymorphisms of hetero-G/T and

homozygous genotypes T/T of the F3 gene are significant prognostic criteria for the risk of developing undeveloped pregnancies in women with thrombophilia among women of the Uzbek population.

Conclusions:

1. Analysis of molecular genetic studies of the frequency distribution of alleles of the G/T polymorphism of the F3 gene in a sample of women from the main group showed that the functional G allele was determined in 72.7% (133/180), and in the control group without thrombophilia - in 100% (30/30) respectively. (χ2=10.65; p<0.001; OR=0.04; 95%CI 0.00 – 0.73). While the mutant allele "T" in the main group was detected in 49 patients (49/180), which accounted for 37.4% of cases. And in the control group in our cases it was not detected. (χ2=10.65; p<0.001; OR=22.96; 95%CI 1.38 – 382.75)

2. Clinical molecular genetic studies indicate that patients with identified non-functional genotypes G/T of the F3 gene have a risk of developing thrombophilia, which amounted to 38.8% of cases. (χ2=11.67; p<0.003; OR=19.83; 95% CI1.15 – 341.95). Variants of polymorphisms of hetero-G/T and homozygous genotypes T/T of the F3 gene are significant prognostic criteria for the risk of developing non-developing pregnancies during IVF in women with thrombophilia among women of the Uzbek population.

Literature:

1. Bakhadurovna, H. D., & Akmalovna, I. G. (2022). THE ROLE OF MULTIGENIC THROMBOPHILIA IN WOMEN WITH UNFAVORABLE OUTCOMES AFTER EXTRACORPOREAL FERTILIZATION. ResearchJet Journal of Analysis and Inventions, 3(1), 44-50.
2. Bakhodirovna, K. D. (2022). Thrombophlebia and Pregnancy, Predicting Perinatal Complications and Optimizing Administration Tactics. International Journal of Culture and Modernity, 13, 130-137.
3. Dustova, N. K., Hafizova, D. B., Jalolova, V. Z., & Raxmatova, M. R. (2018). Prevention of complications of varicose veins of pelvic organs in women of reproductive age. Asian Journal of Multidimensional Research (AJMR), 7(11), 54-59.
4. Hafizova, D. B. (2023). EVALUATION OF THE SIGNIFICANCE OF THE G/A POLYMORPHISM OF THEF7 GENE IN THE DEVELOPMENT OF AN UNFAVORABLE IVF OUTCOME IN WOMEN WITH THROMBOPHILIA. British Medical Journal, 3(2).
5. Hui, X. U., Maiti, G., Shanmugan, K., Prakash, B. B., Dustova, N. K., Hafizova, D. B., ... & Nurmamatovna, I. S. Asian Journal of Multidimensional Research (AJMR).
6. Ihtiyarova, G. A. (2013). Modern and differentiated approaches to the management of pregnant with a dead fetus. International Journal of Applied and Fundamental Research, (2), 191-191.
7. Ikhtiyarova, G. A. (2016). Differentiation of approaches to the management of pregnant women with antenatal fetal death. News of Dermatology and Reproductive Health, (1-2), 73-74.
8. Ikhtiyarova, G. A. (2018). Early diagnosis of complications of varicose veins in pregnant.
9. Ikhtiyarova, G. A. (2019). HORMONAL METHODS OF ABORTION IN WOMEN WITH ANTENATAL FETAL DEATH. PROBLEMS AND SOLUTIONS OF ADVANCED SCIENTIFIC RESEARCH, 1(1), 288-293.

10. Ikhtiyarova, G. A. (2022). A NEW VIEW ON THE PATHOLOGY OF ANTIPHOSPHOLIPID SYNDROME COMBINED WITH PRE-ECLAMPSIA OF PREGNANCY. World Bulletin of Public Health, 9, 84-87.
11. Ikhtiyarova, G. A. (2022). Assessment of Risk Factors for Intrauterine Fetal Malformations. International Journal of Formal Education, 1(4), 22-28.
12. Ikhtiyarova, G. A. (2022). EARLY PREGNANCY LOSS AFTER TREATMENT WITH ASSISTED REPRODUCTIVE TECHNOLOGIES. Asian journal of pharmaceutical and biological research, 11(1).
13. Ikhtiyarova, G. A. (2022). OUTCOMES OF ASSISTED REPRODUCTIVE TECHNOLOGY PROGRAMS IN PATIENTS WITH A HISTORY OF RELATED PREGNANCY MISSION. Thematics Journal of Microbiology, 6(1).
14. Ikhtiyarova, G. A. Diagnostics, treatment and obstetric tactics for fetal loss syndrome. F: News of Dermatology and reproductive health, (1.2016), S74-75.
15. Ikhtiyarova, G. A., & Aslanova, M. (2019). Zh., Dustova NK Microbiological changes in pregnant women with antenatal fetal death. Euaropean journal of research, (2), 102-109.
16. Ikhtiyarova, G. A., Dustova, N. K., Kudratova, R. R., Bakhramova, S. U., & Khafizova, D. B. (2021). Pre-Course Training of Women With Reproductive Loss of Fetus in Anamnesis. Annals of the Romanian Society for Cell Biology, 6219-6226.
17. Ikhtiyarova, G. A., Karimova, G. K., & Navruzova, N. O. (2019). KhairullaevCh. K. Ultrasound diagnostics of diabetic fetopathy in pregnant women with metabolic syndrome on the background of diabetes mellitus. Medicine and sports2019,(3-4), 56-58.
18. Ikhtiyarova, G. A., Khafizova, D. B., & Ikhtiyarova, D. F. (2019). Criteria For prediction of complications in pregnant women with antenatal fetal death. TOM VI, 67.
19. Ikhtiyarova, G. A., Kilicheva, V. A., & Hafizova, D. A. MODERN VIEWS OF CAUSES DYSMENORRHEA AND ITS CORRECTION. ЗАМАНУИ МЕДИЦИНА: ДӘСТУРЛЕР МЕН ИННОВАЦИЯЛАР, 514.
20. Juraboyevna, A. M. (2022). Comparative Analysis of ITGB 3 Gene Polymorphism in Fetal Growth Retardation Syndrome. Research Journal of Trauma and Disability Studies, 1(12), 64–72.
21. Karimova, G. K., Ikhtiyarova, G. A., & Muminova, N. K. (2021). Early biochemical markers and screening diagnosis of Gestional diabetes mellitus and its prevention during pandemic period. Journal of Natural Remedies, 22(1 (1)), 17-26.
22. Karimova, G. K., Navruzova, N. O., & Nurilloyeva Sh, N. (2020). An individual approach to the management of gestational diabetes. European Journal of Molecular & Clinical Medicine, 7(2), 6284-6291.
23. Komilovna, G. K. (2023). Clinical and Anamnestic, Laboratory and Instrumental Indicators of Pregnant Women with Gestational Diabetes. Central Asian Journal of Medical and Natural Science, 4(5), 390-398.
24. Komilovna, G. K. (2023). Clinical and Anamnestic, Laboratory and Instrumental Indicators of Pregnant Women with Gestational Diabetes. Central Asian Journal of Medical and Natural Science, 4(5), 390-398.

25. Sh, I. A., Ikhtiyarova, G. A., Musaeva, D. M., & Karimova, G. K. (2020). Assessment of the status of pregnant women with diabetes mellitus infected with COVID-19. New day in medicine, 2, 30.
26. Аслонова , М. (2022). ҲОМИЛА ЎСИШИ ЧЕГАРАЛАНИШ СИНДРОМИ МАВЖУД ҲОМИЛАДОРЛАРДА ҲОМИЛАДОРЛИК ВА ТУГРУК КЕЧИШ ХУСУСИЯТЛАРИ, ЯНГИ ТУГИЛГАН ЧАКАЛОКЛАР ҲОЛАТИНИ БАҲОЛАШ НАТИЖАЛАРИ. Евразийский журнал академических исследований, 2(13), 1211–1218.
27. Аслонова М.Ю. (2022). ПРИРОДА НАРУШЕНИЙ В СИСТЕМЕ МАТЬ-ПЛАЦЕНТА-Плод И ИХ РОЛЬ В РАЗВИТИИ СИНДРОМА ЗАДЕРЖКИ РОСТА ПЛОДА. Сеть ученых: Международный научно-исследовательский журнал , 3 (12), 1037–1047.
28. Аслонова Махлиё Джурабоевна. (2022). Оценка выявляемости полиморфизма гена интегрина альфа-2 (гликопротеина тромбоцитов Ia/IIa) (ITGA2) у беременных с синдромом задержки роста плода. Глобальное научное обозрение , 10 , 140–144.
29. Аслонова, М. Ж., Ихтиярова, Г. А., Хафизова, Д. Б., & Мирзоева, М. Р. (2018). Микробиологическая и гормональная характеристика формирования неразвивающейся беременности. In Фундаментальные и практические вопросы иммунологии и инфектологии. Сб. науч. статей участников междунар. науч.-практ. конф (pp. 9-15).
30. Ихтиярова, Г. А., Каримова, Г. К., Наврузова, Н. О., & Хайруллаев, Ч. К. (2019). Ультразвуковая диагностика диабетической фетопатии у беременных с метоболическим синдромом на фоне сахарного диабета. Тиббиѐт ва спорт,(3-4), 56-58.
31. Ихтиярова, Г. А., Курбанова, З. Ш., & Хафизова, Д. Б. (1999). СОВРЕМЕННЫЕ АСПЕКТЫ ВОСПАЛИТЕЛЬНЫХ ИЗМЕНЕНИЙ В СИСТЕМЕ МАТЬ-ПЛАЦЕНТА-ПЛОД ПРИ АНТЕНАТАЛЬНОЙ ГИБЕЛИ ПЛОДА. ИНФЕКЦИЯ, ИММУНИТЕТ и ФАРМАКОЛОГИЯ, 132.
32. Ихтиярова, Г., Курбанова, З., & Хафизова, Д. (2019). Воспалительные изменения в системе мать-плацента-плод при антенатальной гибели плода. Журнал вестник врача, 1(2), 61-68.
33. Ихтиярова, Г., Хафизова, Д., & Аслонова, М. (2020). ПАТОМОРФОЛОГИЧЕСКИЕ И МИКРОБИОЛОГИЧЕСКИЕ ПАРАЛЛЕЛИ ПУТЕЙ ИНФИЦИРОВАНИЯ ПЛАЦЕНТЫ У ЖЕНЩИН С РЕПРОДУКТИВНЫМИ ПОТЕРЯМИ ПЛОДА В ПЕРИОД ПАНДЕМИИ. Журнал вестник врача, 1(3), 54-58.
34. Каримова, Г. К. (2022). Гестацион Қандли Диабетда Ҳомиладорлик Ва Туғруқни Олиб Бориш. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 1(6), 180-192.
35. Каримова, Г. К. (2022). Гестацион қандли диабетни эрта ташхислашнинг биокимёвий скрининги. Barqarorlik va yetakchi tadqiqotlar onlayn ilmiy jurnali, 2(8), 199-212.
36. Каримова, Г. К., & Каримова, Г. К. (2023). Лаборатор-Инструментальные Показатели Беременных С Гестационным Диабетом. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(10), 1-8.
37. Каримова, Г. К., & Ихтиярова, Г. А. (2021). ПОПУЛЯЦИИ И РАННИЕ ПРЕДИКТОРЫ ГЕСТАЦИОННОГО САХАРНОГО ДИАБЕТА В ПЕРИОД ПАНДЕМИИ. Журнал теоретической и клинической медицины, (6-1), 77-80.
38. Каримова, Г. К., Ихтиярова, Г. А., & Муминова, Н. К. (2021). Ранние биохимические маркеры и скрининг-диагностика гессионального сахарного диабета и его профилактика в период пандемии. Журнал природных средств правовой защиты, 22(1), 1.

39. Каримова, Г. К., Ихтиярова, Г. А., & Наврузова, Н. О. (2020). Скрининг диагностика гестационного диабета. Новый день в медицине, (1), 220-222.

40. Каримова, Г. К., Наврузова, Н. О., & Нуриллоева, Ш. Н. (2020). Индивидуальный подход к ведению гестационного диабета. Европейский журнал молекулярной и клинической медицины, 7(2), 6284-6291.

41. Хафизова, Д. Б., & Ихтиярова, Г. А. (2022). Оценка Роли Генетического Полиморфизма Факторов Системы Гемостаза Гена F3 В Развитии Тромбофилии У Женщин Узбекской Популяции. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 1(5), 20-28.

42. Хафизова Д.Б. (2023). Оценка Роли Генетического Полиморфизма Факторов Системы Гемостаза Гена F3 в Развитии Тромбофилии у Женщин Узбекской Популяции. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(11), 225–234.

43. Tosheva, I. I. (2022). Research Article: Study of Obstetric and Somatic History in Women with Discharge of Amniotic Fluid. International Journal of Clinical Reports and Studies, 1(2).