ISSN: 2776-0960 Volume 3, Issue 1 Jan., 2022

THE ROLE OF MULTIGENIC THROMBOPHILIA IN WOMEN WITH UNFAVORABLE OUTCOMES AFTER EXTRACORPOREAL FERTILIZATION

Hafizova Dilnoza Bakhadurovna

Ikhtiyarova Gulchehra Akmalovna
Bukhara State Medical Institute named after Abu Ali ibn Sina

Relevance

Recently, the role of hereditary thrombophilia in recurrent IVF failure has been clarified. The association between thrombophilia and recurrent невынашиваниеммiscarriage or poor pregnancy outcome is well known. This may act by disrupting the initial vascularization processthat occurs during implantation, which is necessary for a successful pregnancy (6-9). However, there is limited evidence for an association between thrombophilia, whether inherited or acquired, with female infertility and IVF failure (7, 8, 10-12). The total number of assisted reproductive technology (ART) procedures has grown steadily over the past decades, but the average success rate remains relatively low (1.3,3).

The causes of high implantation rates andplacental failuresremain largely unknown.(9,10). Procoagulant state can lead to thrombotic occlusion of maternal vessels, which will lead to impaired perfusion of the intervillous space and placental insufficiency.(11,13). Both hereditary and acquired thrombophilia have been associated with recurrent pregnancy loss and its complications, and preliminary evidence suggests that thrombophilia may increase the risk of IVF failure, although data remain contradictory (6-8).

Despite multiple embryo transfers in most fertility treatment centers, only one-third of all in vitro fertilization (IVF) cycles achieve clinically achieved pregnancies, and most still fail (1,6,17). The largest percentage of unsuccessful IVF cycles is associated with a lack of implantation. In some patients, the failure of theirplantation occurs repeatedly (18,20). Recurrent IVF failure is usually defined as the inability to become pregnant after 2-6 IVF cycles in which more than 10 high-grade embryos were transferred to the uterus(18,25).

Embryo quality and endometrial susceptibility are two important factors that are considered key during implantation. Possible causes of repeated failed embryo implantation have been extensively investigated. The most frequently identified

ResearchJet Journal of Analysis and Inventions
https://reserchjet.academiascience.org

causes are reduced endometrial susceptibility, fetal defects, and factors with a combined effect [19,24].

Goal

To study the role of the distribution of allelic polymorphism of "vascular system" genes in the occurrence of unfavorable outcomes of in vitro fertilization.

.

Materials and methods

The patient group consisted of 96 infertile women with a history of IVF failure. The control group consisted of 30 healthy women with proven fertility, conceived spontaneously. All participants were evaluated for hereditary thrombophilia, including: Leiden factor V, antithrombin III deficiency (AT-III) mutation. The presence of thrombophilia was compared between the groups.

Examination and treatment were carried out in clinics: " Carmen plus" in the cityBukhara, Uzbekistan. IVF failure was determined by at least three consecutive unsuccessful IVF cycles. A failed IVF cycle was defined as an inability to achieve a clinical pregnancy in a cycle in which at least three good-quality (Grade I or II) embryos were transferred. Indications for IVF were male factor, ovulatory factor, tubal factor, and unexplained infertility. In our center, all fertilizations are performed by intracytoplasmic sperm injection (ICSI).

The control group consisted of 30 healthy women with proven fertility, age-appropriate, without a history of thromboembolic events, who became pregnant spontaneously and had at least one pregnancy without any complications (such as preeclampsia, intrauterine growth retardation, and intrauterine pregnancy). rfruit dumbbell).

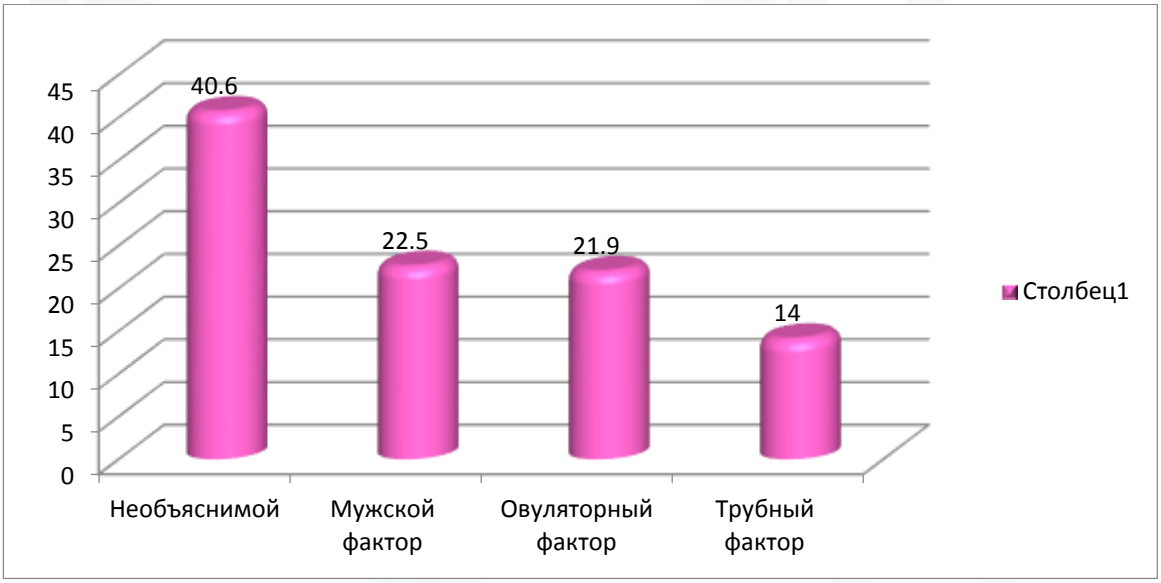
All participants were tested for antiphospholipid antibodies, and they were excluded from the study if they had positive results. Others were evaluated for hereditary thrombophilia, including: factor V Leiden, a prothrombin 20210A mutation. All laboratory tests were performed and repeated after 6 weeks in cases of abnormalities in the same laboratory using the Leiden factor V PCR method, the chromogenic method for antithrombin 3, and the ELISA method for prothrombin 20210G.

Numerical variables were presented as the mean ± standard deviation. We used the independent sampling t-test and chi-square test to compare quantitative and qualitative variables, respectively. To assess whether hereditary thrombophilia can predict the recurrence of failed IVF, we used logistic regression analysis. A univariate analysis was performed in which the odds ratio (ORS) and 95%

confidence interval (95% CI) were calculated. A P-value < 0.05 was considered statistically significant. All analyses were performed using the SPSS software.

P Research results исследования

The analysis was performed on the complete data of 126 patients (96 in the observation group and 30 in the control group). The average age of the study population was 34.59 ± 5.11, which was comparable between the groups. The group of cases included couples with primary and secondary infertility in 67.7% and 32.2%, respectively. The average duration of infertility was 8.7 ± 3.6 years. The most common cause of infertility was unexplained infertility in 39 (40.6%) patients. Other causes were male factor in 22 (22.9%), ovulatory factor in 21 (21.9%), and tubal factor in 14(14.6%) patients.(Figure 1) The prevalence of thrombophilia differed in infertility groups with different etiologies. Fifty-nine patients in the case group (61.5%) had at least one hereditary thrombophilia, compared to 11 women (32.61%) in the control group.



Rice.1. Characteristics of the infertile main group

When the effect of hereditary thrombophilia on recurrent IVF failure was assessed by regression, there was a significant association and presence of at least one thrombophiliaknown as a risk factor for recurrent IVF failure (OR = 3.15, p = 0.000). (Table1). The Leiden factor V mutation (found in 11%) and the MTHFRC677T mutation (homozygous form found in 6.3% and heterozygous form in 11.5%) were the most common hereditary thrombophilia.

ResearchJet Journal of Analysis and Inventions
https://reserchjet.academiascience.org

Table 1Hereditary thrombophilia in the study population

		Group of recurrent IVF failures (N = 96)	Healthy women (N = 30)	p-value
1	Factor V of Leiden mutation	16(16.7%)	1(3.3%)	0.01
2	MTHFR C677T mutation			0.05
	- Homozygote	11(11.5%)	1(3.3%)	
	- Heterozygote	11(11.5%)	2(6.6%)	
3	Prothrombin 20210A9 mutation(	9.4%)	2(6.6%)	0.16
4	Protein C deficiency	4 (4.2%)	1(3.3%)	0.71
5	Protein S Deficiency	4 (4.2%)	1(3.3%)	0.42
6	AT-III deficiency	2 (2.1%)	0	0.57

MTHFR: Methylenetetrahydrofolate reductase
AT-III: antithrombin-III.

The prevalence of Leiden factor V mutation and MTHFR C677T mutation in the group of repeated unsuccessful IVF attempts was significantly higher compared to the control group (p The Leiden factor V mutation and the homozygous form of the MTHFR C677T mutation were risk factors for repeated IVF failure. However, we were unable to find this difference in other hereditary thrombophilias, including prothrombin mutation, hyperhomocysteinemia, S and C protein deficiency, and AT-IIIdeficiency.

Conclusion

Our results showed a higher prevalence of hereditary thrombophilia in women with a history of IVF failure compared to normal women. This fact confirms the connection of this pathology with vascular disorders and, as a result, difficulties in embryo implantation. The Leiden factor V mutation is significantly more common in the group of failed IVF attempts, in contrast to the antithrombin III deficiency (AT-III) mutation in thrombophilia. The presence of at least one thrombophilia, a Leiden factor V mutation, and a homozygous form of the MTHFR C677T mutation were risk factors for repeated IVF failure. Recurrent pregnancy loss and pregnancy complications, such as severe preeclampsia, fetal growth retardation, and stillbirth, are more common in patients with a hereditary or acquired thrombophilic defect. A possible responsible mechanism may be maternal vascular thrombosis, which reduces the perfusion of the intervillous space, which leads to a violation of placentation. IVF embryo implantation and

early placentation failures can be caused by similar mechanisms. Thrombosis of placental vessels leads to hypoperfusion of the intervillous space and can cause a violation of placentation.

List of Literature

1. Shmeleva V. M. The role of hyperhomocysteinemia in the formation of prothrombotic disorders of the hemostatic system... Dr. med. nauk. - SPb., 2010. - 30 p.
2. Antigenic profile, prevalence, and clinical significance of antiphospholipid antibodies in women referred for in vitro fertilization / Sanmarco M. [et al.] // Ann. N. Y. Acad. Sci. — 2007. — Vol. 1108. — P. 457–465.
3. Antinuclear antibody reduces the pregnancy rate in the first IVF-ET treatment cycle but not the cumulative pregnancy rate without specific medication / Kikuchi K. [et al.] // Am. J. Reprod. Immunol. — 2003. — Vol. 50, N 4. — 363–367.
4. Antiphospholipid antibodies and pregnancy rates and outcome in in vitro fertilization patients / Denis A. L. [et al.] // Fertil. Steril. — 1997. — Vol. 67. — P. 1084–1090.
5. Аслонова М.Ж., Ихтиярова Г.А., Хафизова Д.Б., Мирзоева М.Р. Микробиологическая и гормональная характеристика формирования неразвивающейся беременности// Фундаментальные и практические вопросы иммунологии и инфектологии. Сборник научных статей участников международной научно-практической конференции. УФА. - 2018. - С. 9-15.
6. Кудратова Д.Ш. М.Ж. Аслонова, Г.А. Ихтиярова, Хафизова Д.Б. Клинико-гемодинамические и ультразвуковые признаки при гибели плода в различные сроке гестации// Республиканский научный журнал "Vestnik". Казахстан, 2017. № 4(81).-С. 93-95
7. Аслонова М.Ж., Ихтиярова Г.А., Хафизова Д.Б., Мирзоева М.Р. Микробиологическая и гормональная характеристика формирования неразвивающейся беременности// Фундаментальные и практические вопросы иммунологии и инфектологии. Сборник научных статей участников международной научно-практической конференции. УФА. - 2018. - С. 9-15.
8. Aslonova MJ, Ikhtiyarova GA, Mavlyanova NN. Association of ITGB3 gene polymorphisms with the risk of developing fetal growth restriction syndrome.

MOJ Women's Health. 2021;10(4):97–100. DOI: 10.15406/mojwh.2021.10.00296

9. Кудратова Д. Ш., Ихтиярова Г. А. Современный взгляд на диагностику врожденных пороков развития плода //Вестник Ташкентской медицинской академии. – 2020. – №. 2. – С. 147-153.

10. Achilova D. N. SPECIFIC COURSE OF ALLERGIC REACTIONS IN CHILDREN //Web of Scientist: International Scientific Research Journal. – 2021. – Т. 2. – №. 09. – С. 10-17.

11. Khodzhaeva D. I. Changes in the Vertebral Column and Thoracic Spinecells after Postponement of Mastoectomy //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 4. – С. 109-113.

12. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //Барқарорлик ва Етакчи Тадқиқотлар онлайн илмий журнали. – 2021. – Т. 1. – №. 1. – С. 85-89.

13. Mamedov U. S., Khodjaeva D. I. Modern Diagnostic Approachкetreatment of Thyroid Cancer //International Journal of Development and Public Policy. – 2021. – Т. 1. – №. 4. – С. 101-105.

14. Ilkhomovna K. D. Morphological Features of Tumor in Different Treatment Options for Patients with Locally Advanced Breast Cancer //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 2. – С. 4-5.

15. Ходжаева Д. И. СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ УЛЬТРАЗВУКОВОЙ ДИАГНОСТИКИ ПРИ РАКЕ КОЖИ ЛИЦА //Жизнеобеспечение при критических состояниях. – 2019. – С. 111-112.

16. Hemostasis parameters during ovarian stimulation for in vitro fertilization: results of a prospective study / Biron C. [et al.] // Fertil. Steril. — 1997. — Vol. 67. — P. 104–109.

17. In vitro fertilization. Do short-term changes in estrogen levels produce increased fibrinolysis? / Magnani B. [et al.] // Am. J. Clin. Pathol. — 1999. — Vol. 112. — P.485–491.

18. In vitro fertilization-induced alterations in coagulation and fibrinolysis as measured by thromboelastography / Harnett M. J. [et al.] // Anesth. Analg. — 2002. — Vol. 95, N 4. — P.1063–1066.

19. Incidence of autoimmune antibodies in failed embryo transfer cycles / Birkenfeld A. [et al.] // Am. J. Reprod. Immunol. — 1994. — Vol. 31. — P. 65–68.

20. Increased rates of thrombophilia in women with repeated IVF failure / Azem F. [et al.] // Hum. Reprod. — 2004. — Vol. 19. — P. 368–370.

ResearchJet Journal of Analysis and Inventions
https://reserchjet.academiascience.org

21. Low-molecular-weight heparin in the treatment of recurrent IVF-ET failure and thrombophilia: a prospective randomized placebo-controlled trial / Qublan H. // Hum. Fertil. — 2008. — Vol. 11, N 4. — P. 246–253.
22. Lox C., Canez M., Prien S. The influence of hyperestrogenism during in vitro fertilization on the fibrinolytic mechanism // Int. J. Fertil. Womens Med. — 1998. — Vol. 43. — P. 34–39.
23. Luteal phase empirical low molecular weight heparin administration in patients with failed ICSI embryo transfer cycles: a randomized open-labeled pilot trial / Urman B. [et al.] // Hum. Reprod. — 2009. — Vol. 24, N 7. — P. 1640–1647.
24. More on: the 'ART' behind the clot – solving the mystery / Bauersachs R. M.[et al.] // J. Thromb. Haemost. — 2007. — Vol. 5. — P. 438–439.
25. Gulchekhra Ikhtiyarova, Makhliyo Aslonova, Dilnoza Khafizova, Klichova Feruza Karimovna, Ashurova Nigora. CRITERIA FOR PREDICTION OF COMPLICATIONS IN PREGNANT WOMEN WITH ANTENATAL FETAL DEATH. 2 European Journal of Research P. 101-109 (2019).