

Clinical and Genetic Aspects of Women with Thrombophilia Who Cannot Carry a Pregnancy

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Abstract Thrombophilia is a condition characterized by an increased tendency to form abnormal blood clots, which can significantly affect reproductive health in women. This article examines the clinical and genetic aspects of thrombophilia in women who experience recurrent pregnancy loss or are unable to carry a pregnancy to term. The study highlights the importance of early diagnosis, comprehensive genetic screening, and individualized treatment approaches. Understanding the underlying genetic mutations and coagulation disorders can help in developing targeted therapies, thereby improving pregnancy outcomes and supporting reproductive success. The article also emphasizes the role of multidisciplinary collaboration in managing such cases effectively.

Keywords Thrombophilia, Pregnancy loss, Infertility, Genetic mutations, Coagulation disorders, Recurrent miscarriage, Clinical diagnostics, Prenatal care, Inherited thrombophilia, Maternal health, Risk factors, Individualized therapy

1. Introduction

Thrombophilia is a group of hereditary or acquired conditions that predispose individuals to thrombosis, or the formation of abnormal blood clots in blood vessels. In women of reproductive age, this condition poses a serious threat to successful conception and the maintenance of a healthy pregnancy [1,2,3,4,5]. Recurrent pregnancy loss (RPL), intrauterine growth restriction, preeclampsia, placental abruption, and stillbirth have all been associated with thrombophilic disorders. Despite advances in obstetrics and maternal-fetal medicine, many women continue to experience repeated miscarriages or pregnancy complications with unknown causes until thrombophilia is identified. In recent years, increasing attention has been given to the genetic basis of thrombophilia. Mutations such as Factor V Leiden, prothrombin gene mutation (G20210A), and deficiencies in natural anticoagulants like protein C, protein S, and antithrombin III are considered major inherited causes. These genetic abnormalities affect the coagulation cascade and increase the likelihood of thrombotic events in the placenta, impairing blood flow and nutrient exchange essential for fetal development [6,7,8]. Clinical management of women with thrombophilia requires a multidisciplinary approach that includes obstetricians, hematologists, and geneticists. Proper diagnosis involves a detailed medical history,

coagulation tests, and genetic screening, especially in patients with a history of unexplained pregnancy losses or thrombosis [9,10]. Once diagnosed, individualized treatment regimens such as low molecular weight heparin (LMWH) and low-dose aspirin can significantly improve pregnancy outcomes [11]. This article aims to explore the clinical manifestations and genetic mechanisms of thrombophilia in women who are unable to carry pregnancies to term [12,13,14]. It emphasizes the importance of early diagnosis, the role of genetic counseling, and evidence-based therapeutic strategies to reduce pregnancy-related complications and improve maternal and fetal prognosis [15].

Main Body

1. Understanding Thrombophilia and Its Types. Thrombophilia refers to a hypercoagulable state in which the blood has an increased tendency to form clots. It can be categorized into inherited and acquired forms. Inherited thrombophilias are genetic disorders passed from parents to offspring, whereas acquired forms develop due to external factors or underlying diseases. The most common inherited thrombophilias include: Factor V Leiden mutation – the most prevalent genetic thrombophilia, causing resistance to activated protein C. Prothrombin G20210A mutation – associated with increased prothrombin levels and clot formation. Protein C, Protein S, and Antithrombin III deficiencies – rare but highly significant in increasing thrombotic risk. Acquired thrombophilia includes: Antiphospholipid syndrome (APS) – an autoimmune disorder where antibodies attack phospholipids in cell membranes, leading to clotting. Hyperhomocysteinemia – elevated

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- levels of homocysteine, often linked to MTHFR gene mutations and nutritional deficiencies. These conditions interfere with the normal coagulation pathway and increase the likelihood of blood clots in the placental circulation, leading to miscarriages and other pregnancy complications.
2. **Thrombophilia and Pregnancy Loss.** Pregnancy is a naturally hypercoagulable state due to hormonal changes and physiological adaptations that protect the mother from bleeding during childbirth. However, in women with thrombophilia, this pro-thrombotic environment can become pathologically exaggerated, leading to: Placental insufficiency – where blood clots obstruct the maternal-fetal interface, impairing oxygen and nutrient supply. Recurrent miscarriage – often occurring in the first trimester but also in later stages of pregnancy. Intrauterine growth restriction (IUGR) – due to poor placental perfusion. Preeclampsia and eclampsia – potentially life-threatening conditions for both mother and fetus. Stillbirth – due to severe placental thrombosis. Studies have shown that up to 50% of women with unexplained recurrent miscarriages may have an underlying thrombophilic disorder.
 3. **Genetic Screening and Diagnosis.** Timely diagnosis of thrombophilia in women with pregnancy complications is critical. The diagnostic process involves: Detailed patient history – including previous miscarriages, thrombotic events, family history, and autoimmune diseases. Laboratory tests – such as activated protein C resistance, antithrombin activity, homocysteine levels, lupus anticoagulant, and anticardiolipin antibodies. Genetic testing – to detect mutations like Factor V Leiden, prothrombin gene mutation, and MTHFR polymorphisms. Genetic counseling is essential for affected women and their partners, helping them understand inheritance patterns, risks for future pregnancies, and preventive strategies.
 4. **Clinical Management and Treatment Strategies.** Once thrombophilia is diagnosed, an individualized treatment plan is developed, focusing on minimizing thrombotic risk during pregnancy. Common therapeutic approaches include: Low molecular weight heparin (LMWH) – a safe anticoagulant that does not cross the placenta, widely used during pregnancy. Low-dose aspirin – helps improve placental blood flow and reduce clot formation. Close monitoring – through regular ultrasounds, fetal growth assessments, and coagulation profiles. Lifestyle modifications – such as avoiding smoking, maintaining a healthy weight, and staying physically active. For women with antiphospholipid syndrome, combination therapy with LMWH and aspirin has been shown to significantly improve pregnancy outcomes.
 5. **Psychological and Emotional Impact.** Recurrent pregnancy loss and the stress of managing a high-risk pregnancy have profound psychological effects. Many women experience anxiety, depression, and emotional trauma. Therefore, psychological support and counseling are vital components of holistic care.
 6. **Research and Future Perspectives.** Ongoing research aims to improve diagnostic precision through advanced genetic testing, including whole genome sequencing and personalized medicine approaches. Investigations into novel anticoagulants, immune-modulating therapies, and the role of the microbiome are opening new frontiers in the treatment of thrombophilia-related pregnancy loss.
 7. **Thrombophilia in Assisted Reproductive Technologies (ART).** Women with thrombophilia often face difficulties not only in natural conception but also in assisted reproductive procedures such as in vitro fertilization (IVF). Studies have shown that thrombophilia can negatively affect: Embryo implantation – due to microthrombi formation in the endometrium. Early pregnancy development – through impaired uterine blood flow. Ovarian hyperstimulation syndrome (OHSS) – which carries a higher risk of venous thromboembolism in women with thrombophilia. Pre-implantation screening, anticoagulant therapy before and after embryo transfer, and a personalized ART protocol are essential to improve the success rates in such patients.
 8. **The Role of Inflammation and Immunology.** Thrombophilia is not only a disorder of coagulation but also closely linked to immune system dysregulation. Chronic inflammation and autoimmune responses can amplify thrombotic processes, especially in: Antiphospholipid syndrome (APS) – where antibodies trigger an inflammatory cascade that damages placental tissues. Combined thrombophilia – where genetic thrombophilia coexists with immunological abnormalities such as lupus or rheumatoid arthritis. Cytokines, endothelial dysfunction, and activated platelets contribute to a pro-inflammatory and pro-thrombotic state, increasing the risk of pregnancy complications.
 9. **Ethnic and Geographic Variations in Thrombophilia Prevalence.** The frequency and types of thrombophilic mutations vary among different populations: Factor V Leiden is more common in European populations (up to 15% carrier rate) but rare in Asian and African groups. Prothrombin G20210A mutation is most prevalent in Mediterranean countries. MTHFR polymorphisms have a high occurrence in Central and South Asian populations. These geographic and genetic variations underscore the importance of population-specific screening guidelines and culturally appropriate medical counseling.
 10. **Thrombophilia and Other Pregnancy Complications.** Apart from miscarriage, thrombophilia is associated with several late pregnancy complications, such as: Placental abruption – where the placenta detaches prematurely, leading to heavy bleeding and fetal distress. Preterm labor – often triggered by inflammation and

placental dysfunction. Oligohydramnios – reduced amniotic fluid levels due to compromised placental function. Gestational hypertension – which can progress to life-threatening eclampsia. Early identification and proactive management of thrombophilic women can reduce these risks substantially.

11. **Multidisciplinary Care Approach.** Optimal management of pregnant women with thrombophilia requires a collaborative, team-based approach involving: Obstetricians and Maternal-Fetal Medicine specialists – for high-risk pregnancy monitoring. Hematologists – for coagulation management and anticoagulant therapy oversight. Geneticists – for mutation analysis, family history evaluation, and reproductive planning. Psychologists – for emotional and mental health support. Nutritionists – to manage dietary factors that may influence homocysteine levels and clotting risk. This team-based strategy ensures a comprehensive, patient-centered treatment plan that maximizes both maternal and fetal health outcomes.
12. **Preventive Measures and Long-Term Outlook.** For women diagnosed with thrombophilia prior to pregnancy, preventive strategies play a critical role. These include: Preconception counseling and risk assessment. Starting prophylactic anticoagulation early in pregnancy. Continued monitoring postpartum, since the thrombotic risk remains elevated for at least 6 weeks after delivery. In most cases, with proper diagnosis and individualized treatment, a successful full-term pregnancy is achievable. Women who receive timely and effective management often go on to have healthy pregnancies and children. Furthermore, ongoing long-term follow-up is recommended to monitor for future thrombotic events, especially in women with strong genetic predisposition or a family history of cardiovascular disease.
13. **Gaps in Knowledge and Future Directions.** Despite significant progress, many aspects of thrombophilia remain under-researched. Areas that warrant further investigation include: Gene-gene and gene-environment interactions in pregnancy-related thrombosis. The impact of micronutrient deficiencies (e.g., folate, vitamin B6 and B12) on thrombophilic outcomes. Emerging biomarkers for early detection and prognosis. New-generation anticoagulants and their safety in pregnancy. Epigenetic modifications affecting coagulation genes during pregnancy. Future research efforts must focus on personalized medicine, using genetic profiles and risk stratification tools to guide therapy and reduce adverse outcomes.

2. Conclusions

Thrombophilia represents a significant risk factor in women experiencing recurrent pregnancy loss or pregnancy-related complications. Both inherited and acquired forms of

thrombophilia can disrupt the delicate balance of coagulation and placental function, leading to adverse reproductive outcomes. Early diagnosis through comprehensive clinical assessment and genetic screening is essential for identifying at-risk individuals. Personalized treatment plans, including anticoagulant therapy and close monitoring throughout pregnancy, have proven effective in improving maternal and fetal outcomes. Moreover, multidisciplinary care involving obstetricians, hematologists, genetic counselors, and mental health professionals is crucial for holistic management. Despite advancements, many aspects of thrombophilia remain poorly understood, and further research is needed to explore genetic interactions, optimize treatment protocols, and improve screening strategies. By continuing to investigate and address the clinical and genetic dimensions of thrombophilia, healthcare providers can offer better reproductive support to affected women, ultimately enhancing their chances of carrying a pregnancy to term successfully.

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