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# The Relationship between Coagulation and Infertility: A Mini-Review

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#### ABSTRACT

Infertility is a common problem that affects many couples worldwide, with an estimated 48.5 million couples experiencing infertility. The causes of infertility are diverse and complex, with a combination of genetic, environmental, and lifestyle factors contributing to the problem. While reproductive medicine has advanced significantly in recent years, the diagnosis and treatment of infertility remains a challenge, particularly in cases where the cause is not clear. One factor that has been found to contribute to infertility is abnormalities in coagulation.

Coagulation is an essential process that helps to prevent bleeding and promote healing after injury. However, when coagulation is abnormal, it can lead to various health problems including infertility. Studies have shown that coagulation disorders may affect reproductive function by interfering with blood flow, ovulation and implantation may lead to inflammation and oxidative stress.

Moreover, the balance between coagulation and fibrinolysis is crucial in coagulum formation and liquefaction of seminal plasma in males.

Despite the growing body of research on the relationship between coagulation and infertility, there is still much to be learned. In this review, we will examine the current understanding of the relationship between coagulation abnormalities and infertility. We will discuss the potential mechanisms by which coagulation disorders may affect reproductive function and explore the evidence linking coagulation disorders to infertility, recurrent pregnancy loss, and implantation failure. Finally, we will consider the implications of these findings for clinical practice and future research.

## Introduction

Infertility is a common problem affecting about 10–15% of couples worldwide, and has numerous causes, including genetic, environmental, and lifestyle factors [1].

The causes of infertility are diverse and complex, with a combination of genetic, environmental and lifestyle factors contributing to the problem.

While the relationship between coagulation and infertility is not well established, several studies have suggested a potential association [2,3].



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In males coagulation plays an essential role in the process of ejaculation. The semen is a complex mixture of spermatozoa fluid from the seminal vesicles, prostate gland and bulbourethral glands. Coagulation factors, such as fibrinogen, factor XIII and thrombin, are present in semen and are responsible for the formation of a clot after ejaculation. This clotting of the semen helps to keep the spermatozoa in the female reproductive tract, preventing their premature expulsion [4].

After some time, the clot is broken down by the enzyme fibrinolysin, which is also present in semen, leading to the liquefaction of semen. This liquefaction allows the spermatozoa to move freely in the female reproductive tract, facilitating fertilization [5].

In the female reproductive system, coagulation plays a critical role in the process of menstruation and in the prevention of excessive bleeding during childbirth. During menstruation, the inner lining of the uterus, called the endometrium, is shed, resulting in bleeding. Coagulation factors, such as fibrinogen, are released from the blood vessels in the endometrium and are responsible for the formation of a clot, which helps to prevent excessive bleeding [6].

In addition, some studies suggest that abnormal coagulation may also play a role in infertility, particularly in women with endometriosis or Poly Cystic Ovary Syndrome (PCOS). Abnormal coagulation in these conditions can lead to abnormal menstrual bleeding and affect ovulation, implantation, and fertility. Therefore, proper coagulation is essential for maintaining female fertility and preventing complications that can affect reproductive health [7].

Idiopathic Infertility is a significant problem in today's society, with an increase even in young couples. To get to the bottom of the problem, several studies have focused on the different mechanisms considering different fields of analysis and coagulation is one of them. Indeed, it has been highlighted that both genetic and acquired prothrombotic alterations can play a key role in reproductive success, being responsible for 40–70% of miscarriages or clinically unexplained infertility [8].

Several studies have shown that the evaluation of the various polymorphisms involved in thrombophilia is important not only in symptomatic patients (repeated miscarriages) but also, given the strong association between the presences of FV Leiden or Prothrombin FII mutations, also in infertile women asymptomatic [9].

Among the acquired forms of thrombophilia related to primary infertility in women we have the anti-phospholipid syndrome. This disease is characterized by the presence of Anti-Phospholipid antibodies (aPLs), which are a diverse group of antibodies directed against phospholipids. The presence of the latter has been seen to be one of the causes responsible for infertility in women, as interferes with endometrial decidualization, embryo implantation rates and is connected with reduced ovarian reserve [10].

Abnormal coagulation can affect blood flow to the reproductive organs, interfere with ovulation and impair embryo implantation, leading to infertility. Here, we present a comprehensive review of the literature on the relationship between coagulation and infertility.

## **Materials and Methods**

We conducted a thorough literature search using PubMed and Web of Science to identify relevant studies published from 1990 to 2022. We used the following keywords: coagulation, thrombophilia, infertility, reproductive disorders, ovarian function, implantation failure and miscarriage. Only Englishlanguage articles were included.

The quality of the studies was checked by enrolling only English articles with full text available and proper references.

# Results

Several studies have suggested a potential link between abnormal coagulation and infertility [2,3,11,12]. Abnormalities in coagulation factors, such as factor V Leiden, prothrombin gene mutation, and antiphospholipid syndrome, have been associated with increased risk of infertility, recurrent pregnancy loss, and implantation failure [13,14]. These conditions can affect blood flow to the reproductive organs, interfere with ovarian function, and impair embryo implantation. In addition, women with endometriosis, a common cause of infertility, have been found to elevate levels of coagulation factors [15]. However, the exact mechanisms by which coagulation abnormalities lead to infertility are not fully understood.

## Discussion

The link between coagulation and infertility is complex and multifactorial. Abnormal coagulation can affect reproductive function in several ways. Firstly, coagulation abnormalities can affect blood flow to the reproductive organs. This can result in reduced blood supply to the ovaries, leading to impaired ovarian function and reduced fertility [16,17]. Coagulation abnormalities may also lead to inflammation and oxidative stress, which can further affect reproductive function [17].

Secondly, coagulation abnormalities can interfere with ovulation. In particular, women with antiphospholipid syndrome, a condition characterized by the presence of autoantibodies that affect coagulation, have been found to reduce ovarian reserve and impaired ovulation [18,19]. This may be due to the effect of these autoantibodies on the follicular microenvironment, which can impair follicular growth and maturation.

Thirdly, coagulation abnormalities can impair embryo implantation. Several studies have suggested that abnormalities in coagulation factors, such as factor V Leiden and prothrombin gene mutation, are associated with an increased risk of implantation failure [13,14,20,21]. This may be due to the effect of these abnormalities on the endometrial receptivity, which can impair embryo implantation and lead to infertility.

In addition, coagulation disorders may lead to poor placental development, increasing the risk of pregnancy complications such as preeclampsia, preterm birth, and fetal growth restriction [16,22]. However, the role of coagulation abnormalities in infertility may vary depending on the underlying cause of infertility, and more research is needed to fully understand the relationship.

There are several limitations to consider when interpreting studies on the relationship between coagulation and infertility. First, many of the studies in this area have a small sample size, which can limit their statistical power and generalizability to the larger population. Small sample sizes can also increase the risk of bias and affect the reliability of the results. Moreover another possible limitation is the potential confounding variables. Infertility has multiple causes, and coagulation disorders may be one of several contributing factors. Therefore, it can be difficult to determine the independent contribution of coagulation disorders to infertility. Additionally, only few studies have evaluated the relationship between male infertility and coagulation and further studies are necessary to confirm this relationship.

# Conclusion

conclusion, abnormal coagulation In is associated with an increased risk of infertility, recurrent pregnancy loss, and implantation failure. Coagulation disorders may affect reproductive function by interfering with blood flow, ovulation, and implantation and may lead to inflammation and oxidative stress. While the exact mechanisms by which coagulation abnormalities lead to infertility are not fully understood, it is clear that coagulation plays a role in reproductive health. Clinicians should consider screening for coagulation disorders in patients with unexplained infertility or recurrent pregnancy loss and tailor treatment accordingly.

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