CASE REPORT

# The role of male factors in possible recurrent implantation failure: a case report.

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**Introduction**: Recurrent implantation failure (RIF) poses a significant challenge in in vitro fertilization (IVF) procedures. Although maternal factors are often considered, the role of male factors, particularly sperm quality, remains under investigation.

**Material and Methods:** This case report aims to evaluate the potential relationship between male factors and recurrent implantation failure in IVF.

**Results:** We present the case of a 33-year-old male partner of a couple experiencing RIF in IVF who underwent semen analysis and additional functional tests to assess sperm quality. Despite normal conventional semen analysis parameters, functional tests revealed abnormalities, including high levels of DNA fragmentation, low percentage in the hypoosmotic test, and low concentrations of inorganic phosphorus.

**Conclusions:** The identification of functional sperm alterations underscores the importance of tailored approaches to address male infertility and improve the success rates of assisted reproductive technologies.

**Keywords:** Case reports; Fertility; Semen analysis; Fertilization in vitro; Embryo implantation.

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## Introduction

In events following fertilization, sperm can generate early negative paternal effects, including both poor zygote or embryo morphology and low cleavage speed, or late negative effects related to poor embryo development, which may lead to implantation failure [1, 2].

The management of couples with fertility problems sometimes leads to the use of assisted reproductive technology (ART), especially in vitro fertilization (IVF), and with its development, maternal and paternal factors are considered crucial and can influence the success of the process [3].

Recurrent implantation failure (RIF) affects approximately 10% of couples undergoing IVF [1]. It is a complex clinical phenomenon arising from maternal, paternal, and/or embryonic factors and is defined as the inability to become clinically pregnant after the transfer of at least three good-quality embryos in three fresh or frozen cycles in women under 40 years of age [4].

The most important clinical laboratory test for evaluating male factors related to reproductive success is conventional semen analysis, which provides valuable information on sperm volume, viscosity, pH, sperm concentration, motility, and morphologically normal sperm; however, it has been assumed that many individuals with normal semen analysis parameters cannot become pregnant. This indicates that conventional semen analysis does not detect some functional alterations [5], thereby highlighting the need to implement additional, more specific semen quality function tests that evaluate, for example, defects in functional sperm membrane integrity, sperm DNA fragmentation, the presence of antisperm antibodies (ASA), and biochemical characteristics of the seminal fluid.

Therefore, this case report aims to present the semen analysis of an apparently healthy 33-year-old man whose partner underwent three IVFs with implantation failure.

## Case presentation

A 33-year-old man was referred to the Lisa Andrology Laboratory for semen analysis. During the clinical examination, he reported having no children and no reports of miscarriages or ectopic pregnancies. His 31-year-old partner underwent three IVF procedures in which there was embryo development with no implantation. No maternal infertility factors were detected (uterine anatomical abnormalities, thrombophilia, nonreceptive endometrium, or immunological factors), and chromosomal abnormalities were not observed in either individual. and to identify possible male infertility factors, the patient was referred for conventional and functional semen analysis. The authors have obtained the patient's informed consent.

The semen sample was collected after four days of sexual abstinence and processed following the recommendations of the World Health Organization manual for semen analysis [6]; in addition, complementary functional tests. The primary results are shown in Table 1.

The patient had normal parameters on conventional semen analysis (pH, volume, sperm count, viability, progressive

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motility, normal morphology, and leukocyte count). However, the complementary functional tests are altered, as the patient presents with high sperm DNA fragmentation, a low percentage in the hypoosmotic test (HOST), low inorganic phosphorus concentrations, and a lower testis/epididymis index (Table 1).

Table 1. Results of the patient's semen analysis.

| Parameter | Result | Lower reference limit or reference value |
|---|---|---|
| Volume, mL | 2.6 | 1.5 mL |
| Viscosity | Increased | Normal |
| pH | 7.4 | 7.2 |
| Concentration, spermatozoa/mL | 42,5 x $10^6$ | 15 x $10^6$ |
| Total concentration, spermatozoa/ejaculate | 110.5 x $10^6$ | 39 x $10^6$ |
| Sperm agglutination | Grade 2 | |
| Vitality, % | 84 | 54 |
| Leukocyte count, $10^6$/mL | < 5 | < 5 |
| Progressive fast motile, % | 22 | Fast progressive + slow |
| Slow progressive motile, % | 28 | Progressive = 42% |
| Non-progressive motile, % | 10 | |
| Immotile, % | 40 | |
| Normal morphology, % | 8,6 | 4 |
| Sperm DNA fragmentation, % | 35.1 | < 30 |
| HOST, % | 29 | > 58 |
| Testicle/epididymis index | 0.54 | 1.23 to 1.53 |
| Inorganic phosphorus, ug/mL | 288 | 691 – 887 |
| Acid phosphatase, U/mL | 1182 | 135 – 1129 |

## Discussion

Conventional semen analysis is also pivotal for investigating male infertility; however, it often does not provide sufficient information on the functional ability of the spermatozoa to fertilize the egg, produce a good-quality embryo with implantation potential, and ultimately, a live birth. Therefore, other tests that provide more information on sperm metabolism and the physical and biochemical characteristics of seminal fluid are needed to improve the diagnostic capacity for investigating male infertility [5].

In the semen analysis routine, the HOST evaluates the membrane's ability to transport compounds; however, it was initially unclear whether this ability predicted successful sperm head membrane reactions during capacitation and the acrosomal reaction. However, a high percentage of HOST was reported in patients with globozoospermia [7] after excluding a possible association between acrosomal or postacrosomal sheath abnormalities and low HOST percentages.

Similarly, a relationship between low HOST levels and low implantation and viable pregnancy rates has been shown [8]. In a prospective study, they demonstrated that a mean HOST score of 36.7% and a mean sperm concentration of 34.0 million/mL did not affect the mean number of oocytes retrieved, fertilization rate, or number of embryos transferred compared to high HOS scores; however, viable clinical pregnancy rates and implantation rates were considerably lower, indicating that low HOST levels may be associated with defective embryo formation, resulting in low implantation and pregnancy rates but normal fertilization rates [8].

Low HOST scores are associated with higher sperm DNA fragmentation [9]. High levels of sperm DNA fragmentation have been shown to correlate with poor blastocyst development, lower implantation rates, and increased miscarriage risk in assisted reproduction cycles, as the paternal DNA damage may surpass the oocyte's repair mechanisms during early embryogenesis [10]. Therefore, sperm DNA fragmentation analysis is a diagnostic method for identifying late paternal effects that lead to RIF in IVF [11, 12].

On the other hand, sperm agglutination has been associated with ASA; however, it is insufficient for diagnosing immunological infertility, as ASA can also occur in the absence of sperm agglutination and can affect motility [13].

Regarding the biochemical properties of seminal plasma, it has been observed that the amount of inorganic phosphorus (Pi) in semen samples from men with and without vasectomy is similar, indicating that the supply of Pi comes from the accessory glands (prostate and seminal vesicles), even Pi content correlates positively with fructose levels, a biochemical marker of seminal vesicle function [14, 15]. In turn, hypofunction of the seminal vesicles, determined by low fructose levels, affects the stability of sperm chromatin and generates high levels of acid phosphatase [15]. However, Pi is also essential for the activity of prostatic acid phosphatase, which is associated with the process of semen liquefaction and the activity of the enzyme adenylyl cyclase, which is essential for the motility and maturation

of spermatozoa [16].

In addition to these tests, analyses that allow us to evaluate the health and function of the male reproductive system, such as the concentration of inorganic phosphate, which is an indicator of the function of seminal vesicles, and biochemical markers of the prostate, which may influence semen viscosity and sperm motility, are important. Likewise, the testicle/epididymis index may suggest abnormal testicular function [17], affecting sperm membrane integrity, as assessed by the HOST. Indeed, semen analysis has many more attributes for investigating male infertility and couples who submit to ART technologies than the single assessment of sperm characteristics, as focused on clinical practice.

In the present case report, semen analysis revealed normal sperm count, vitality, motility, and morphology, but abnormal results in complementary tests; a low percentage of HOST is not necessarily associated with abnormal sperm morphology, which has been associated with high levels of DNA fragmentation [18]. This could be involved with the generation of embryos that lack implantation potential through IVF, preventing reproductive success and the appearance of RIF in three attempts. The limitation of this case report is the lack of information on the effects of treatment on sperm DNA fragmentation [18]. Evidence indicates that lifestyle and dietary changes—rich in antioxidants (fruits, vegetables, nuts, sources of vitamins C/E, zinc, selenium, and omega-3 fatty acids)—can significantly reduce DNA fragmentation by mitigating oxidative stress [19-21]. Furthermore, it was not possible to assess the effect of any treatment on subsequent reproductive cycles, as they did not wish to continue trying to conceive.

## Conclusion

In conclusion, it is crucial to perform not only conventional semen analysis but also complementary tests that provide supplementary information for estimating sperm fertilization potential and even for determining embryo development, implantation potential, and the live pregnancy rate to reduce risks and successfully overcome male infertility barriers through ART.

## Authors' contributions

FTA-R: Conceptualization, Formal Analysis, Data curation, Writing – original draft, Writing – review & editing
AVH: Conceptualization, Formal Analysis, Data curation, Writing – original draft, Writing – review & editing
WDCM: Conceptualization, Formal Analysis, Data curation, Writing – original draft, Writing – review & editing

## Conflict of interest

None to declare.

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