



Is there a Relationship between Chronic Endometritis Diagnosis and Spermogram Alterations?

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Abstract

Background: Chronic endometritis (CE) plays a significant role in couple infertility, affecting female reproductive health. While CE directly impacts the uterine environment, there's no direct evidence suggesting it causes male factor infertility.

Objective: The aim of this study is to examine the relationship between CE seen during hysteroscopy and spermogram alterations (rising white blood cell counts and pH, asthenospermia, hyperviscosity, modified fluidification).

Methods: This study involved 22 infertile couples who had hysteroscopy during fertility evaluation of recurrent implant failure (RIF), recurrent pregnancy loss (RPL) or idiopathic infertility. The semen analysis was conducted at least twice over a two-week period, one from the other in accordance with WHO criteria. Hysteroscopy was conducted at the time of endometrial growth.

Results: The result showed that in case of CE, the high endometrial inflammation intensity correlate with the high number of spermogram alterations. Leukocytospermia, high pH and asthenospermia are the most common altered factors in semen analysis.

Conclusion: In case of RIF, RPL or idiopathic couple infertility, flogistic alterations in sperm may lead to suspicious of CE in women.

Keywords: Chronic Endometritis (CE); Hysteroscopy; Assisted Reproductive Technologies (ART)

Introduction

Chronic endometritis (CE) plays a significant role in couple infertility, primarily by affecting the female partner's reproductive health. While CE directly impacts the uterine environment, crucial for conception and pregnancy, there's no direct evidence suggesting it causes male factor infertility. However, its impact on the female partner can indirectly contribute to the couple's overall infertility challenges. While CE is a condition affecting the female reproductive tract, primarily the uterus, there isn't a direct "cause-and-effect" relationship where a woman's CE causes alterations in her partner's spermogram. Spermogram alterations are indica-

tive of male factor issues, arising from conditions within the male reproductive system. We present below a brief case history of 22 couples with histological diagnosis of endometritis. We evaluated the characteristics of the male partners' spermograms and identified the most recurrent alterations presented by the seminal fluid at the time of andrological evaluation.

Materials and Methods

Our evaluation involved 22 consecutive infertile couples in which the female partner underwent hysteroscopy with endometrial biopsy during the diagnostic process in case of recurrent im-

plantation failure (RIF), recurrent pregnancy loss (RPL), idiopathic infertility. In all cases a diagnosis of endometritis was performed by the same pathologist. The couple included had a normal sexual life with a period of intercourse 2-3 times per week; had no major diseases and active infectious diseases. All couples never used antibiotic treatment prior to hysteroscopy. Semen analysis was performed within the last six months and male partner had at least two semen analyses according to WHO 2021 reference values. The endocrine problem or another disease causing infertility were excluded. The patient has had an intrauterine operation or procedure in the last two months in which ultrasonography revealed uterine malformation, fibroids, intrauterine adhesion, and tubal effusion. No birth control pills or other hormonal drugs in the last three months was taken. The male partner collected sperm samples after 2–4 days of sexual abstinence accompanied by masturbation without the use of any substances that could compromise sperm quality. On samples, the pH, viscosity, fluidification, total count, concentration, total motility, progressive motility, and concentration of round sperm cells were evaluated as part of standard inspection. The hysteroscopy was done during the endometrial growth phase. All surgical procedures were carried out by the same surgeon.

Results

The female age range was 25-47 years, 36.1 ± 5.55 years, and the male partner age was 28-52 years, 37 ± 9 years. All couple had not conceived within 12 months without contraception or after escaping their contraception uses. Of 22 couples, 11 (50%) were involved in an ART program (82% suffered by RIF), 9 (41%) had RPL, 2 (9%) were diagnosed for idiopathic infertility. The result showed that in case of endometritis the white blood cell range in semen specimens from endometritis female patients was high ($>200.000/\text{ml}$) in variable association with asthenospermia (98%), iperviscosity (25%), fluidification abnormalities (10%), $\text{pH} > 8$ (95%), spermatic count reduction (21%). Only 10 (45%) women are symptomatic for CE. All men are asymptomatic for male gland infections (MAGI) or uro-genital symptoms. Higher plasma cell count was recorded in 11 (50%) endometrial samples. In case of lower plasma cell count, we recorded minimal sperm alterations.

Discussion

Chronic endometritis (CE) is an infectious disease characterized by persistent inflammation of the endometrial lining. The preva-

lence in the general population is still not entirely clear, although the prevalence of CE in infertile patients, particularly among those with recurrent implantation failure (RIP), is reported to range from 14% to 58% [1]. Clinically, CE has subtle symptoms, such as dysfunctional uterine bleeding, pelvic discomfort, and leukorrhea, making it likely that it is underdiagnosed in the general population. The diagnostic gold standard for CE is endometrial biopsy with histologic analysis, with the detection of endometrial stromal plasma cells representing the histologic diagnostic marker [2]. However, it remains unclear whether treating CE improves livebirth rates in subsequent ART cycles [3]. The primary mechanism by which CE contributes to infertility is the persistent inflammation of the inner lining of the uterus [4].

Meta-analyses consistently show a higher prevalence of CE in women experiencing RIF during assisted reproductive technologies (ART) like *in vitro* fertilization (IVF). The inflamed endometrium struggles to support the embryo, leading to repeated failed attempts at implantation. The compromised endometrial environment may not be able to sustain a pregnancy, leading to early pregnancy losses [5]. Studies and meta-analyses demonstrate that women with untreated CE have significantly lower clinical pregnancy rates and live birth rates, both in natural conception and with ART. CE is often linked to an altered uterine microbiome, with an imbalance of bacterial communities. This dysbiosis can negatively impact endometrial receptivity and immune responses, crucial for successful pregnancy [6]. A significant challenge with CE is its often asymptomatic nature. Many women with CE experience no noticeable symptoms, making routine screening important in cases of unexplained infertility, RIF, or RPL [7]. The gold standard for diagnosing CE involves identifying plasma cells in the endometrial stroma through endometrial biopsy, often performed with hysteroscopy. Immunohistochemical staining (e.g., for CD138) is crucial for accurate detection [8]. Some meta-analyses suggest that the negative impact of CE on IVF outcomes may be more pronounced in cases of severe CE (higher plasma cell count), while mild CE might have a less significant effect [9].

In our small case series, we observed all of these characteristics reported in the scientific literature. In most cases, CE is asymptomatic, or at least suggestive symptoms must be carefully investigated in the medical history. Greater intensity of endometrial inflammation appears to be associated with a greater number of inflamma-

tory alterations in the semen analysis. In this context, arise the pivotal role of urologists in the evaluation and treatment of couple infertility, within the context of ART also. Reproductive urologists have the expertise to diagnose and manage male infertility, identify reversible causes, provide appropriate consultations, and perform surgical techniques such as sperm retrieval to enable ART or ICSI [10]. Furthermore, they can recognize irreversible reasons for testis failure and provide guidance on the most suitable treatment options for couples seeking fertility assistance. Based on a holistic view of the case, the anamnesis, the evaluation and exclusion of infertility factors, predicts the presence of a CE, optimising therapy times and success in achieving a pregnancy with a child in arms. In fact, our experience shows that there can be an indirect relationship and important considerations for couples where one partner has CE and the other has spermogram alterations. Some studies suggest a correlation between CE in women and the presence of leukocytospermia (elevated white blood cells in semen) in their male partners. Leukocytospermia indicates inflammation or infection within the male reproductive tract (male accessory gland infection - MAGI). Leukocytospermia can negatively affect sperm parameters, including reduced progressive motility (how well sperm swim forward), altered sperm shape, potentially lower sperm count, increased levels of sperm DNA fragmentation, which is a significant factor in RIF and RPL. Leukocytes produce reactive oxygen species (ROS), which can damage sperm. While not always the case, some microorganisms involved in CE (e.g., certain bacteria) could theoretically be transmitted back and forth between partners, potentially contributing to or perpetuating inflammatory conditions in both. However, this is a complex area and not a universal finding. In couples experiencing infertility, RIF or RPL, both partners undergo thorough evaluation. If CE is diagnosed in the female, the male partner's semen quality becomes even more critical. Subtle male factor issues that might be overlooked in a "normal" couple may become more significant in the context of CE, where the uterine environment is already compromised. CE itself can significantly impair endometrial receptivity, leading to reduced implantation rates and increased miscarriage rates, even with seemingly normal embryos. When CE is combined with sub-optimal sperm quality (e.g., high DNA fragmentation), the cumulative effect on reproductive outcomes can be even more detrimental. Addressing both factors simultaneously becomes crucial for improving success rates in assisted reproductive technologies (ART). Therefore, for couples struggling with infertility or RPL, if CE is diagnosed in the female partner, it is highly recommended

that the male partner undergoes a thorough andrological evaluation, including advanced sperm function tests like DNA fragmentation, even if standard semen parameters appear "normal." This comprehensive approach ensures that all potential contributing factors are identified and addressed.

Conclusion

The CE is a critical factor in couple infertility, primarily by compromising the female partner's endometrial receptivity and increasing the risk of implantation failure and miscarriage. Its diagnosis and timely, effective treatment are crucial steps in improving reproductive outcomes for couples struggling with infertility. The role of uro-andrologists in the evaluation and diagnosis of infertility in the era of ART is crucial. They play a key role in identifying and addressing male factor infertility issues, which can significantly impact the success of ART treatments. Through a comprehensive evaluation process, uro-andrologists can provide valuable insights and recommendations. To date, CE in a woman does not directly cause her partner's spermogram to be abnormal. Spermogram alterations are a male factor issue. In our experience, we consider possible to suspect a CE starting from the sperm alterations like for example leukocytospermia associated with high pH, hyperviscosity, impaired fluidification and oligo-asthenospermia. When both CE and spermogram alterations are present in a couple, it creates a more complex fertility challenge, often requiring a comprehensive approach to diagnosis and treatment for both partners to optimize reproductive outcomes.

Authors' Contributions

All authors participated in the design and conduct of the study. All authors reviewed and approved the final version of the manuscript.

Authors' Disclosure

No conflict of interest declared.

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