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# IMMUNOLOGICAL INFERTILITY CAUSED BY ANTISPERM ANTIBODIES AFFECTING FERTILIZATION

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**Abstract**
Immunological infertility is a multifaceted condition resulting from the production of antisperm antibodies (ASA), which can significantly impair the fertilization process. These antibodies are produced by the immune system of either the male or female partner in response to sperm cells, which are mistakenly recognized as foreign agents. Their impact varies, ranging from direct sperm damage to impaired motility and fertilization potential.
Understanding the role of ASA and cytokines in sperm functionality is crucial for developing effective diagnostic and therapeutic approaches. This article provides a comprehensive review of the mechanisms of ASA formation, their impact on sperm structure and function, and the role of inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Additionally, the study explores the correlation between ASA levels and pregnancy outcomes, including the risk of spontaneous miscarriages and preterm births, as well as the effectiveness of various therapeutic strategies in enhancing conception rates in assisted reproductive technologies (ART).

**Keywords**: Infertility, cytokines, antisperm antibodies (ASA), IL-1β, IL-6, TNF-α, reproductive immunology.

## Introduction

Immunological infertility is a growing concern in reproductive medicine due to its significant impact on conception and pregnancy outcomes. Antisperm antibodies (ASA) can interfere with





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sperm function by causing agglutination, increased oxidative stress, and DNA fragmentation, all of which can reduce fertilization rates and embryo viability.

Recent studies indicate that approximately 10-15% of infertile couples have detectable ASA levels in either semen or serum, leading to reduced sperm motility and viability. Moreover, heightened levels of inflammatory cytokines in seminal plasma have been linked to chronic inflammatory conditions, further exacerbating sperm dysfunction.

## Materials and Methods

This study included 120 men aged 22 to 38 years who were diagnosed with infertility and referred to the Bukhara Medical Center for Obstetrics and Gynecology for diagnostic evaluation. All participants provided written informed consent. Inclusion criteria were at least one year of regular unprotected intercourse without conception, absence of genetic disorders or severe systemic diseases affecting fertility, and normal reproductive hormonal profiles.

Semen analysis was conducted according to WHO (2010) guidelines, assessing volume, sperm concentration, motility, and morphology. The presence of ASA was determined using the mixed antiglobulin reaction (MAR) test, where a threshold of >50% ASA-bound sperm was considered indicative of immunological infertility.

Cytokine profiles in blood serum and seminal plasma were measured using enzyme-linked immunosorbent assay (ELISA) to quantify levels of pro-inflammatory (IL-1β, IL-6, TNF-α) and anti-inflammatory (IL-10) cytokines. Testicular biopsy samples were obtained from a subset of 30 patients to evaluate histological and immunohistochemical changes associated with ASA presence. Correlation analysis was performed to determine associations between ASA levels, cytokine expression, and sperm parameters. Descriptive statistics, including mean values, standard deviations, and proportional distributions, were applied to summarize findings.

## Results and Discussion

Among the 120 men evaluated, 48 (40%) had ASA levels exceeding the diagnostic threshold. A strong negative correlation ($r = -0.76$, $p < 0.01$) was observed between ASA levels and total sperm motility. Specifically, in the ASA-positive group, progressive motility was reduced to 22.5% ± 4.1%, compared to 51.2% ± 5.7% in the ASA-negative group ($p < 0.001$). Additionally, sperm DNA fragmentation rates were significantly higher in ASA-positive individuals (38.4% ± 6.3%) versus ASA-negative individuals (14.6% ± 3.2%) ($p < 0.001$). Increased oxidative stress, as indicated by elevated reactive oxygen species (ROS) levels in seminal plasma, further supported the detrimental impact of ASA on sperm integrity.

The analysis of cytokine profiles revealed significant differences between ASA-positive and ASA-negative individuals. IL-1β, a pro-inflammatory cytokine involved in immune response modulation, was found at elevated levels in seminal plasma of ASA-positive individuals, averaging 54.2 ± 8.7 pg/mL compared to 23.1 ± 5.3 pg/mL in ASA-negative cases ($p < 0.001$). IL-6, a cytokine that plays a critical role in chronic inflammation and immune regulation, was also significantly increased in ASA-positive patients, with mean levels reaching 68.9 ± 9.4 pg/mL, in contrast to 29.7 ± 6.1 pg/mL in ASA-negative individuals ($p < 0.001$). This cytokine is known to



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contribute to sperm dysfunction by promoting oxidative stress and disrupting the blood-testis barrier, leading to further immune activation.

TNF-α, a cytokine involved in cellular apoptosis and immune response, exhibited an even more pronounced elevation, averaging 72.4 ± 10.2 pg/mL in ASA-positive men compared to 31.8 ± 6.4 pg/mL in ASA-negative subjects ($p < 0.001$). Elevated TNF-α has been associated with increased germ cell apoptosis and impaired spermatogenesis, further exacerbating infertility. The presence of these cytokines in excessive amounts suggests that immunological infertility is driven not only by direct ASA-mediated sperm dysfunction but also by a broader inflammatory milieu that further compromises male reproductive potential.

Testicular biopsies from 30 ASA-positive individuals revealed increased infiltration of immune cells, including macrophages and T-lymphocytes, around seminiferous tubules. These findings underscore the immune-mediated disruption of spermatogenesis, contributing to reduced sperm quality and function. Among 48 ASA-positive couples who proceeded with ART, 19 (39.6%) achieved pregnancy, compared to 52 out of 72 (72.2%) in the ASA-negative group ($p < 0.001$). The miscarriage rate in the ASA-positive group was notably higher (37.2%) than in ASA-negative pregnancies (12.5%), suggesting a potential link between ASA and early pregnancy loss.

Therapeutic interventions, including corticosteroid treatment and immunomodulatory therapy, improved conception rates among ASA-positive patients. Following a 3-month treatment regimen, ASA levels decreased in 65% of treated individuals, correlating with a 27% increase in sperm motility and a reduction in DNA fragmentation rates.

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Additionally, sperm DNA fragmentation rates were significantly higher in ASA-positive individuals (38.4% ± 6.3%) versus ASA-negative individuals (14.6% ± 3.2%) ($p < 0.001$). Increased oxidative stress, as indicated by elevated reactive oxygen species (ROS) levels in seminal plasma, further supported the detrimental impact of ASA on sperm integrity.

Elevated levels of IL-1β, IL-6, and TNF-α were detected in the seminal plasma of ASA-positive individuals. IL-1β concentrations averaged 54.2 ± 8.7 pg/mL in ASA-positive cases, significantly exceeding the 23.1 ± 5.3 pg/mL observed in ASA-negative subjects ($p < 0.001$). Similarly, TNF-α levels were markedly elevated (72.4 ± 10.2 pg/mL vs. 31.8 ± 6.4 pg/mL; $p < 0.001$), highlighting a pro-inflammatory immune environment in these patients.

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## Conclusion

This study highlights the critical role of antisperm antibodies and inflammatory cytokines in immunological infertility. The negative impact of ASA on sperm motility, integrity, and fertilization potential underscores the importance of early and accurate diagnosis. The strong correlation between elevated cytokine levels and impaired sperm function further suggests that immune modulation may be a valuable therapeutic approach.

Future research should focus on refining immunotherapeutic strategies to mitigate ASA-related infertility and improve ART outcomes. A multidisciplinary approach integrating immunogenetic screening, cytokine profiling, and personalized treatment protocols may enhance fertility prospects for affected individuals.

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