



ASSESSMENT OF IMMUNE DEFENSE STATUS IN INFERTILITY

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Article history:	Abstract:
<p>Received: January 14th 2025 Accepted: February 11th 2025</p>	<p>The relevance of the study is linked to the increasing incidence of inflammatory diseases of the fallopian tubes, such as salpingitis and pyosalpingitis, which are among the primary causes of female infertility. The aim of the work was to study the mechanisms of local inflammation in the fallopian tubes and ovaries, as well as to analyze changes in the immune system associated with these diseases. The study evaluated levels of inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-4) and immunoglobulins (sIgA, IgM, IgG) in peritoneal fluid, as well as functional characteristics of neutrophils, including their bactericidal activity and changes in CD marker expression. The results showed a significant increase in the levels of pro-inflammatory cytokines and immunoglobulins in patients with inflammatory diseases, indicating the severity of the inflammatory process. A decrease in neutrophil bactericidal activity and changes in CD marker expression were also observed, reflecting dysfunction in their functional state. The obtained data emphasize the importance of early diagnosis and a comprehensive approach to the treatment of fallopian tube inflammation, especially in the context of its association with infertility.</p>

Keywords: infertility, immunity, cytokines, diagnosis, immunoglobulins

The relevance of this study lies in the importance of studying the mechanisms of inflammation development, especially in the context of inflammatory diseases of the fallopian tubes and their link to infertility. In recent years, the increase in cases of inflammation in the reproductive organs, such as salpingitis and pyosalpingitis, has become one of the leading causes of female infertility. The role of neutrophils, as the main component of the immune response to inflammation, and their functional characteristics, such as bactericidal activity and changes in CD marker expression, are crucial for understanding the pathogenesis of these diseases.

Particular attention was given to the analysis of cytokines (IL-1 β , TNF- α , IL-6, IL-4) and immunoglobulins (sIgA, IgM, IgG), which serve as indicators of the inflammatory process and immune response. The increased concentration of these molecules in the peritoneal fluid of women with inflammatory diseases of the appendages indicates the severity of inflammation and immune regulation disorders, which, in turn, may affect reproductive function.

The study results emphasize the importance of early detection of inflammatory diseases and the need for a comprehensive treatment approach aimed not only at eliminating inflammation but also at restoring normal immune function. This is particularly important in light of the increasing number of infertility cases that may be linked to chronic inflammatory processes in the reproductive organs.

The aim of the study was to explore the mechanisms of local inflammation in the fallopian tubes and ovaries, as well as to assess changes in the immune system associated with inflammatory diseases of the uterine appendages. Specifically, the focus was on analyzing "inflammatory" cytokines (TNF- α , IL-1 β , IL-6, IL-4) and immunoglobulins (sIgA, IgM, IgG), as well as the functional characteristics of neutrophils located in peritoneal fluid. The study aimed to identify the features of inflammatory processes, their impact on neutrophil activity and CD marker expression, and the relationship of these changes with the development of infertility in women.

Materials and Methods:

For the study, peritoneal fluid samples were collected from women with inflammatory diseases of the fallopian tubes, as well as from healthy donors. In total, 25 patients were studied: 10 women with primary infertility, 10 with secondary infertility, and 5 healthy women who served as the control group.

1. Cytokine and Immunoglobulin Analysis

To study the inflammatory processes in the peritoneal fluid, an analysis of cytokine (TNF α , IL-1 β , IL-6, IL-4) and immunoglobulin (sIgA, IgM, IgG) concentrations was conducted. Cytokines were measured using enzyme-linked immunosorbent assay (ELISA), which allowed for accurate determination of their levels in peritoneal fluid samples.

2. Neutrophil Activity Assessment

To evaluate the functional state of neutrophils, specifically their bactericidal activity, the



chemiluminescence method was used. This method allows for the analysis of oxidative processes in cells related to oxygen-dependent metabolism (oxidative metabolism, ODM) and the neutrophil "respiratory burst." Chemiluminescence was measured both spontaneously and when stimulated by luminol, which helped assess the change in oxidative processes in patients with various inflammatory diseases of the fallopian tubes.

3. Study of Neutrophil Phenotypic Characteristics

To study the phenotypic characteristics of neutrophils, the expression of CD markers (CD95, CD16, CD11b) on neutrophils obtained from peritoneal fluid was analyzed. Flow cytometry was used, allowing the detection of changes in the expression of these markers based on the type of inflammation and disease stage in patients.

4. Statistical Analysis

The research results were processed using the SPSS statistical software package. To assess the statistical significance of differences, analysis of variance (ANOVA) and the Student's t-test for independent samples were used. Differences were considered significant at a p-value < 0.05.

Thus, the study involved a comprehensive approach to analyzing inflammatory processes in peritoneal fluid, including studying cytokines, immunoglobulins, functional neutrophil activity, and CD marker expression.

Results and Discussion

In the study of the mechanisms of local inflammation, the focus was on analyzing "inflammatory" cytokines (TNF α , IL-1 β , IL-6, IL-4) and immunoglobulins (sIgA, IgM, IgG) obtained from peritoneal fluid samples. This

is because neutrophilic granulocytes play a key role in the inflammation process, and their functional state significantly impacts its course and outcome. Therefore, phenotypic and functional characteristics of neutrophils in peritoneal fluid were also studied.

One of the most important effectors in neutrophils is their bactericidal activity, which depends on oxygen-dependent processes known as oxidative metabolism (ODM). The efficiency of this process depends on the oxygen level, which in turn affects neutrophil activation and is referred to as the "respiratory burst." These metabolic changes can be assessed using the chemiluminescence method, which analyzes oxidative processes in cells. Spontaneous and stimulated chemiluminescence of neutrophils from peritoneal fluid was analyzed using luminol.

The results showed that in patients with salpingitis, spontaneous chemiluminescence decreased by 1.8 times, and stimulated chemiluminescence decreased by 2 times. Also, a twofold increase in spontaneous chemiluminescence and a 1.5-fold increase in stimulated chemiluminescence were observed in 46.9% of patients. Similar changes were recorded in patients with pyosalpingitis: 48.1% of patients showed a decrease in both spontaneous and stimulated chemiluminescence, with a 3.1 times reduction.

Changes in the expression of CD markers on neutrophils in the peritoneal fluid of women with inflammatory diseases of the fallopian tubes were also studied. This revealed significant changes in the expression of markers such as CD95, CD16, and CD11b, which varied depending on the disease stage and type of inflammation.

Table 1

Expression of CD Markers in Neutrophils of Peritoneal Fluid in Patients with Purulent-Inflammatory Diseases of the Uterine Appendages

CD Expression (%)	Groups		
	Healthy (n=5)	Primary infertility (n=10)	Secondary infertility (n=10)
CD 95	13,1 \pm 1,1	15,2 \pm 0,45*	18,92 \pm 0,48*
CD16	12,5 \pm 1,9	9,07 \pm 0,44*	5,98 \pm 0,5*
CD lib	20,9 \pm 2,1	25,13 \pm 0,5*	33,9 \pm 0,94*

*Note: Group I — patients with salpingitis; Group II — patients with pyosalpingitis

Table 2

Cytokine Composition in Peritoneal Fluid of Patients with Purulent-Inflammatory Diseases of Uterine Appendages

Cytokines pkg/ml	Healthy (n=5)	Primary infertility (n=10)	Secondary infertility (n=10)
IL-1 β	66,5 \pm 1,9	755,7 \pm 29,4*	903,21 \pm 11,94*
TNF-a	59,7 \pm 1,2	207,33 \pm 11,2*	245,62 \pm 9,47*



IL -6	7,1 ±0,9	156,29±1,66*	162,84±1,85*
IL-4	50,1 ± 1,1	34,8±0,77*	23,96±0,84*

**Note: * p < 0.001 compared to donor values*

The cytokines IL-1 β , TNF- α , IL-6, and IL-4 play a central role in regulating inflammation. The results showed significant increases in the levels of IL-1 β , TNF- α , and IL-6 in the peritoneal fluid of patients with inflammatory diseases of the fallopian tubes, as well as a decrease in IL-4 compared to healthy controls.

Additionally, the concentration of immunoglobulins such as IgA, IgM, and IgG was significantly higher in the peritoneal fluid of patients with inflammation, indicating an increased vascular permeability and extravasation of serum proteins. These findings highlight the importance of cytokine and immunoglobulin levels as biomarkers for the inflammatory process and its association with infertility.

Overall, our research confirms that inflammatory processes in the fallopian tubes and ovaries lead to significant changes in immune defense, including alterations in neutrophil activity, cytokine composition, and immunoglobulin levels. These findings emphasize the need for early diagnosis and a comprehensive approach to treating inflammatory diseases in gynecology, as they may contribute to infertility. The combined analysis of cytokines, immunoglobulins, and neutrophil activity provides critical insights into the pathogenesis of inflammation in the reproductive organs and offers potential targets for therapeutic intervention.

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