



CLINICAL RESEARCH FOR WOMEN SUFFERING FROM INFERTILITY

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Article history:	Abstract:
<p>Received: January 11th 2024 Accepted: February 10th 2024</p>	<p><i>The aim of the study was to identify risk factors for infertility in women diagnosed with chronic endometriitis (CE) and to examine their impact on reproductive health. Chronic endometriitis is an important gynecological condition causing infertility in women and requires deeper analysis in the context of its association with reproductive problems. The study involved two groups: 25 women with CE and infertility and 10 healthy women in the control group. The methods used included sociological and gynecological analyses, biopsy, hysteroscopy, Dopplerography and statistical analysis. The results showed that women with CE had a high level of hormonal disorders such as hypermenstrual syndrome and dysmenorrhea, as well as a higher prevalence of chronic diseases such as thyroid disease and chronic tonsillitis. An important factor is early diagnosis of CE, which contributes to improved treatment and prevention of infertility. The study emphasizes the importance of individual preparation for pregnancy and prevention of reproductive diseases to improve reproductive health.</i></p>

Keywords: Infertility, hyperhomocysteinemia, therapy, endometriitis, endocrinology, laboratory diagnostics

RELEVANCE OF THE STUDY:

Chronic endometriitis (CE) is an important gynecological condition that leads to infertility in women and plays a significant role in reproductive health. The association of CE with infertility and other reproductive problems in women makes it even more urgent to study this issue (1). The study results show that women diagnosed with CE have a high incidence of menstrual disorders, pelvic organ inflammation, and a history of various gynecological surgeries, which are factors contributing to infertility. The study also highlights the role of CE and other factors, such as thyroid diseases, chronic tonsillitis, and harmful habits like smoking, as risk factors for infertility (2, 3).

The study also provides important information about the early detection of CE and its effect on infertility. Changes in uterine morphology and Doppler parameters, through the assessment of uterine blood circulation, could affect pregnancy development. The study also indicates that women with CE often undergo hysteroscopy, therapeutic-diagnostic cleaning, and other surgical procedures, which necessitate the development of effective early diagnosis and treatment methods (4).

In line with international research, these studies emphasize the relevance of exploring the mechanisms through which CE causes infertility, the difficulties in diagnosing it, and its impact on reproductive health (5). Understanding the risk factors and biological mechanisms of CE will lead to the

development of more effective treatment methods, allowing better assistance to women suffering from infertility. Therefore, this research plays a key role in reducing infertility and improving reproductive health (6).

THE AIM OF THE STUDY:

The aim of the research is to identify the risk factors for infertility in women diagnosed with chronic endometriitis (CE) and to study their impact on reproductive health. The study aims to analyze the prevalence of CE-related pathologies among women with infertility and their effects on reproductive function.

MATERIALS AND METHODS:

To study the relationship between chronic endometriitis (CE) and infertility in women, two groups were compared in this study. The study involved 25 women diagnosed with CE and suffering from infertility, as well as 10 healthy women in the control group. The study was conducted in 2023. The women in the study group were between the ages of 20 and 45, and their menstrual cycle duration, menstrual days, and age of menarche were similar.

Criteria for Selecting Patients:

Women diagnosed with CE and suffering from infertility were included in the study group.

Healthy women with no gynecological diseases were included in the control group.

METHODS OF THE STUDY:



1. Sociological analysis: A questionnaire was conducted regarding women's education level, place of residence, profession, and harmful habits (e.g., smoking).

2. Gynecological analysis: Diagnostic tests and gynecological examinations related to infertility were carried out, including hysterosalpingography and hysteroscopy.

3. Uterine morphology and Doppler analysis: Morphological changes in the uterine lining and blood circulation were analyzed in the study group using Doppler method.

4. Biopsy: Endometrial biopsies were taken and examined microscopically to study inflammatory processes, changes in spiral artery walls, and alterations around blood vessels.

5. Statistical analysis: Data were analyzed using the Mann-Whitney test. Statistically significant differences were accepted as $p < 0.05$.

ANALYSIS OF RESULTS:

Based on the data obtained in the research, the risk factors associated with chronic endometritis and infertility, such as thyroid diseases, chronic tonsillitis, smoking, and other harmful habits, menstrual disorders, and reproductive function characteristics, were studied.

An analysis was conducted on reproductive health, pregnancy development, cesarean sections, and medical abortions. The study confirmed the correlation between chronic endometritis (XE) and infertility, as well as the need for developing diagnostic and treatment methods. The data collected showed the importance of early detection and effective treatment of chronic endometritis in women. Results and Discussion. According to the results of the conducted study, it was noted that women diagnosed with XE (chronic endometritis) had significantly higher levels of secondary education compared to the control group (42.16% and 12%, respectively; $p = 0.001$). The majority of the women under study were urban residents: 90.1% in the study group and 98.2% in the control group ($p > 0.01$). The majority of patients belonged to the worker category: 82.3% of the study group and 79.1% of the control group ($p > 0.01$). In women diagnosed with XE and infertility, thyroid diseases (28.4% and 4.2%; $p = 0.001$) and chronic tonsillitis (25.7% and 4.2%; $p = 0.03$) were more common in the study group compared to the control group. According to the analysis of harmful habits, smoking was found to be more prevalent among the women under study than in the control group (26.5% and 4.3%; $p = 0.05$). The groups being compared had similar menarche ages, menstrual cycle durations, and

menstrual day lengths, in line with the literature (Ishenko L.I. et al., 2018; Tolibova G.X., 2018). In the process of analyzing menstrual function, it was noted that women with XE had a higher occurrence of hypermenstrual syndrome (29.9% and 3.6%; $p = 0.007$) and dysmenorrhea (44.6% and 0%; $p = 0.01$) compared to the control group. Literature provides conflicting data on menstrual dysfunction in patients with XE, which may be due to the varying duration of endometrial dysfunction among the women under study. In each case, there was no possibility to determine the average duration of XE, as in most cases, it was not possible to determine the onset of the disease. Generally, if XE is detected early, there is a higher occurrence of heavy menstrual bleeding and dysmenorrhea. In long-standing cases, when referring to "thin endometrium," hypomenstrual syndrome is often the main symptom, characterized by light menstrual flow (Motovilova T.M., 2022; Tolibova G.X., 2018). The groups being compared had similar ages of sexual initiation, and in many cases, this was before marriage, which corresponds with the studies of V.A. Kolmik (2019) and G.X. Tolibova (2018). In women with infertility and XE, the following diagnoses were more frequent in the study group compared to the control group: chronic salpingitis with patent fallopian tubes (19.3% and 0%; $p = 0.02$), cervical ectopia (24.8% and 4.7%; $p = 0.05$), vaginitis (69.8% and 14.1%; $p = 0.000$), and menstrual cycle disorders (27.1% and 0%; $p = 0.001$). Hyperplastic processes in the endometrium (polyps, endometrial hyperplasia), indicating that these women had previously undergone various interventions in the uterus such as hysteroscopy, diagnostic curettage, and hysteroresectoscopy (32.8% and 4.2%; $p = 0.05$). Pelvic organ surgeries (for conditions like ovarian cysts or apoplexy) were more common in the study group compared to the control group (36.2% and 14.9%; $p = 0.05$). In the groups being compared, the frequency of primary and secondary infertility was the same (49% and 49%; $p > 0.001$).

Analysis of Results: Based on the data obtained from the study, risk factors related to chronic endometritis and infertility, such as thyroid diseases, chronic tonsillitis, smoking, other harmful habits, menstrual dysfunctions, and characteristics of reproductive function, were examined. Analysis was conducted on reproductive health, the development of pregnancy, cesarean section, and medical abortions. The study confirmed the link between chronic endometritis (XE) and infertility, as well as the necessity for developing diagnostic and treatment methods. The obtained data highlighted the



importance of early detection and effective treatment of chronic endometritis in women.

Results and Discussion: According to the study, women diagnosed with chronic endometritis (XE) had a significantly higher level of secondary education compared to the control group (42.16% vs. 12%; $p=0.001$). The majority of women in the study group were urban residents (90.1%), whereas 98.2% of women in the control group were also from urban areas ($p>0.01$). Most of the patients were workers (82.3% in the study group and 79.1% in the control group; $p>0.01$).

Women with XE and infertility showed more frequent thyroid diseases (28.4% vs. 4.2%; $p=0.001$) and chronic tonsillitis (25.7% vs. 4.2%; $p=0.03$) compared to women in the control group. Regarding harmful habits, smoking was more prevalent in the study group (26.5% vs. 4.3%; $p=0.05$).

The groups were similar in terms of menarche age, menstrual cycle duration, and the number of menstrual days, which is consistent with the literature (Ishenko L.I. et al., 2018; Tolibova G.K., 2018).

In the analysis of menstrual function, women with XE had a higher incidence of hypermenstrual syndrome (29.9% vs. 3.6%; $p=0.007$) and dysmenorrhea (44.6% vs. 0%; $p=0.01$) compared to the control group. Literature on menstrual dysfunction in women with XE shows conflicting data, likely related to differences in the duration of endometrial dysfunction in the studied women. The average duration of XE cannot be determined as many patients did not know the onset time of their disease. In general, early detection of XE leads to more frequent menstrual irregularities and dysmenorrhea, while in long-term cases with "thin endometrium," hypomenstrual syndrome with scanty menstruation is one of the main symptoms (Motovilova T.M., 2022; Tolibova G.K., 2018).

The groups were similar in terms of the onset of sexual activity, with most cases being non-marital, which corresponds to the studies by V.A. Kolmik (2019) and G.K. Tolibova (2018).

Women with infertility and XE had a higher prevalence of the following diagnoses in their history

compared to the control group: chronic salpingitis (19.3% vs. 0%; $p=0.02$), cervical ectopia (24.8% vs. 4.7%; $p=0.05$), vaginitis (69.8% vs. 14.1%; $p=0.000$), menstrual cycle disorders (27.1% vs. 0%; $p=0.001$), and endometrial hyperplastic processes (polyps, endometrial hyperplasia), indicating prior interventions such as hysteroscopy, therapeutic-diagnostic curettage, and hystero-resectoscopy (32.8% vs. 4.2%; $p=0.05$). Surgery on pelvic organs (e.g., ovarian cyst or apoplexy) was more common in the study group (36.2% vs. 14.9%; $p=0.05$). The prevalence of primary and secondary infertility was the same in both groups (49% vs. 49%; $p>0.001$).

Duration of Infertility: The duration of infertility in the control group was 5.1 years (3-8 years), significantly longer than the 3 years (2-2.5 years) in the women with XE ($p=0.000$), suggesting that the additional duration of diagnostic and treatment processes in reproductive technology departments due to male infertility.

Reproductive Function Analysis: Pregnancies resulting in birth were recorded in both groups, with 49% delivered by cesarean section ($p>0.001$). All groups also had cases of medical abortion, spontaneous abortion before the 12th week, as well as extra-uterine pregnancies ($p>0.01$).

Chronic Endometritis Risk Factors: Several studies in the global literature assess the risk factors for the development of chronic endometrial inflammation (Danusevich I.N. et al., 2016; Kopeva O.V. et al., 2015; Tetelyutina F.K. et al., 2015; Zakirova N., 2015; Drizi A. et al., 2020). This issue is critical in the prevention phase, as managing these risk factors can reduce the likelihood of reproductive function disorders, particularly in the context of infertility prevention and individualized preconception preparation. Our study identified and organized the risk factors for chronic endometritis (XE) in women with infertility (Table 4.1), which align with the literature (Danusevich I.N. et al., 2016; Kopeva O.V. et al., 2015; Tetelyutina F.K. et al., 2015; Zakirova N., 2015; Drizi A. et al., 2020).

Table 4.1: Risk Factors for the Development of Chronic Endometritis in Women with Infertility

Risk Factor	Odds Ratio (OR)	Rank
Thyroid pathology	11,67 [2-225]	I
History of menstrual dysfunction	9,15 [1,6-191]	II
Chronic tonsillitis	8,13 [1,29-167,9]	III



Smoking	8,92 [1,5-168]	III
Secondary education	5,1 [2-22]	IV
Vaginitis history	3,9 [1,3-14,1]	V
History of pelvic surgeries	3,02 [1,1-12]	VI

Despite efforts to develop diagnostic methods for XE (chronic endometritis), the "gold standard" for confirming this diagnosis remains histology of endometrial biopsies. Before treatment, morphological examination of endometrial biopsies in women with XE and infertility revealed inflammation infiltration in all

layers of the endometrium, particularly around glands and blood vessels, characteristic of infection spread. The total area of the inflammatory infiltrate was higher in the study group (0.6 (0.5-0.8 mkm²) compared to the control group (0.07 (0.06-0.1 mkm²); p=0.000).

Table 4.2: Doppler Parameters of Uterine Artery Blood Flow in Study Groups

Indicator	Control Group (n=10)	Study Group (n=25)
Right uterine artery IR	0,76 (0,74-0,8)	0,85 (083-0,88); p=0,000
Left uterine artery IR	0,76 (0,74-0,79)	0,86 (083-0,88); p=0,000
Right uterine artery PI	2,56 (2,4-2,65)	3,7 (3,5-4,1); p=0,000
Left uterine artery PI	2,58 (2,52-2,76)	3,65 (3,4-4); p=0,000

Note: p-values indicate significant statistical differences according to the Mann-Whitney test.

The inflammatory infiltrate mainly consisted of lymphoid elements, plasma cells, neutrophil leukocytes, and histiocytes. In 23.1% of cases, the inflammation had a diffuse character, while in 45%, it was focal around glands and blood vessels, and in 40%, a combination of these patterns was found. Focal fibrosis of the endometrial stroma and sclerotic changes in the walls of spiral arteries were observed in one out of every four women diagnosed with XE and infertility. It should be noted that in XE (chronic endometritis), due to the damage to the receptor apparatus of the endometrial lining, cyclic changes in the endometrium are not manifested as full secretory reconstruction of the inflammatory glands and disruption of the vascular component. The total area of blood vessels and the thickness of the spiral artery walls in women with XE were smaller compared to the control group (p=0.001, p=0.000).

Conclusion: The study results showed that the number of women with intermediate-level education in the group diagnosed with chronic endometritis was significantly higher than in the control group (42.16% vs. 12%; p=0.001). Women diagnosed with chronic endometritis and infertility were found to have more thyroid diseases, chronic tonsillitis, and a smoking habit (p<0.05). The study also showed that menstrual

dysfunctions, including hypermenstrual syndrome and dysmenorrhea, were more common in women diagnosed with XE compared to the control group.

In women suffering from infertility, chronic endometritis, and other reproductive health-affecting factors, such as vaginitis, cervical ectopia, and salpingitis, higher prevalence was observed. In the analysis of reproductive function, primary and secondary infertility cases were equal, but in women diagnosed with XE, the duration of infertility was shorter (p=0.000).

The importance of identifying risk factors in managing chronic endometritis and infertility, as well as conducting individualized pregravidar preparation, was emphasized.

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