Summary

The diagnosis of chronic endometritis is problematic because of its asymptomatic course and the need for invasive uterine procedures to confirm the diagnosis histologically. Therefore, it is important to identify factors that indicate a high risk of this condition.

Aim: The aim of this study is to identify factors that have a statistically significant correlation with the presence of CE in women of reproductive age and to validate them by histologic examination of the endometrium.

Material and Methods. A retrospective analysis of 400 histories of women of reproductive age who underwent hysteroscopy and endometrial biopsy for histologic examination was performed. Histologically, 154 women (38.5%) were found to have chronic endometritis (the group of women with chronic endometritis), while 246 women (61.5%) were found to have other conditions unrelated to chronic endometritis (the group of women without chronic endometritis). Analysis of anamnestic factors and ultrasound criteria associated with an increased likelihood of chronic endometritis was performed when comparing data from women in these groups.

The strength of the relationship between these factors on the one hand and the development of chronic endometritis on the other hand was assessed by calculating the Kendall’s τ (tau) rank correlation coefficient. The strength of the relationship between the mentioned factor and CE was considered strong (+++) with a τ coefficient of 0.5 or higher; moderate (+++) with a τ coefficient in the range of 0.2 to 0.499, weak (+) with a τ coefficient in the range of 0.1 to 0.199. A τ-coefficient value between 0 and 0.099 indicated no correlation between the factor and chronic endometritis.

The study was conducted in accordance with the principles of patient-centered care, the requirements of the Tokyo Declaration of the World Medical Association, the international recommendations of the Helsinki Declaration of Human Rights, the Convention of the Council of Europe on Human Rights and Biomedicine, the laws of Ukraine, and the Code of Ethics of the Ukrainian Physician.

The paper is an excerpt from the initiative scientific research project of the Department of Obstetrics and Gynecology No. 2 at Poltava State Medical University, entitled «Optimization of approaches to the management of pregnancy in women at high risk of obstetric and perinatal pathology» (State registration number 0122U201228, duration: 10.2022-09.2027) in collaboration with the Department of Pathological Physiology at Poltava State Medical University.

Results and Discussion. The determination of the correlation coefficient allowed us to identify the factors with the strongest association with chronic endometritis. Among them are 5 infectious factors: cervicitis in the past medical history (τ coefficient 0.6252245229; p<0.0000000001); chronic inflammation of the uterine appendages (τ coefficient 0.52536031; p<0.00000000001); sexually transmitted diseases in the past medical history (τ coefficient 0.547218916; p<0.00000000001); chronic urogenital inflammatory diseases in the sexual partner (τ coefficient 0.529314979; p<0.00000000001); previous multiple use of intrauterine contraception (τ coefficient 0.502383401; p<0.00000000001); 4 symptomatic consequential factors: infertility in past medical history (τ coefficient 0.683492482; p<0.00000000001); missed miscarriages in past medical history (τ coefficient 0.644489429; p<0.00000000001); recurrent early pregnancy loss (τ coefficient 0.625942138; p<0.00000000001); abnormal uterine bleeding (τ coefficient 0.650850348; p<0.00000000001); and 4 ultrasound criteria, such as the presence of local endometrial thickening (τ coefficient 0.665245229; p<0.00000000001); increased echogenicity of the endometrium (τ coefficient 0.650850348; p<0.00000000001); heterogeneity of the endometrial echo structure with areas of increased and decreased echogenicity (τ coefficient 0.693152163; p<0.00000000001); hyperechogenic structures in the basal layer of the endometrium (τ coefficient 0.521658745; p<0.00000000001). In our opinion, the combination of an infectious or symptomatic factor with an ultrasound criterion indicates a high probability of chronic endometritis. In the absence of ultrasound signs, the combination of 1 infectious and 1 symptomatic-consequential factor indicates a high risk of chronic endometritis.

To confirm the representativeness of this method, we analyzed endometrial biopsies obtained by curettage in 100 women with this combination of factors. The diagnosis was confirmed histologically in 87 women.

Conclusion. Our proposed assessment of high-risk criteria for chronic endometritis, based on the combination of infectious, symptomatic-consequential, and ultrasound criteria, allows predicting the presence of this pathology in 87 % of patients without the need for invasive interventions. This helps to improve patient selection for hysteroscopy and avoid unnecessary uterine interventions in the diagnosis of chronic endometritis in women planning pregnancy.

Key words: Chronic Endometriosis; Anamnestic Factors; Ultrasound diagnostics.
and reproductive dysfunction (67%), the formation of infertility (60-87%), unsuccessful attempts at in vitro fertilization and embryo transfer (37%), as well as a high frequency (up to 60. 5-86.7%) of pregnancy loss when it occurs [10-13].

The diagnosis of CE is associated with a number of challenges, primarily due to its asymptomatic nature and the need for invasive uterine procedures for histologic verification [14-17]. Under these circumstances, it is crucial to identify factors that indicate a high risk for the presence of CE. [18-22] Analysis of these factors will allow targeted selection of patients for hysteroscopy or other methods of endometrial biopsy, thereby increasing the effectiveness of diagnostic efforts.

Aim. The aim of this study is to identify factors that have a statistically significant correlation with the presence of CE in women of reproductive age and to validate them by histologic examination of the endometrium.

Material and Methods. A retrospective analysis of 400 cases of women of reproductive age who underwent hysteroscopy and endometrial biopsy for histologic examination was performed. The indications for hysteroscopy were as follows: abnormal uterine bleeding (73 women; (18.25%)), endometrial polyp detected by ultrasound (110 women; (27.5%)), suspected endometrial hyperplasia (50 women; (12.5%)), uterine leiomyoma (128 women; (32.0%)), infertility (22 women; (5.5%)), and adenomyosis (17 women; (4.25%)). Histologic examination of the endometrium obtained during hysteroscopy in 154 women (38.5%) revealed changes characteristic of CE (leukocytic infiltration, plasma cell clusters, stromal swelling, focal endometrial hyperplasia or atrophy associated with inflammatory infiltrates, mismatch of the endometrium to the phase of the menstrual cycle). The remaining 246 women (61.5%) had other conditions unrelated to CE (endometrium in proliferative phase, non-atypical and atypical endometrial hyperplasia, adenomyosis, etc.). Correlation analysis was performed when comparing the medical history of women in whom CE was detected by histologic examination (CE group) and the medical history of patients in whom CE was not detected by histologic endometrial biopsy (non-CE group). The study was conducted in accordance with the principles of patient-centered care, the requirements of the Tokyo Declaration of the World Medical Association, the international recommendations of the Helsinki Declaration on Human Rights, the Convention of the Council of Europe on Human Rights and Biomedicine, the laws of Ukraine, and the Code of Ethics of the Ukrainian Physician.

In order to develop criteria for high risk of the presence of CE, the analysis of factors associated with an increased likelihood of developing this pathology was performed. The strength of the association between these factors and the development of CE was assessed by calculating Kendall’s τ (tau) rank correlation coefficient, which is used in hypothesis testing to determine whether two variables can be considered statistically dependent [23]. The strength of the association between the given factor and CE was considered strong (+++) with τ coefficient ranging from 0.2 to 0.499, weak (−) with τ coefficient values from 0.1 to 0.199, τ coefficient values from 0 to 0.099 indicated a low level of association between the factor and CE.

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Results and Discussion. The mean age of the women was 35.4±9.6 years (ranging from 21 to 45 years). Regarding marital status, the majority of women were married (304 women (76 %)). The mean height was 166.3±6.8 cm and did not differ significantly between the groups. Body weight ranged from 48 to 113 kg, with a mean of 72.1±8.1 kg. There was no significant difference in mean body weight between the group of women with CE (70.4±6.1 kg) and the group without CE (73.1±6.2 kg) (p>0.1). The mean age at menarche was 13.0±2.6 years in the group with CE and 13.4±2.4 years in the group without CE (p=0.5). The menstrual cycle duration ranged from 21 to 35 days. The mean duration in the group of women with CE was 27.3±0.9 days, while in the group without CE it was 29.1±2.6 days (p>0.5). The duration of menstruation was 5.6±1.3 days in the group with CE and 5.9±2.4 days in the group without CE (p>0.5). In the CE group, 24 women (15.6%) experienced intermenstrual bleeding, while the frequency of this symptom was 2.1 times lower in the group without CE (18 women; 7.3 %).

The amount of blood loss was considered normal by 51 women (33.1 %) in the CE group and 131 women (53.3 %) in the group without CE; 35 women (22.7 %) and 42 women (17.1 %), respectively, considered their menstruation to be minimal, whereas 68 women (44.2 %) and 73 women (29.7 %), respectively, complained of significant blood loss during menstruation. Thus, the frequency of significant menstrual bleeding was 1.5 times higher in women with CE than in women without CE. Pain during menstruation was reported by 4 women (3.25 %) in the CE group and 7 women (2.4 %) in the group without CE.

The mean age of sexual debut was 18.6±3.1 years. In the CE group it was earlier with a mean of 16.1±3.3 years, while in the group without CE it was 19.4±3.5 years (p>0.05). Infertility was diagnosed in 31 women (20.1 %) in the CE group, almost twice as many as in the group without CE (27 women; 10.9 %). Among the subjects, 69 women (44.8 %) in the CE group and 99 women (40.2 %) in the no CE group had a history of a first birth. Second or subsequent births were reported by 26 (16.9 %) and 51 (20.7 %) women, respectively. Induced abortion was reported by 26 women (16.8 %) in the CE group and 34 women (13.8 %) in the no CE group. In addition, 10 women (6.5 %) in the CE group and 14 women (5.6 %) in the non-CE group had more than 2 induced abortions. The frequency of inflammatory complications after
childbirth and abortions in the past medical history was slightly higher in the group of women with CE at 21.4 % (33 women) compared to 16.2 % in the group without CE (40 women).

Of the 400 women studied, 54 (13.5 % of the total) had a history of recurrent miscarriage. Notably, miscarriages prior to 8 weeks’ gestation were almost three times more common in the CE group (14 women; 9.1 %) than in the non-CE group (9 women; 3.7 %). 16 women in the CE group (10.4 %) reported a missed miscarriage in their medical history. This is twice the rate of the no CE group, where missed miscarriages occurred in 4.9 % of cases (12 women).

Among the gynecological diseases in the past medical history of the studied patients, inflammatory processes of the vagina, endocervix and uterine appendages were the most frequent. Recurrent vaginitis was reported by 120 patients (30 % of the total): 56 women (36.4 %) in the CE group and 64 (26.01 %) women in the group without CE. Cervicitis was reported by 122 patients (30.5 %): 63 (40.9 %) women in the CE group and 59 (23.9 %) women in the no CE group. In addition, 27 patients (6.75 %) had cervical scar deformities: 9 (5.8 %) women in the CE group and 18 (7.3 %) women in the non-CE group. A history of acute salpingo-oophoritis was reported by 56 women (14 %): 18 (11.7 %) women in the CE group and 38 (15.4 %) women in the group without CE. Chronic inflammatory diseases of the uterine appendages were reported by 195 women (48.74 %): 98 (63 %) women in the CE group and 97 (39.4 %) women in the no CE group.

95 women (23.7 % of the total) reported various sexually transmitted diseases in their past medical history: 58 patients (37.7 %) in the CE group and 37 patients (15 %) in the group without CE. Approximately one third of the women (31.5 % of the total) reported the presence of urogenital inflammatory diseases in their sexual partners: 62 (40.2 %) women in the CE group and 64 (26.5 %) women in the group of women without CE.

Almost half of the women reported a history of chronic pelvic pain (189 women; 47.2 % of the total). The frequency of this condition did not differ significantly between the comparison groups, with 45.4 % (70 women) in the CE group and 48.4 % (119 women) in the group without CE. The presence of cystic changes in the ovaries in the past medical history was equally distributed: 19 women (12.3 %) in the CE group and 28 women (11.4 %) in the group without CE. In contrast, the frequency of pathology such as endometriosis was higher in patients without CE (31 women; 12.6 %) and 7 women (4.5 %) in the CE group.

A significant difference was found between the comparison groups in the frequency of repeated intrauterine interventions in the past medical history (such as hysterosalpingography, therapeutic and diagnostic curettage of the uterine cavity, hysteroscopy, insertion of intrauterine contraceptive devices, etc.). In women with CE, it was 12.3 % (19 women), which is 2.1 times higher than in patients in the group without CE (5.6 %; 12 women).

Of the total number of women, 84 individuals (21 %) reported intrauterine contraception in their past medical history. In 69 cases (17.2 %), intrauterine contraception was a one-time procedure, while in 15 women (3.8 %) it was repeated for a longer period of time. It is noteworthy that the frequency of one-time contraception was evenly distributed between the comparison groups: 17.53 % (27 women) in the CE group and 17.1 % (42 women) in the group without CE. However, the frequency of repeated insertion and long-term use of intrauterine contraception was significantly higher in women with CE compared to the group without CE (6.4 %; 10 women) vs. 2.0 % (5 women), respectively. History of surgery on the uterine appendages (ovarian resection, salpingolysis, cystectomy) was reported by 2 women in the CE group (1.3 %) and 8 women in the group without CE (3.25 %).

The most common extragenital diseases were acute respiratory viral infections (ARVI), influenza, tonsillitis, and respiratory diseases (acute and chronic bronchitis). The above-mentioned were detected in 171 women (42.7 % of the total), predominantly in the group of women with CE (49.3 % (76 women) compared to 38.6 % (95 women) in the group without CE). Chronic inflammatory diseases of the kidneys and urinary tract were the second most common with a frequency of 38 % (152 women): 74 women (48.1 %) in the CE group and 78 women (31.7 %) in the no CE group.

Chronic diseases of the gastrointestinal tract and intestinal dysbiosis (144 patients; 36.0 % of the total) were the third most common diseases. In the CE group, their frequency was 42.8 % (66 women) compared to 31 % (78 patients) in the group without CE.

The frequency of anemia was low (20 %; 80 women), as were cardiovascular (11.5 %; 45 women) and neurological (4 %; 16 women) diseases. The incidence of these conditions was not significantly different between the groups compared.

Thus, the analysis of age composition, social background, marital status, menstrual and reproductive functions, obstetric and gynecologic history, and extragenital diseases showed that, on the one hand, the groups of women studied were homogeneous. On the other hand, it showed that some factors were more frequent in women with EC than in those who did not have this pathology (infertility, recurrent pregnancy loss or missed abortion in the past medical history, presence of chronic inflammatory diseases of internal genital organs, sexually transmitted diseases in the past medical history, as well as repeated intrauterine interventions, including multiple insertions and long-term use of intrauterine contraception).

The results of general clinical examination (including complete blood count, biochemical blood analysis, coagulogram, bacteriological and bacterioscopic examination of lower parts of genital tract, cytological examination of cervical canal contents) performed before hysteroscopy did not show any differences between groups.

The analysis of the ultrasound data revealed several notable signs that were most common in women in the CE group and almost absent in the control group. At this point, the following were identified in the CE group: increased echogenicity of the endometrium (72 patients; 46.7 %), heterogeneity of the echo structure of the endometrium accompanied by the appearance of areas of increased and
decreased echogenicity within the central structure (96 patients; 62.3%), the presence of hyperechoic structures in the basal layer of the endometrium (63 patients; 40.9%), enlargement of the uterine cavity with the presence of fluid content 3-5 days after the end of menstruation (61 patients; 39.6%), the presence of local thickening of the endometrium in the form of polyps (110 patients; 71.4%). Ultrasound examination of women with endometriosis showed endometrial thickening of more than 15 mm compared to the group without endometriosis (66 women in the CE group (42.8%) vs. 29 women (11.7%) in the group without CE), as well as a decrease in endometrial thickness of less than 5 mm (25 women in the CE group (16.2%) vs. 11 women (4.7%) in the group without CE). Inconsistencies in the endometrial condition with the day of the menstrual cycle occurred in 87% of cases (134 women) in the women with CE, compared to 23.5% of cases (58 women) in the group without CE.

It is noteworthy that ultrasound criteria indicating CE were observed in only 114 of 154 women (74.0%) in whom this pathology was confirmed histologically. In the remaining 26% of subjects, CE was not detected by ultrasound. This suggests the use of other diagnostic methods for CE, not relying solely on ultrasound criteria to diagnose this pathology, and emphasizes the need for their combined use (along with the analysis of other risk factors) for diagnostic purposes in cases of CE.

Therefore, we calculated the Kendall’s τ coefficient to evaluate the strength of the correlation between the anamnestic factors and the ultrasound signs on the one hand and the histologically confirmed CE on the other hand. Among the factors analyzed, some showed a weak correlation with CE (τ coefficient ranged from 0 to 0.099); single use of intrauterine contraception in the past medical history, expulsion of intrauterine contraception in the past medical history, single intrauterine procedure, cervical scar deformation, anemia in the past medical history, amenorrhea, hypomenstrual syndrome, dyspareunia, chronic pelvic pain. In addition, there were factors with a slightly stronger correlation with CE (τ coefficient ranged from 0.1 to 0.199). These included frequent respiratory infections, chronic inflammatory processes of the respiratory system, previous acute salpingo-oophoritis, malnutrition, obesity, diabetes mellitus, history of spontaneous or induced abortion, or inflammatory complications after childbirth or abortion.

The correlation between CE and early onset of sexual activity, the presence of chronic inflammatory diseases of the kidneys, urinary tract, gastrointestinal tract or intestinal dysbiosis, as well as multiple (3 or more) intrauterine interventions in the past medical history showed a moderate correlation (τ coefficient ranging from 0.2 to 0.499). A moderate correlation of CE with certain ultrasound signs, such as enlargement of the uterine cavity with the presence of fluid content 3-5 days after menstruation, inconsistency of the endometrium with the day of the menstrual cycle, endometrial thickness less than 5 mm or greater than 15 mm, was also found. The strongest correlation (τ coefficient is 0.5 or higher) with CE was noted in 9 anamnestic factors (which we categorized into infectious and symptomatic-consequential) and in 4 ultrasound criteria, presented in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Anamnestic factors (τ coefficient)</th>
<th>Ultrasound criteria (τ coefficient)</th>
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<tbody>
<tr>
<td>Infectious</td>
<td>Symptomatic-consequential</td>
</tr>
<tr>
<td>• cervicitis in the medical history (τ=0.625; p&lt;1*10^-2);</td>
<td>• localized thickening of the endometrium in the form of a polyp (τ=0.642; p&lt;1*10^-3);</td>
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<tr>
<td>• chronic inflammatory processes in the uterine appendages (τ=0.523; p&lt;1*10^-2);</td>
<td>• elevated echogenicity of the endometrium (τ=0.665; p&lt;1*10^-2);</td>
</tr>
<tr>
<td>• sexually transmitted infections in the medical history (τ=0.547; p&lt;1*10^-2);</td>
<td>• inhomogeneity of the echo structure of the endometrium with areas of increased and decreased echogenicity (τ=0.693; p&lt;1*10^-2);</td>
</tr>
<tr>
<td>• chronic urogenital inflammatory conditions in the sexual partner. (τ=0.529; p&lt;1*10^-2);</td>
<td>• hyper-echogenic structures in the basal layer of the endometrium (τ=0.521; p&lt;1*10^-2);</td>
</tr>
<tr>
<td>• past history of recurrent use of intrauterine contraceptive device in the past. (τ-coefficient=0.502; p&lt;1*10^-2);</td>
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<tr>
<td>• infertility in the medical history (τ=0.683; p&lt;1*10^-2);</td>
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<tr>
<td>• history of missed miscarriage (τ=0.644; p&lt;1*10^-2);</td>
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<tr>
<td>• recurrent pregnancy loss in the medical history (τ=0.624; p&lt;1*10^-2);</td>
<td></td>
</tr>
<tr>
<td>• abnormal uterine bleeding (τ=0.651; p&lt;1*10^-2);</td>
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</table>

In our opinion, there is a high likelihood of CE when one of the 5 infectious risk factors or one of the 4 symptomatic-consequential factors is combined with one of the 4 ultrasound criteria. In the absence of ultrasound signs, the combination of one infectious and one symptomatic-consequential factor indicates a high risk of CE.

To evaluate the effectiveness of our proposed criteria for assessing the risk of CE development in women planning pregnancy, and with the intention of determining the representativeness of this method, we performed endometrial biopsies obtained by pipelle biopsy on days 5-10 of the menstrual cycle in 100 women at high risk of developing the mentioned pathology. Signs of CE were detected histologically in 87 women. They were mainly represented by leukocytic and plasma infiltration, stromal swelling, sclerotic changes in spiral vessels and narrowing of their lumen. Significant destruction of endometrial glands was observed in 97.7% of women with CE, with varying degrees of severity. Localized endometrial hyperplasia or atrophy with leukocytic infiltration was observed in 81.6% of women with CE. These changes represent a typical picture of long-term chronic inflammation of the endometrium occurring in cases of this pathology and do not differ from the histologic description of the endometrium in this condition provided by other researchers [24, 25].
Conclusions. Statistically significant correlations were found between CE and anamnestic factors of infectious origin (cervicitis, chronic inflammation of the uterine appendages, history of sexually transmitted infections of an infectious origin (cervicitis, chronic inflammation), as well as symptoms (history of infertility, history of miscarriages or incomplete pregnancies, abnormal uterine bleeding) and ultrasonographic characteristics of the endometrium (increased or heterogeneous echo structure, hyperechogenic inclusions in the basal layer, local thickening resembling a polyp). The combination of one or more anamnestic factors with ultrasound criteria makes it possible to predict the presence of this pathology in 87% of patients without the need for invasive procedures. This helps to improve patient selection for hysteroscopy and to avoid unnecessary uterine interventions in the diagnosis of CE in women planning pregnancy.

Prospects for further research. The obtained results indicate the need for further study of the causes of the development of chronic endometritis in order to develop effective means of treatment and prevention of this pathology.

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