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Particularities of gynecological history in patients with primary infertility associated with endometrial dysfunction

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Abstract

Background: Despite the positive dynamics of global demography, infertility remains one of the current challenges of contemporary gynecology. The endometrium represents the mirror that reflects the state of the pathological processes that occur in the pelvic organs, and the frequency of morphofunctional disorders of the endometrium in infertility is quite high. The aim of the study was to assess the gynecologic history in primary infertility patients.
Material and methods: The study included 96 patients divided into 2 groups. The study group - 48 patients with primary infertility and the control group – 48 fertile patients. The patients were interrogated according to a questionnaire that included 130 questions.
Results: The evaluation of menstrual function revealed that according to the following criteria: age of menarche, duration of menstruation, study groups were homogeneous. The age of onset of menarche was within the normal range in 97.9% (n = 47) of patients in both groups and averaged 12.77±1.27 years. Patients in the study group had regular menstrual cycle in 70.8% (n = 34) of cases, and those in the control group in 93.8% (n = 45) of cases, c^2 = 8.649; p = 0.003. The duration of the menstrual cycle averaged 35.23 ± 12.54 days in Study group (L_1) versus 28.33 ± 3.09 days in Control group (L_0), p <0.001. The duration of menstruation was between 2 and 7 days in both groups with a mean of 4.35±1.12 in the study group and 4.73±1.12 in the control group, p = 0.1.
Conclusions: Patients in the study group reported more often an irregular menstrual cycle and a prolonged interval between menstrual periods, hypomenorrhea, intermenstrual and postcoital bleeding, algodysmenorrhea, dyspareunia, premenstrual syndrome indicating the existence of endometrial dysfunction at the basis of infertility pathogenesis.
Key words: endometrial disfunction, primary infertility, endometrium.

Introduction

The fertility rate is a fundamental and integral criterion in the socio-economic wellbeing of a country. Despite the positive dynamics of the global demography, infertility remains one of the current challenges of contemporary gynecology [1, 2]. Despite the fact that the etiological factors and the pathogenetic mechanisms of infertility are diverse, the fundamental mechanisms in pregnancy occurrence are represented by the quality of the embryo and the morphofunctional state of the endometrium [3, 4, 5, 6]. For many decades, researchers have shown a special interest for the study of the endometrium, in which complex molecular interactions of biologically active substances take place in order to create optimal conditions for the most important function - implantation of the embrio and pregnancy occurance, but so far it was not possible to disclose its functional activity until the end [7, 8]. It is necessary to note that the first mention about the endometrium, especially its pathology as a cause of infertility is found in the works of Hippocrates [7]. With the development of medicine, subsequent knowledge about the structure and functional activity of the endometrium has been refined and expanded. The endometrium is the mirror that reflects the state of the pathological processes that occur in the female genital organs, and the frequency of the morphofunctional disorders of the endometrium in infertility is quite high [9, 10].

Endometrial dysfunction represents the morphofunctional changes of the endometrium, which can be reversible or irreversible, based on disorders of molecular mechanisms, which subsequently lead to infertility, disturbances in the implantation of the embryo and placenta [5, 10, 11, 12, 13]. Factors that contribute to the development of endometrial dysfunction are chronic inflammatory processes of the endometrium. The most important signs of chronic endometrial inflammatory processes and endometrial dysfunction are disturbances of the reproductive function in women (infertility, miscarriages, missed abortion), disturbance of menstrual function (irregular menstrual cycle, abnormal uterine bleeding), pain syndrome (dysmenorrhea, dyspareunia) and dysregulation of secretory functions [4, 14, 15, 16, 17, 18, 19, 20].

Material and methods

A prospective cohort study was conducted at the Department of Obstetrics, Gynecology and Human Reproduction at the clinical base of Municipal Clinical Hospital No.1, and Maternity No.2, Nicolae Testemitsanu State University of Medicine and Pharmacy. The study included 96 patients divided into 2 groups. The study group (L_1) included 48 patients with the established diagnosis of primary infertility and the control group (L_0) included 48 fertile patients.

The protocol of this study was approved by the Research Ethics Committee of the Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova (no. 79/62 of 26.04.2017). Patients signed informed consent for participation in the research.

The inclusion criteria for the study group were: patients suffering from primary infertility with indications for laparoscopy and hysteroscopy, age of the patient 20 - 40 years, lack of hormone and antibiotic therapy during the last 6 months, lack of intrauterine manipulations in anamnesia, agreement to participate in the research. Inclusion criteria for the control group: patients who have had a live birth in the last 2 years and are not breastfeeding, patients who do not have complicated reproductive gynecological anamnesis (infertility, miscarriage, missed abortion), lack of hormonal and antibiotic therapy in the last 6 months, research participation agreement. The exclusion criteria from the research were: patients with acute genital infection, age < 20 years and > 40 years, patients suffering from congenital uterine malformations, patients who have had previously intrauterine surgical manipulations, atypical endometrial hyperplasia, patients who refused voluntary participation in the research.

The clinical examination consisted of the evaluation of patient's complaints and the anamnesis. Assessment of the average age of menarche, establishment of menstrual function, duration and variations of the menstrual cycle and menstrual flow. Evaluation of the regularity of the menstrual cycle and the presence of such characteristics as: dysmenorrhea, the onset of pain syndrome with menarche, dyspareunia, the presence of pain and their nature during the menstrual cycle. In the study of the anamnestic data, attention was paid to the premorbid background, gynecological and extragenital disorders, reproductive and menstrual function. Were determined the factors that contributed to the onset of the disease. A general physical and gynecological examination was performed in the patients from the examined groups.

Statistical data processing was performed using Microsoft Excel 2016 and SPSS 20. The results are expressed as mean values ± standard deviation for the parametric variables and for the categorical variables as a percentage. The Pearson test was applied for correlation analysis. The values $p<0.05$, were considered statistically significant.

Results

The study included 48 patients in each group who met the inclusion criteria, the study group – patients with the diagnosis of primary infertility and the control group – fertile patients.

According to the age criterion, marital status, living environment, the examined lots were homogeneous. The age of the patients included in the study group was between 22 and 39 years with an average of 29.00 ± 4.58 years and in the control group was between 20 and 35 years with the average of 29.23 ± 4.29 years p = 0.80 (fig. 1).

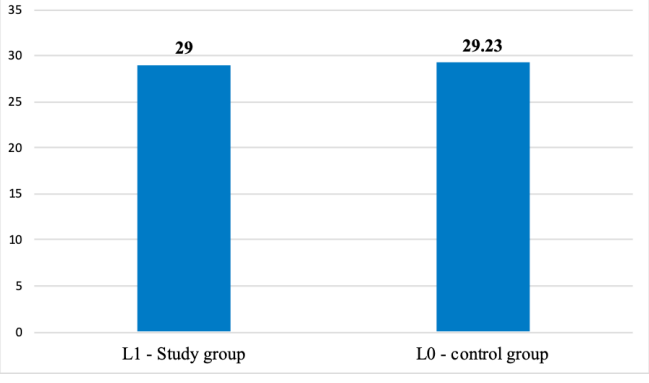

Fig. 1. Distribution of groups according to age criterion (years).

The majority of patients in both groups were from urban area L_1 – 64.6% (n = 31) vs L_0 – 75% (n = 36) (fig. 2).

Each second patient suffering from primary infertility had higher education – 54.2% (n = 26) whereas in the control group only 43.8% (n = 21) of patients and 54.2% (n = 26) of the patients in the study group reported the presence of harmful factors at work, while patients in the control group only – 22.9% (n = 11).

The evaluation of menstrual function in the patients included in the study revealed that according to criteria such

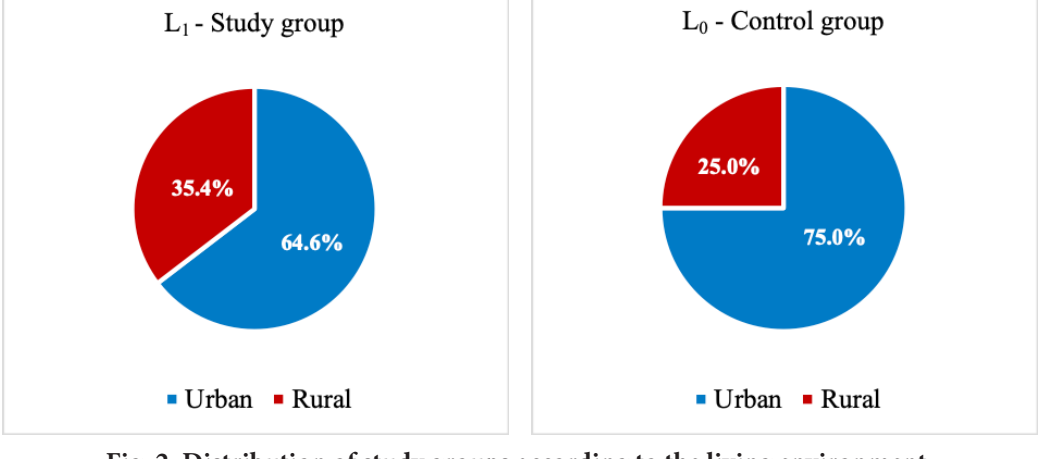

Fig. 2. Distribution of study groups according to the living environment.

as the age of menarche, the duration of menstruation the study groups were homogeneous. The age of onset of the menarche was within the norm within 97.9% (n = 47) of patients in both groups and constituted on average 12.77±1.27 years. Patients in the study group had a regular menstrual cycle in 70.8% (n = 34) cases, and those in the control group – in 93.8% (n = 45) of cases, c^2 = 8.649; p = 0.003. The duration of the menstrual cycle was on average 35.23 ± 12.54 days in L_1 versus 28.33 ± 3.09 days in L_0, p<0.001. The duration of menstruation was between 2 – 7 days in both groups with the average of 4.35 ± 1.12 in the study group and 4.73±1.12 in the control group, p = 0.1.

As a result of the study of the peculiarities of the menstrual cycle, we found that every 5th patient suffering from primary infertility reported hypomenorrhea compared with the fertile patients – 18.8% (n = 9) vs 2.1% (n = 1), c^2 = 7.839; p = 0.020, the presence of intermenstrual and postcoital bleeding was reported only by patients in the study group with a frequency of 14.6% (n = 7), c^2 = 7.551; p = 0.006 and 4.2% (n = 2) c^2 = 2.043; p = 0.15 in the control group. Algosdymenorrhea was more frequent in patients in the study group – 60.4% (n = 29) vs the control group – 35.4% (n = 17), c^2 = 6.010; p = 0.014. Each of the 2 patients in the study group reported premenstrual syndrome – 47.9% (n = 23) vs 29.2% (n = 14), c^2 = 3.562; p = 0.059, and each 5th patient – dyspareunia 20.8% (n = 10) vs. 4.2% (n = 2), c^2 = 8.095; p = 0.014 (table 1).

Table 1

The complaints of the patients included in the study

The evaluated criterion	Study group L_1 %(n)	Control group L_0 %(n)	p
Regular menstrual cycle	70.8 (34)	93.8 (45)	0.003
Hypomenorea	18.8 (9)	2.1 (1)	0.020
Intermenstrual bleeding	14.6 (7)	0	0.006
Postcoital bleeding	4.2 (2)	0	0.15
Algodysmenorrhea	60.4 (29)	35.4 (17)	0.014
Premenstrual syndrome	47.9 (23)	29.2 (14)	0.059
Dyspareunia	20.8 (10)	4.2 (2)	0.014

The analysis of the gynecological pathologies that had an impact throughout the life of the patients included in the study revealed the following: the pathology of the fallopian tubes was found in 68.8% (n = 33) L_1 vs 0% (n = 0) L_0, c^2 = 50.286; p < 0.001, ovarian pathology was reported by patients in 52.1% (n = 25) L_1 vs 8.3% (n = 4) L_0, c^2 = 21.789; p < 0.001, uterine pathology – 16.7% (n = 8) L_1 vs 2.1% (n = 1) L_0, c^2 = 6.008; p = 0.014; of which endometrial polyps in 2.1% (n = 1) vs 0% (n = 0), intramural myoma – 2.1% (n = 1) vs 0% (n = 0), subserous myoma – 14.6 % (n = 7) vs. 2.1% (n = 1), multinodular myoma in 2.1% (n = 1) vs. 0% (n = 0) (fig. 3). Each 5th patient in the study group had a sexually transmitted disease during her lifetime – 22.9% (n = 11) L_1, vs 6.3% (n = 3) L_0, c^2 = 5.352; p = 0.021, of which chlamydiosis – 12.5% (n=6) vs 2.1% (n=1), trihomonia – 2.1% (n = 1) vs 0% (n = 0), genital herpes – 2.1% (n = 1) vs 2.1% (n = 1), human papilloma virus (HPV) – 2.1% (n = 1) vs 2.1% (n = 1), mycoplasmosis – 8.3% (n = 4) vs 0% (n = 0), ureaplasmosis – 12.5% (n = 6) vs 0% (n = 0).

In the study group the duration of primary infertility was 4.2% (n = 2) up to 1 year, 10.4% (n = 5) one year, 20.8% (n = 10) - 2 years, 22.9% (n = 11) – 3 years, 6.3% (n = 3) – 4 years, 8.3% (n = 4) – 5 years and 27.1% (n = 13) more than 5 years (fig. 4).

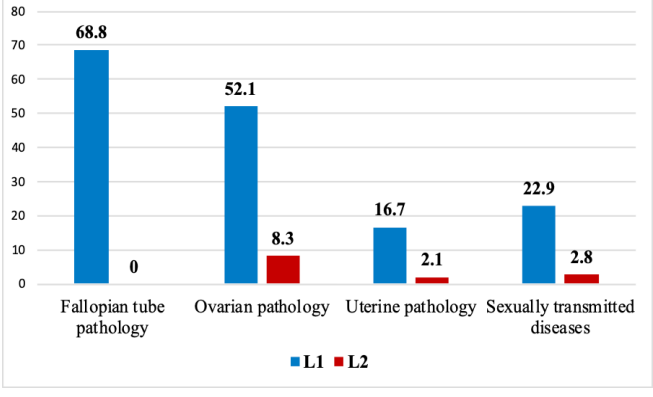

Fig. 3. Structure of gynecological history in patients included in the research (%).

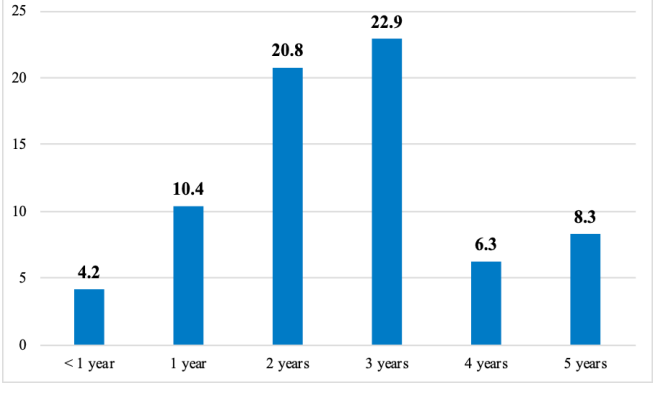

Fig. 4. Duration of primary infertility in patients in the study group (%).

Discussion

The endometrium is a complex, hormone-dependent functional tissue, which undergoes cyclic and structural changes under the influence of sex steroid hormones. Optimal morphofunctional characteristics of the endometrium are the basic elements in the occurrence and development of pregnancy [5, 7]. The pathological processes of the pelvic organs have both a direct and indirect effect on the state of the endometrium. Changes in their structural and functional characteristics determine the development of infertility, spontaneous abortions and implantation defects [14, 21, 22].

In the presented study we evaluated the clinical-anamnestic characteristics in patients with primary infertility in order to determine which conditions most frequently lead to the development of endometrial dysfunction. Currently, an important social factor is the fact that women delay the planning of a pregnancy closer to 30 years, which leads to the accumulation of both somatic and gynecological pathologies [22, 23]. The socio-economic factors of a woman's life such as studies, career, lack of life partner, often become fundamental moments in the process of performing the reproductive function [24]. The results of the study showed that most of the women suffering from infertility and included in the research were between 25 and 34 years of age (73%), of which 41.7% were between the age of 25-30 years and 31.3% of the patients were 30-34 years old, a share of 14.6% occupied the patients included in the age category of 35-40 years.

The assessment of the menstrual function of the patients showed that the age of onset of menstruation and the duration of menstruation in both groups correspond to normal sexual development. Thus, the average values of the studied parameters were not statistically significant and were within the average range. Menstrual function in patients suffering from primary infertility is the mirror of the morphofunctional status of the endometrium and denotes the degree of its impairment by a number of pathological factors mentioned by the patients throughout their life. According to different studies, the main complaints of patients suffering from infertility and endometrial damage are the following menstrual disorders: the presence of hypomenorrhea, oligomenorrhea, intermenstrual bleeding, bleeding or postcoital spotting [9, 10, 25, 26]. These results were also obtained in our study, so patients with primary infertility reported more frequently, compared with fertile patients: hypomenorrhea (18.8%), intermenstrual bleeding (14.6%), postcoital bleeding (4.2%). Another important factor that leads to changes in quality of life and working capacity in infertile patients is the presence of chronic pain syndrome with such manifestations as algodysmenorrhea, dyspareunia, dysuria, premenstrual syndrome, these complaints have also been more frequently reported by patients in the study, compared to the control group. Premenstrual syndrome and algodysmenorrhea have been reported 2 times more frequently by patients suffering from infertility, whereas dyspareunia have been accused 5 times more frequently, which is consistent with other international studies [12, 14].

According to some authors, early sexual onset and lack of knowledge about appropriate contraception methods are responsible for the development of a series of infectious gynecological pathologies that have serious repercussions on women's reproductive health [21]. International studies broadly describe the association of sexually transmitted diseases, pelvic inflammatory disease with the development of endometrial dysfunction in patients with infertility, in particular the pathological and cytopathic action of viral infection (herpesvirus, cytomegalovirus, HPV) on the endometrium [27, 28, 29]. The results of our study indicated a high incidence among patients with primary infertility of the sexually transmitted diseases (22.9%), especially those with silent evolution and with cytopathic effect on the endometrium such as chlamydiosis – 12.5%, genital herpes – 2.1%, HPV – 2.1%, mycoplasmosis – 8.3% and ureoplasmosis – 12.5%. This subsequently led to the high frequency of repeated pelvic inflammatory diseases such as salpingitis (52.1%), salpingoophoritis (12.5%), endometritis (6.3%), cervicitis (33.3%). The results obtained coincide with the data obtained by other researchers [12, 28, 30, 31]. The high frequency of urogenital infections independent of the causal factor ultimately leads to endometrial damage and the development of endometrial dysfunction with infertility, spontaneous abortions, missed abortion, premature births, intrauterine growth restriction of the fetus, fetal death.

Conclusions

Patients suffering from primary infertility more often reported irregular and prolonged menstrual cycle. Also, the patients in the study group reported a series of menstrual cycle disorders such as: hypomenorrhea, intermenstrual and postcoital bleeding, algodysmenorrhea, dyspareunia, premenstrual syndrome, which indicates the existence of endometrial dysfunction based on the pathogenesis of infertility. Gynecological anamnesis was more frequently complicated with the pathology of the fallopian tubes, ovaries and most importantly was complicated by sexually transmitted diseases.

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