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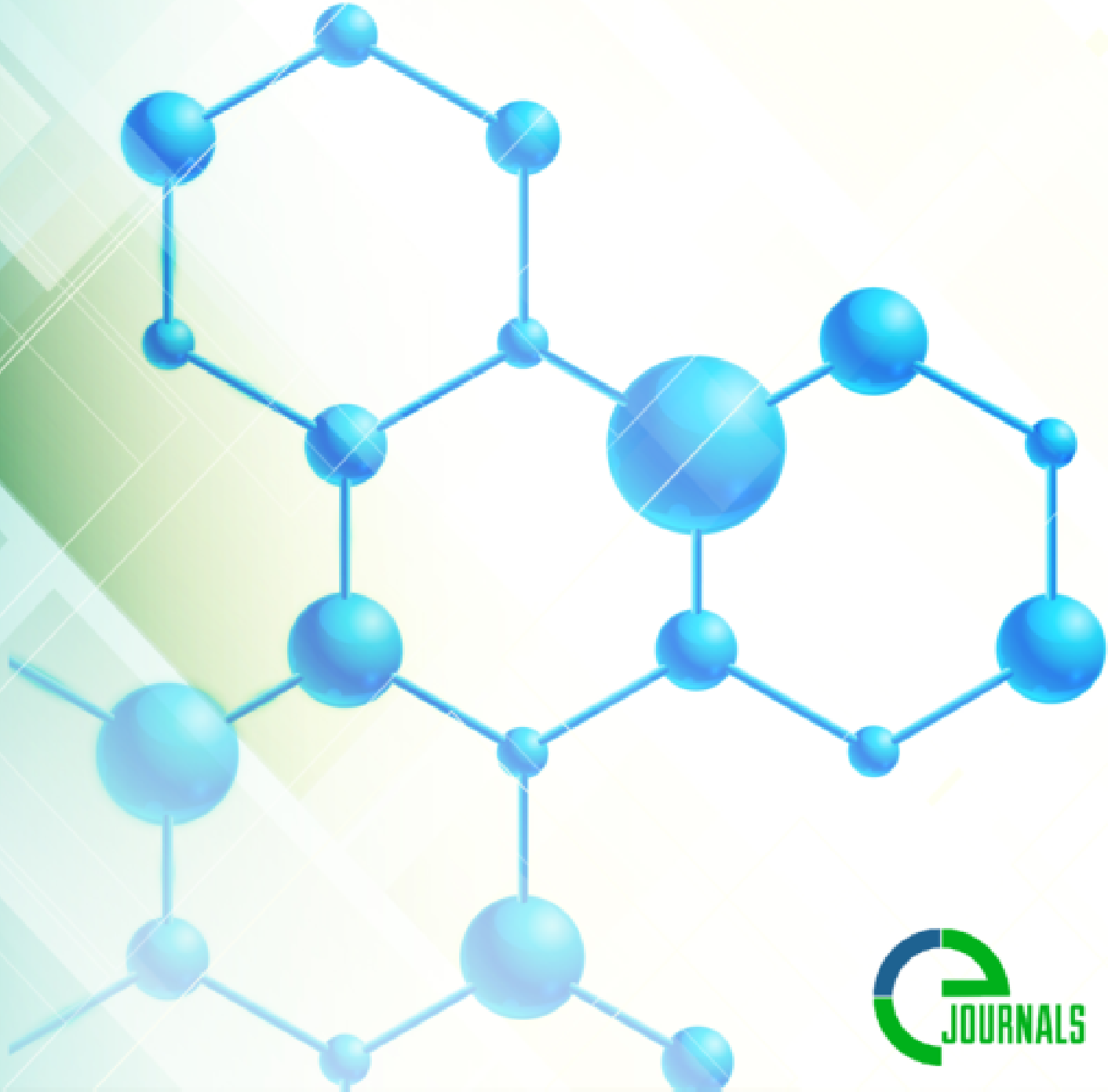

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# ASSESSMENT OF THE HORMONAL STATUS OF WOMEN WITH FAILED OUTCOMES OF ASSOCIATE REPRODUCTIVE TECHNOLOGIES IN THE HISTORY DURING THE BACKGROUND OF A LATENT FORM OF GENITAL TUBERCULOSIS

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*Abstract. During analyzing the hormonal status, we found a significant decrease in the levels of testosterone, estradiol and progesterone in the blood of women in the main group compared to patients with infertility and without GT. Timely detection of a decrease in the level of ovarian hormones in women with reproductive disorders associated with genital tuberculosis will make it possible to rationally and effectively correct hypogonadism and prevent these disorders.*

*Keywords: infertility, genital tuberculosis, history of unsuccessful outcomes of assisted reproductive technologies, hormonal status.*

Today, one of the world's problems is still tuberculosis, and it should be noted that there is a more frequent development of this pathology in females in the age group from 25 to 44 years [4, 6]. According to world statistics, 800,000 new cases of extrapulmonary forms of tuberculosis are registered annually around the world. It is worth noting that most often this pathology is registered at a stage that cannot be effectively treated and occurs with a large number of complications [3, 5].

The effectiveness of assisted reproductive technologies (ART) courses has shown significant positive dynamics over the past few years, but it is worth noting that about 60% of females are not able to achieve pregnancy after one course of treatment, and only every fifth woman achieves pregnancy after three in vitro fertilization (IVF) cycles [2]. It has been proven that transplantation of a structurally high-quality product of conception into the endometrium, the development of which is optimal for the current period of development, does not guarantee the onset of pregnancy, and even at the beginning of pregnancy there is no guarantee that fetal development will stop in the early stages of development [1].

Neuroendocrine regulation contributes to the influence on the entire body, and the pituitary-ovarian and pituitary-thyroid links play a huge role in the metabolic processes of development, maturation and regeneration of all tissues and organs. However, an imbalance in the secretion of gonadotropic and sex hormones in most cases leads to infertility.

Modern diagnosis and effectiveness of treatment for infertility caused by tuberculosis has a number of difficulties. The use of assisted reproductive technologies (ART) increases the effectiveness of therapy aimed at combating infertility, which has developed due to

the presence of genital tuberculosis. It is worth noting that there is a high chance of developing latent tuberculosis of the reproductive system after undergoing in vitro fertilization (IVF) procedures, which may contribute to further failures in IVF [6]. The above facts show the high degree of relevance of this problem and the need for its further study.

**Purpose of the study:** to study the features of hormonal status in women with genital tuberculosis and a history of unsuccessful ART.

**Materials and research methods:** of 309 women with infertility who applied for ART, 120 had a history of unfavorable ART outcomes, which amounted to 38.8%,the average age of all examined women was 31.2ë3.5 years. In the main group the average age was 33.4ë1.5 years, while in the comparison group it was 30.5ë2.4 years

The average number of unsuccessful ART outcomes among 120 women was 1.71ë0.18 times. In 32 cases (26.6%) tuberculosis of the genitals was diagnosed.As a result of the data obtained, 2 groups of subjects were formed: main group: 32 women with a confirmed diagnosis of genital tuberculosis; comparison group: 88 women with excluded diagnosis of genital tuberculosis.

Verification of the diagnosis of genital tuberculosis in the main group was carried out on the basis of a characteristic clinical and radiological picture, as well as specific tests (GeneXpert, PCR, bacteriological).

Hysterosalpingography (HSG) was performed at the Republican Clinical Tuberculosis Dispensary and at the Republican Clinical Gynecological Hospital. We used the Vympel X-ray diagnostic complex (Russia). The study was carried out in phase I of the menstrual cycle - on days 7-12 from the first day of menstruation; in the presence of concomitant gynecological pathology (in particular, adenomyosis), HSG was performed in phase I of the menstrual cycle (days 7-9). Water-soluble contrast agents (Verografin, Urografin, Omnipaque) were used for the study.

Determination of hormones in blood serum was carried out using an enzyme-linked immunosorbent assay on a Cobas 6000 analyzer (Switzerland).Standard indicators for hormone concentrations are as follows: progesterone - ovulatory phase 0.5-6.0 nmol/l, luteal phase 10-89 nmol/l; free testosterone - 0-4.1 pg/ml; estradiol - 13-191 pg/ml.

For statistical calculations, standard functions included in the MS Excel 2017 program were used. The resulting differences were assessed using the Student t-test. To assess the statistical reliability of the results obtained, the following significance levels were accepted: $p<0.05$; $p<0.01$; $p<0.001$.

Research results.Analysis of the duration of infertility revealed that in 59.4% (19 patients out of 32) of women in the main group, the duration of the disease exceeded 5 years (Fig. 1), compared with women in the comparison group - 37.5% (33 patients).

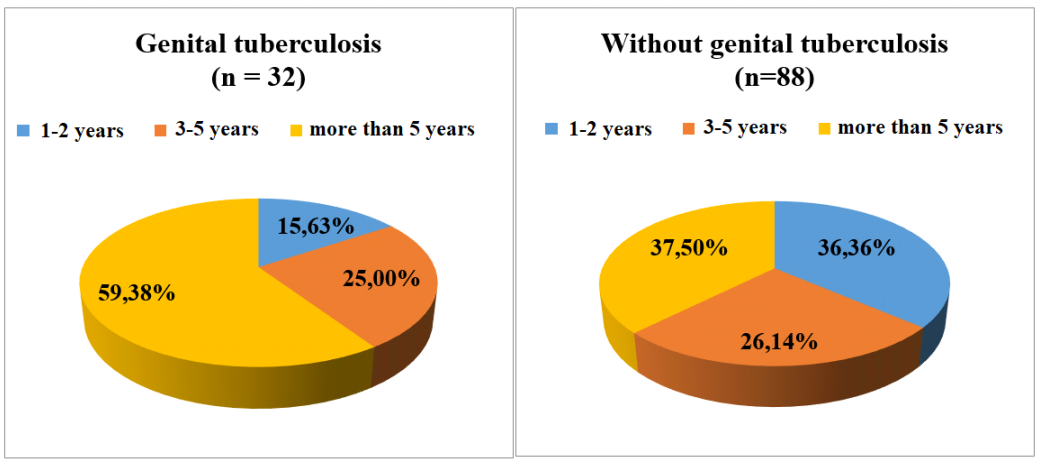


**Figure 1. Duration of infertility in the research groups**

The shortest duration of infertility (1-2 years) was found in the comparison group - 36.3% (32 patients), while in the main group this percentage was 2.3 times less, which was significant (P <0.05) .

An epidemiological history was aggravated in 46.9% (15 out of 32 patients), of which in most cases contact with a patient with tuberculosis was established, and treatment with anti-tuberculosis drugs in childhood was recorded in 37.5% of cases.

Among the diseases suffered in the patients of the main group, PID dominated (65.6%), in contrast to the comparison group (39.4%, p <0.001). Patients of the main group (87.5%) underwent inpatient and outpatient treatment for PID more often than women in the comparison group (60.2%) (p <0.001), while there was a lack of proper effect from treatment in the main group in 65.6 % of cases, in contrast to patients in the comparison group (13.6%, p<0.001).

The number of patients who underwent surgical interventions on the pelvic organs using laparotomy and laparoscopic access in the group of patients with genital tuberculosis was significantly higher (43.8%) than in the group of patients with infertility and an unknown diagnosis of genital tuberculosis (15.9%, p< 0.001).

According to the results of ultrasound examination in the main group, a predominance of calcifications in the myometrium and/or ovaries (62.5%, p<0.001), signs of adhesions (81.3%, p<0.01), unilateral and bilateral hydrosalpinxes ( 18.8%, p<0.01), endometrial hypoplasia (21.9%, p<0.01). The informative value of ultrasound in the complex diagnosis of genital tuberculosis was 78.1%.

When assessing the results of hysterosalpingography in the group of patients with infertility associated with genital tuberculosis, specific symptoms of damage to the fallopian tubes (symptoms of "rosary beads", rigid tubes, "clubs") (71.9%, p<0.001) and uterus (T- shaped uterus) (21.6%, p<0.001) in combination with obstruction of one or both fallopian tubes (75.0%, p<0.001) (Table 1). The informative value of HSG in the complex diagnosis of HT was 87.5%.

**Table 1**

**Results of hysterosalpinography among examined women depending on the diagnosis of genital tuberculosis**

| Results | Main group, n=32 | | Comparison group, n=88 | | Data reliability |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Calcifications in the abdominal cavity | 16 | 50.0±8.8 | 2 | 2.3±1.6 | <0.001 |
| Fallopian tube damage (specific signs) | 23 | 71.9±7.9 | 2 | 2.3±1.6 | <0.001 |
| Synechia/T-shaped uterus | 9 | 28.1±7.9 | 1 | 1.1±1.1 | <0.001 |
| One or more third-party presence of hydrosalpinxes of the fallopian tubes | 9 | 28.1±7.9 | 19 | 21.6±4.4 | >0.05 |
| The patency of the pipes is not impaired | 8 | 25.0±7.7 | 55 | 62.5±5.2 | <0.001 |

According to the laparoscopic study, the most characteristic features for women in the main group were the presence of complete occlusion of the fallopian tubes (62.5%) with bilateral lesions in every second case, tortuosity of the "constriction" type, and tuberculate rashes on the pelvic peritoneum (56.3%), with the possibility of preserved tube patency (25.0%).

Noteworthy was the statistically significant predominance of proximal fallopian tube occlusion in the main group, while in the comparison group this type of occlusion was not noted ($\chi 2 = 8.167$, $p=0.004$).

When analyzing the hormonal status, we found a significant decrease in the levels of testosterone, estradiol and progesterone in the blood of women in the main group compared to patients with infertility and without HT (Fig. 2).

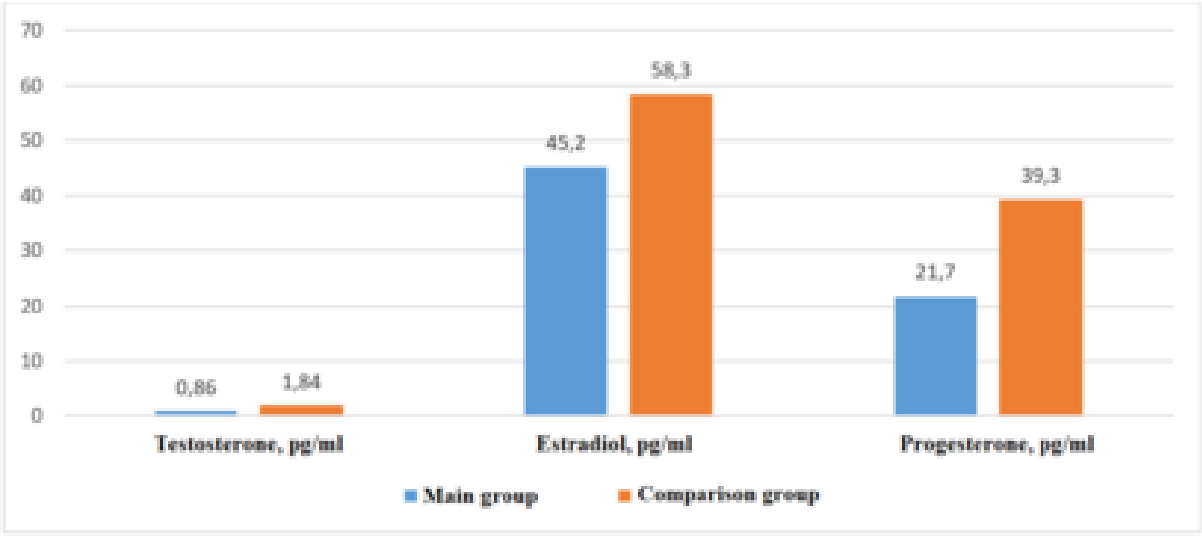


**Figure 2. Indicators of hormonal status in the study groups**

The level of free testosterone in the group of patients with genital tuberculosis was reduced by 2.2 times compared to the comparison group and averaged 0.85±0.4 ng/ml (0.36-2.1 ng/ml) versus 1. 84±0.3 ng/ml (1.3-2.76 ng/ml), respectively; $P < 0.001$.

Estradiol levels in the main group also significantly decreased by 1.3 times compared to the comparison group, averaging 45.2±1.5 pg/ml (24.4-66.5 pg/ml) in the main group and 58.3 ±2.1 pg/ml (45.1-69.4 pg/ml) in the comparison group; $P < 0.05$.

The FSH content in 90.8% of all examined women was within the normal range (109 out of 120 patients), in 5.8% of women the levels were above the upper limit of normal (7 out of 120 patients). However, no statistically significant changes were observed across groups.

As a result, we found that the characteristic features of the hormonal status of women with unsuccessful ART attempts against the background of genital tuberculosis are a decrease in the level of estradiol, progesterone and testosterone in the blood in relation to women without genital tuberculosis. A decrease in these ovarian hormones, in turn, directly affects reproductive dysfunction.

**Conclusions:**

1.It was found that in women with a history of repeated unsuccessful IVF outcomes, one of the causes of unfavorable outcomes in 26.6% of cases is genital tuberculosis.

2.In the hormonal status of women with unfavorable outcomes of ART against the background of genital tuberculosis, disorders of ovarian hormones were revealed, in particular, a decrease in free testosterone by 2.2 times, estradiol by 1.3 times, progesterone by 1.8 times in relation to the group of women without genital tuberculosis .

3.Timely detection of a decrease in the level of ovarian hormones in women with reproductive disorders associated with genital tuberculosis will make it possible to rationally and effectively correct hypogonadism and prevent these disorders.

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