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THE IMPACT OF ENDOCRINE PATHOLOGY ON THE OUTCOMES OF IN VITRO FERTILIZATION PROCEDURE

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The purpose of the study was to find out the influence of endocrine disorders of women on the results of in vitro fertilization procedure. We observed 191 patients undergoing treatment for infertility. Of these, 146 (76.4%) were aged 20–35 years, 45 (23.6%) were aged 36-50 years. The presence and structure of endocrine pathologies and the outcomes of in vitro fertilization were analyzed in the patients. In the structure of somatic diseases in women underwent in vitro fertilization procedure, endocrine pathology predominated: in total 14 of 20 (70 %), 12 (60 %) women had hypothyroidism, 2 (10 %) had type 2 diabetes mellitus. Almost all women with endocrine pathology (12 cases of 14–85.7 %) demonstrated unsuccessful IVF results: a higher IVF failure rate based on absence of transfer was observed in women with hypothyroidism, and based on cycle disruption–in persons with type 2 diabetes mellitus.

Key words: assisted reproductive technologies, hypothyroidism, diabetes mellitus, pregnancy.

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ВПЛИВ ЕНДОКРИННОЇ ПАТОЛОГІЇ НА РЕЗУЛЬТАТИ ПРОЦЕДУРИ ЕКСТРАКОРПОРАЛЬНОГО ЗАПЛІДЕНННЯ

Метою дослідження було встановлення впливу ендокринної патології у жінок на результати процедури екстракорпорального запліднення. Під наглядом перебувала 191 пацієнтка, яка проходила лікування щодо безпліддя. З них 146 (76,4 %) були у віці 20–35 років, 45 (23,6 %) – у віці 36–50 років. У пацієнток проаналізовано наявність та структуру ендокринної патології, а також результати екстракорпорального запліднення. У структурі соматичних захворювань у жінок, які перенесли процедуру екстракорпорального запліднення, переважала ендокринна патологія: у 14 із 20 (70 %), у 12 (60 %) жінок був гіпотиреоз, у 2 (10 %) – цукровий діабет 2 типу. Практично у всіх жінок з ендокринною патологією (12 випадків (14–85,7 %)) відзначено невдалі результати екстракорпорального запліднення: вищий відсоток невдач екстракорпорального запліднення через відсутність переносу спостерігався у жінок з гіпотиреозом, а з порушенням циклу – у осіб з цукром діабетом 2 типи.

Ключові слова: допоміжні репродуктивні технології, гіпотиреоз, цукровий діабет, вагітність.

Infertility still remains one of the problematic fields of modern medicine. Assisted reproductive technologies (ART), mainly intrauterine insemination and in vitro fertilization (IVF), have already helped many couples overcome infertility. According to statistics, millions of children have been born through ART worldwide, currently accounting for >4 % of births in several European countries. It must be remembered that the ultimate goal of ART, in particular in vitro fertilization, is the birth of a living child. As with natural conception, pregnancy failure following IVF may occur, including early miscarriage, ectopic pregnancy, intrauterine fetal death, or stillbirth. In addition to the physical and financial burden, any abortion has a destabilizing emotional impact on couples undergoing IVF cycles [2].

In this regard, the impact of any group of factors that can change the outcome of pregnancy during the process of IVF and its stages should be the subject of close study in order to minimize adverse outcomes.

Some researchers include endocrine factors in the list of such factors. With age, there is an increase in the incidence of endocrine diseases, which can have a further negative impact on fertilization rates.

Ovulatory dysfunction in patients included in assisted reproduction programs is associated with endocrine disorders, among which thyroid diseases, polycystic ovary syndrome and hyperprolactinemia predominate. [3]. There are several reports of a relationship between some endocrine diseases and an increase in adverse outcomes ART [4, 9, 10].

Among women of reproductive age, hypothyroidism is a common cause of infertility due to anovulation (prevalence is 3–5 %). The incidence of autoimmune thyroid disease is higher among infertile women. According to patient registries of assisted reproduction centers, the incidence of thyroid autoimmunity can reach 20% [9, 14].

Studies have demonstrated that reproductive dysfunction is also a common but little studied complication of diabetes [13].

Due to the state of hyperglycemia, women with diabetes may have substantially decreased fecundability and higher proportions of spontaneous losses [7].

Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM), both are equally at risk for reproductive disorders [1]. Endocrine disorders are not the leading indications for ART, but their treatment prior to ART is necessary to achieve optimal results. However, there is little data available to estimate to what extent ART can be successful in association with endocrinopathy.

Given that IVF is itself a stressful situation, assessing the role of various endocrine conditions may be important to improve the effectiveness of the procedure.

The purpose of the study was to find out the influence of endocrine pathologies of women on the results of in vitro fertilization procedure.

Materials and methods. We observed 191 patients who applied to the reproductive department of Caspian International Hospital between 2020 and 2022 for examination for infertility. Of these, 146 (76.4 %) were aged 20–35 years, 45 (23.6 %) were aged 36–50 years. The patients were analyzed based on the presence of somatic diseases (especially, endocrine pathologies).

The subjects underwent IVF procedure according to standard clinical procedures. Ovulation induction was carried out by injection of recombinant follicle-stimulating hormone (daily 225 IU), starting from the third day of the menstrual cycle. Human chorionic gonadotropin (3300–10,000 IU) was administered after observing two follicles reaching a minimum mean diameter of 17 mm. Oocyte collection was carried out 36 hours after the administration of human chorionic gonadotropin with the introduction of progesterone on the day of oocyte collection. Pregnancy assessment was carried out 4–5 weeks after embryo transfer using ultrasound.

The NCSS (Number Cruncher Statistical System) program was used to evaluate the data. The mean, standard deviation, and frequency of the trait (absolute number and percentage) were determined. Compliance of quantitative data with normal distribution was checked using the Shapiro-Wilk test and graphical studies. Comparison of groups with a normal distribution was carried out using the Student's t-test, groups in the absence of a normal distribution–the Mann-Whitney U-test. Differences were considered significant at $p<0.05$.

Results of the study and their discussion. When analyzing anamnestic data, it was found that out of 191 patients who were under observation, 41 (21.5 %) had higher education, 149 (78 %) women had only school education. One of the patients had an incomplete school education. An assessment of social status showed that 70 (36.6 %) had a permanent job, 120 (62.8 %) were not working at the time of the survey. In one of the cases, information could not be obtained. An analysis of the place of residence revealed that 30 (15.7 %) of those who applied lived in Baku, the remaining 161 (84.3 %) lived in the regions. At the same time, 20 (10.5 %) patients rated the living conditions as “good,” 167 (87.4 %) as “satisfactory,” and 4 (2.1 %) as “unsatisfactory.” Accordingly, answers to the question about financial situation were distributed in a similar way. All women denied having bad habits. With regard to marital status, it was revealed that only 1 patient was not married at the time of treatment, the remaining 190 (99.5 %) were married.

Among the infertility factor the we noted several causes of infertility: male factor, the ovarian factor, tube factor. Besides, some cases were related to unexplained reason and gender selection. In a number of couples, infertility depends on both sides.

The menstrual function was regular in 70 women (36.6 %), irregular – in 121 (63.4 %) of 191 patients. 180 (94.2 %) women described the intensity of menstruation as “normal”, in 6 (3.1 %) women hypomenorrhea was registered, in 5 (2.6 %) – hypermenorrhea. 6 patients (3.1 %) of 191 have the history of recurrent miscarriage, 68 of all women observed were treated before the current process of in vitro fertilization. In addition, we revealed that 7 (3.7 %) of patients have the experience of medical abortion, 9 (4.7 %) of them lost pregnancy in previous period due to ectopic pregnancy.

The presence of somatic diseases was confirmed by clinical and laboratory methods in 20 (10.5 %) patients under observation; these patients were mainly in the age group of 36–50 years. In 2 cases (1 %) tuberculosis infection was detected. In addition, arterial hypertension was observed (in 3 (1.6 %) patients), bronchial asthma (in 1 (0.5 %)). All respondents indicated that they had suffered from various infectious diseases in childhood.

In the structure of somatic diseases, endocrine pathology predominated: 12 (60 %) women had hypothyroidism, 2 (10 %) had type 2 diabetes mellitus.

Based on the results of in vitro fertilization, the following outcomes were obtained: no transfer – 8 cases (4.2 %), absence of pregnancy –91 cases (47.6 %), presence of pregnancy – 82 cases (42.9 %), cycle disruption – 10 cases (5.2 %).

It should be noted that almost all women with endocrine pathology (12 cases of 14–85.7 %) demonstrated unsuccessful in vitro fertilization results. Interestingly, a higher IVF failure rate based on absence of transfer was observed in women with hypothyroidism, and based on cycle disruption–in persons with type 2 diabetes mellitus. 9 (64.2 %) of these (even without confirmed diagnosis of diabetes mellitus) had higher baseline glucose and baseline insulin.

Our data coincide with the study by Herman T, et al (2022), who observed 231 patients underwent in vitro fertilization treatment, of these 161 patients (69.7 %) had at least one known and treated endocrine disorder. Comparing the results of IVF in study group to control group without endocrinopathies, the authors revealed that with no difference in the IVF cycles performed, pregnancy rate was lower in the study group (61.43 % vs. 34.16 %; p=0.003). The researchers concluded that even after proper correction, the presence of the endocrine disorder negatively influences the pregnancy rate in in vitro fertilization treatment. In contrast with our work, this study demonstrated high prevalence of endocrine disorders in females participating in in vitro fertilization programs [4].

Several studies showed the role of pathologies of thyroid gland. [8, 9, 14]. Thus, some authors found out that the number of retrieved oocytes was significantly lower in the group with autoimmune thyroid disease (p=0.014) [4]. They supposed the negative impact of hypothyroidism on reproductive health due to related hyperprolactinaemia. It is considered the hyperprolactinaemia causes infertility through the impaired pulsatile secretion of gonadotropin-releasing hormone and its consequences, which leads anovulation.

On the other hand, thyroid hormone is also required for the proper synthesis of estrogen and progesterone. From this position, the level of thyroid hormones may affect the success of IVF treatments and appropriate thyroid hormone replacement is important prior to in vitro fertilization procedure [8].

In our study only 2 women had type 2 diabetes mellitus, but there were 16 women of 191 with impairment glucose tolerance and 9 patients with high baseline glucose and baseline insulin. These women had the negative outcomes, such as absence of transfer and pregnancy.

Mattsson K, et al noted that women with type 2 diabetes with onset before their reproductive “journey” were more often childless compared with women without diabetes and had a higher risk of negative outcomes of pregnancy. The researchers suggested that this patient group may be in need of targeted information regarding potential fertility issues as part of their clinical treatment [6].

The similar with our data were obtained by Qin X, et al, who revealed lower oocyte rate, fertilization rate, and high-quality embryo rate, as indicators of embryo development, in women with type 2 diabetes mellitus compared with the non-T2DM group. [10]. The authors noted that the patients with type 2 diabetes mellitus showed statistically decreased levels of anti-mullerian hormone and during ovarian stimulation they required significantly higher total and initial doses of gonadotropin, although they had fewer retrieved oocytes. Compared to our work, the researchers used multivariate logistic regression analysis adjusting for confounding factors which showed that type 2 diabetes mellitus alone was an independent risk factor for clinical pregnancy rate, live birth rate, and abortion rate. The authors concluded that infertile patients with T2DM have decreased ovarian reserve, and type 2 diabetes mellitus has a deleterious impact on clinical pregnancy outcomes during the assisted reproductive technologies process compared with non-T2DM infertile women.

There are evidences that type 2 diabetes mellitus impairs the function of the female reproductive system and negatively affects fertility [5].

The negative impact of diabetes on female fertility has been identified in a number of studies. In the one cohort study the researches found out that elevated pre-pregnancy maternal glucose levels were associated with the couple’s lower fecundability [15].

Another large prospective cohort study also found that women with T2DM had a higher risk of miscarriage and infertility before birth. In addition, they may face serious problems with ovarian reserve and pregnancy outcomes [6].

This means that the increasing childbearing women with type 2 diabetes mellitus need to rely on assisted reproductive technology to complete fertility. Besides, the incidence of spontaneous abortion and the risk of pregnancy complications [11].

The sources mentioned above supports the results of our study, however, there are still some studies that remain controversial regarding the fertility in patients with type 2 diabetes mellitus, such as an observational, descriptive study, which were conducted in Iran and showed a higher rate of fertility in married women with T2DM [12].

Conclusions

1. In the structure of somatic diseases in women underwent in vitro fertilization procedure, endocrine pathology predominated: in total 14 of 20 (70 %), 12 (60 %) women had hypothyroidism, 2 (10 %) had type 2 diabetes mellitus.

2. Almost all women with endocrine pathology (12 cases of 14–85.7 %) demonstrated unsuccessful IVF results: a higher IVF failure rate based on absence of transfer was observed in women with hypothyroidism, and based on cycle disruption – in persons with type 2 diabetes mellitus.

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