



## OPTIMIZED METHODS OF PREPARATION INFERTILE PATIENTS TO IVF PROGRAMS.

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**Annotation.** Secondary infertility is one of the main indications for in vitro fertilization (IVF). Lack of preconceptional preparation has been associated with significantly higher reproductive risks, ranging from infertility to intrauterine structural defects and diseases . We studied the microelement composition of the blood and follicular fluid of women with tubal infertility. During the study of the microelement composition of peripheral blood, Zinc deficiency was determined in 28% of women and Iron deficiency in 7.14% of women. At the same time, the microelement composition of the follicular fluid was studied and it was determined that zinc was consumed 69% of the initial value. And also the concentration of iron and copper is reduced to 32% and 11.2% accordingly . In this review, we focus on the reproductive risks associated with certain preconception care, which is a critical step in determining fetal development and health due to the potential onset of a number of diseases in women with tubal infertility.

**Key words:** infertility, in vitro fertilization, preconception preparation, folic acid

Infertile marriage is the absence of pregnancy within 12 months of regular unprotected sexual activity. Nowadays, around the world, about 15% of married couples suffer from infertility, and more than 55% of cases are caused by reproductive disorders [1]. The burden of infertility is overwhelmingly higher among women in developing countries; in some regions of South and Central Asia, sub-Saharan and North Africa, the Middle East and Eastern Europe, infertility rates can reach 30% in women of reproductive age [2]. The inability to conceive not only creates a significant cost burden for patients and the healthcare system, but also causes significant psychological distress for millions of couples [3]. In some parts of the world, especially in low- and middle-income countries where biological children are highly valued and expected of married couples, involuntary infertility can lead to stigma, economic deprivation, social exclusion and loss of status, social shame and humiliation, and some cases of violence [4]. Female infertility can be associated with a number of factors, which are generally classified as endocrine, vaginal, cervical, uterine, tubal and pelvic-abdominal, and although estimates vary, approximately 15–30% of cases still remain unexplained [5]. A better understanding of the causes of infertility is needed to alleviate this multifactorial burden on society. To suspect infertility, the patient must have had a failed pregnancy after 12 months or more of regular unprotected intercourse in a woman under 35 years of age and 6 months of unsuccessful pregnancy in a woman aged 35 years or older. WHO estimates that 50 to 80 million women worldwide and 11.3% of married women suffer from infertility, and only 35% of them seek medical help [6]. Tubal subfertility or infertility is attributed to 30% of the etiologies of infertility [7]. Tubal peritoneal infertility (TPI) is one of the most common causes of infertility in women of reproductive age. Tubal disease may involve the proximal, distal, or entire tube and can vary in severity. Pelvic inflammatory disease is the most common cause of

tubal disease, accounting for more than 50% of cases, and can affect the fallopian tubes in many locations [8].

Fertility, conception, implantation, fetal organogenesis, and placentation are critical stages that can potentially be affected by nutrition during the preconceptional period. The preconception period is particularly important as it affects both fertility and early pregnancy. Dietary micronutrient intake and maternal status influence the various phases of pregnancy and development, as well as fetal health. Micronutrients are essential vitamins and minerals that are required in small quantities as dietary components. Although these microelements do not provide the body with energy, they are necessary for catabolic and anabolic processes and must be supplied externally. The importance of proper nutrition during pregnancy has already been established, influencing embryonic and intrauterine development and therefore pregnancy outcomes. Pre-conceptual preparation is preventive measures aimed at leveling the risks in the implementation of the reproductive function of a young couple. The need for pre-conceptual preparation of future parents is due to the fact that both the young husband and the young wife equally transfer genetic material to the embryo and are jointly responsible for the optimal condition of the fetus.

A global study found that the global prevalence of infertility remained virtually unchanged between 1990 and 2010, with an estimated 48.5 million couples worldwide having difficulty having a child over 5 years of age in 2010. Morphological and functional disorders of the fallopian tubes, such as obstruction, rigidity deformation and peristaltic imbalance, occurring in various diseases, account for 25–30% of all cases of infertility [9]. Accurate assessment of tubal patency can be important evidence for targeted clinical treatment. Laparoscopy and dye intubation (knees and dye) have long been considered the gold standard for tubal patency testing; but in the public sector there are concerns about long delays and costs, as well as risks associated with anesthesia and surgery [10]. The more accessible hysterosalpingography involves X-ray exposure and the risk of hypersensitivity reaction to iodinated contrast agents. Compared to these procedures, transvaginal Hysterosalpine contrast sonography (HSCS) is a non-invasive, safe and cost-effective method that provides rapid, easy and reliable diagnosis of tubal patency [11]. So far, some studies have attempted to evaluate the accuracy of GCS in diagnosing tubal patency compared with traditional methods.

Tubal infertility (TB) is one of the most common causes of infertility, accounting for 30% of female infertility worldwide, and is even more common in some communities [12]. Bacteria travel up the mucosal surface from the cervix to the endometrium and ultimately to the fallopian tubes. This causative pathway manifests clinically as pelvic inflammatory disease (PID), which in turn is closely associated with subsequent TB. In fact, about 15% of women with PID have a BMI, and the number of episodes of PID a woman experiences is directly proportional to her risk of infertility [13]. However, most women with a history of ID do not have a clinically diagnosed acute PID, but rather develop asymptomatic or minimally symptomatic salpingitis as a result of an upper genital tract infection [14]. Testing the patency of the fallopian tubes is an integral part of the assessment of subfertility in women. Fallopian tube anomalies are observed in 30-40% of women with infertility. Laparoscopy (LS) with chromopertubation is considered the gold standard for diagnosis [15].

The study of ME metabolism in the body of people of different ages, professions, during pregnancy, and also depending on other factors is currently attracting the attention of many researchers. The great interest in this problem is explained by the high biological activity of

MEs, their participation in a number of important biochemical processes: redox, various types of metabolism (protein, fat, carbohydrate, vitamin, mineral), gas exchange, tissue respiration, tissue permeability, cell division, hematopoiesis, growth, immunological reactions, etc.

In addition, a number of researchers believe that increased or decreased percentages of trace elements in the blood and in the VF are predictors of a negative outcome of in vitro fertilization (IVF).

**The purpose of our study** was to study the importance of microelements in women with tubo- peritoneal infertility to predict the effectiveness of an IVF program.

**Materials and methods of research.** We examined 74 patients undergoing IVF treatment for infertility, 26 of them with tubal factor infertility with a deficiency of certain microelements (main group) and 48 with tubal factor infertility with normal values of certain microelements (comparison group). Examination and treatment were carried out in clinics " Consultative medical group ", " Istanbul Eku markazi " and " Ankalife " in Tashkent, Uzbekistan. Depending on the effectiveness of the IVF program, two subgroups were prospectively formed in each group. The 1st (main) group included 26 patients with tubal infertility with a deficiency of individual microelements, of which 7 (26.9%) had a positive IVF result and 19 (73%) women in whom pregnancy did not occur (confirmed by echography ). The age of the women interviewed ranged from 25 to 35 years. The average age of the subjects was  $27.1 \pm 2.3$  years. The average duration of infertility was  $5.6 \pm 1.3$  years. The comparison group (group 2) consisted of 48 patients of comparable age (from 26 to 35 years) with tubal infertility (obstruction or absence of the fallopian tubes). Of these, 17 (35.4%) patients became pregnant, 31 (64.6%) cases did not. After completing the treatment and preparatory procedures, all women underwent an IVF program. To induce superovulation in both groups, a short-short protocol was used using gonadotropin- releasing hormone antagonists according to the standard method. Fertilization of oocytes was carried out using IVF. Before stimulation in the IVF program, 50 women began supplementation with a German high-quality microelement preparation for 2 months. Selective transfer of one blastocyst - on the 5th day of cultivation. Blood serum is collected on an empty stomach from the ulnar vein before transvaginal puncture of preovulatory follicles. Follicular fluid (FF) was obtained by transvaginal puncture of preovulatory follicles. If blood entered the contents of the follicles, this material was not examined. Biological materials were examined at the Swiss clinic Lab " in Tashkent. The concentration of trace elements in blood serum and follicular fluid was studied using standard biochemical methods.

**Research results.** Based on our data, it was established that in groups of women formed depending on the result of IVF ( echographically confirmed pregnancy), the pregnancy rate in the main group (with tubal factor infertility and a deficiency of certain microelements) was significantly lower. (26.9%) than in the comparison group (tube factor with normal values of microelements) -35.4%. When studying the microelement composition of peripheral blood, zinc deficiency was detected in 28% of women, iron deficiency - in 7.14% of women. In all women, the concentration of copper and folic acid did not exceed control values. The concentration remained unchanged and did not differ from the values in patients in the comparison group ( $0.01 \pm 0.002$  g/l - indicator in patients in the comparison group). Factors predicting a negative outcome of IVF programs are: decreased zinc levels in the blood and mixed types of micronutrient deficiencies worsen reproductive outcomes. In case of shortage

microelements in the blood of infertile women with tubal infertility, the reproductive outcome in ART programs is reduced in all respects. Follicular fluid is a diagnostic indicator of tubal

Embryological results	Main group	Comparison group
Number of eggs collected	7.48+-0.67	12.19+-0.93
Mature eggs (M2)	5.87+-0.64	9.31+-0.73
Fertilized eggs (2PN)	4.03+-0.56	6.60+-0.62
Frozen eggs	2.19+-0.30	4.15+-0.45
Number of implanted embryos	1.41+-0.13	1.41+-0.12
number of pregnancies	7 -22.6 %	17 -33.4%

factor infertility.

#### Ultrasound of the first trimester of the fetus

Ultrasound of the first trimester of the fetus	Main group	Comparison group
Hypertonicity of the uterus	6	5
Progresses without pathology	21-67.7 %	42 -82.4%
Pregnancy 4-6 weeks . In the uterus	0	0

NB. According to the type of anembryonia	0	0
NB. Fetal death	0	2
Hydatidiform mole	0	0
Chorionic detachment	1	0
Cervical digroma	0	0
Retrochorial hematoma	2	2
Ectopic pregnancy	1	0
Chorion water turbidity	0	0

As we can see , according to ultrasound findings of the first trimester of the fetus, the level of reproductive losses in the main group was significantly increased than in the comparison group. Upon receipt of the above results, it is advisable to consider the possibility of conducting delayed ovulation stimulation cycles in order to conduct a course of pre-conceptual preparation before IVF programs.

**Conclusion.** In the course of our research, it was found that microelement support with a microelement containing preparation for infertile women with tubal factor occurs, and improves the primary results by affecting the overall well-being of the human body. Their insufficient levels can negatively affect the ability to conceive a child. A recommended approach to the management of the first trimester in women after an IVF cycle for tuboperitoneal infertility is necessary. The new data obtained form the basis of practical recommendations for practical healthcare for the prevention and treatment of infertile women with tubal- peritoneal factor. If the results described above are obtained , it is advisable to consider the possibility of delayed cycles of ovulation stimulation in order to conduct a course of preconception preparation in IVF programs. Nutritional deficiencies, identifying target groups at high risk of suboptimal nutrition, and implementing practical, safe and effective nutrition policy solutions can help improve the resilience of infertile couples. We decided that analysis of published series is necessary to assess the consistency of published results and to enable patients to receive more accurate information about their prognosis for IVF in the presence of tuboperitoneal infertility .

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