The Austrian Journal of Technical and Natural Sciences, No 7–8
ISSN 2310-5607

PREMIER Publishing
ppublishing.org

DOI:10.29013/AJT-25-7.8-105-112

EFFECTIVENESS OF IN VITRO FERTILIZATION IN WOMEN WITH HYPOTHYROIDISM-RELATED ENDOCRINE INFERTILITY

Jilonova A. N. [1]***, Nasirova K. K.*** [1]***, Shodieva K. T.*** [2]

[1] Endocrinology, pediatric endocrinology department, Tashkent State Medical University, Uzbekistan

[2] Obstetrics and gynecology in family medicine department, Tashkent State Medical University, Uzbekistan

Cite: *Jilonova A. N., Nasirova K. K., Shodieva K. T. (2025). Effectiveness of in vitro fertilization in women with hypothyroidism-related endocrine infertility. Austrian Journal of Technical and Natural Sciences 2025, No 7–8.* https://doi.org/10.29013/AJT-25-7.8-105-112

Abstract

Hypofunction of the thyroid gland leads to changes in the menstrual cycle – most often manifesting as menorrhagia – and is accompanied by increased prolactin levels that adversely affect the ovarian reserve, ultimately necessitating in vitro fertilization. An increase in gonadotropin levels and a decrease in progesterone indicates more pronounced menstrual cycle disorders and an increase in anovulatory cycles in patients, which dictates the need to correct hormonal status for the effectiveness of IVF.

Keyword: *hypothyroidism, fertility, in vitro fertilization*

I. Introduction

In medicine the absence of pregnancy after regular unprotected sexual intercourse for 12 or more months is classified as a infertility, and it is a disorder of the female or male reproductive system (Infertility prevalence estimates, 1990–2021. Geneva: World Health Organization; 2023; Purity Njagi, Wim Groot, Jelena Arsenijevic, Silke Dyer, Gitau Mburu, James Kiarie). Diagnostics and infertility remain one of the pressing problems of modern medicine. Methods of prevention, diagnostics and treatment of infertility, including assisted reproductive technologies such as in vitro fertilization (IVF), are often unavailable due to high cost and limited number of clinics providing such services (Infertility prevalence estimates, 1990–2021. Geneva: World Health Organization; 2023; Purity Njagi, Wim Groot, Jelena Arsenijevic, Silke Dyer, Gitau Mburu, James Kiarie).

Although the prevalence of infertility increases depending on the methodology, according to global data, from 48.5 to 72.4 million couples suffer from this condition (Boivin, Jacky & Bunting, L. & Collins, J.A. & Nygren, Karl-Gösta. 2007; Infertility prevalence estimates, 1990–2021. Geneva: World Health Organization; 2023; Purity Njagi, Wim Groot, Jelena Arsenijevic, Silke Dyer, Gitau Mburu, James Kiarie). Among couples

of reproductive age, infertility is from 12.6% to 17.5%, which means that approximately every sixth person in the world faces this problem. Thus, infertility is not only a medical but also a major social problem.

The causes of infertility are varied. According to the European Society of Human Reproduction and Embryology (ESHRE) in 2018, the male factor accounts for 20–30% of cases, and the female factor accounts for 20–35%. Infertility affecting both partners occurs in 25–40% of cases, and the remaining 10–20% is unexplained infertility. A study of infertility factors has shown that the main causes of female infertility in 38–40% of cases are endocrine disorders, 30% fallopian tube obstruction, 18% uterine diseases, 7% idiopathic causes and in 5% of cases psychological and immunological factors (London: National Institute for Health and Care Excellence (NICE); 2017).

Hypothyroid conditions play an important role among endocrine infertility. According to foreign researchers, the prevalence of hypothyroidism in women with infertility ranges from 2 to 34%; the variability of hypothyroidism prevalence in different populations is directly related to the endemicity of the zone for iodine deficiency (Poppe K., Velkeniers B., Glinoer D., 2007).

Thyroid hormones play a crucial role in the interaction with follicle-stimulating hormone, promoting the differentiation of granulosa cells. This process is vital for normal follicular development, which is necessary for ovulation and the formation of the corpus luteum. Therefore, adequate levels of thyroid hormones are essential for effective ovulation stimulation.

Given the high rates of infertility in various forms, there is an increasing demand for assisted reproductive technologies (ART). ART encompasses a range of effective strategies and interventions designed to address infertility, involving medical technologies, therapies, and procedures that facilitate pregnancy, often with some or all conception processes occurring outside the woman's body (Systematic review, Human Reproduction Open, Volume 2023).

The course of thyroid pathology among patients in ART programmes and the peculiarities of these programmes have not been sufficiently studied. One of the stages of in vitro fertilisation (IVF) is superovulation stimulation, which leads to hyperestrogenemia, which causes relative hypothyroxinemia and an increase in the concentration of TTG in the blood due to a decrease in the reserve capacity of the thyroid gland. A large number of thyroid gland pathologies, more often hypothyroidism, have been studied as a factor of infertility, which affects the outcomes of ART programmes, but their results are contradictory. Despite the achievements of modern reproductology, the parameters of monitoring and screening of thyroid function at the pregravidar stage, in IVF protocols and during pregnancy have not been defined.

The issue of management of patients planning IVF with hypothyroidism, as well as deterioration of thyroid function after these procedures is urgent.

Objective. To evaluate the efficacy of in vitro fertilization programmes in women with endocrine infertility in hypothyroidism.

II. Aim of the work

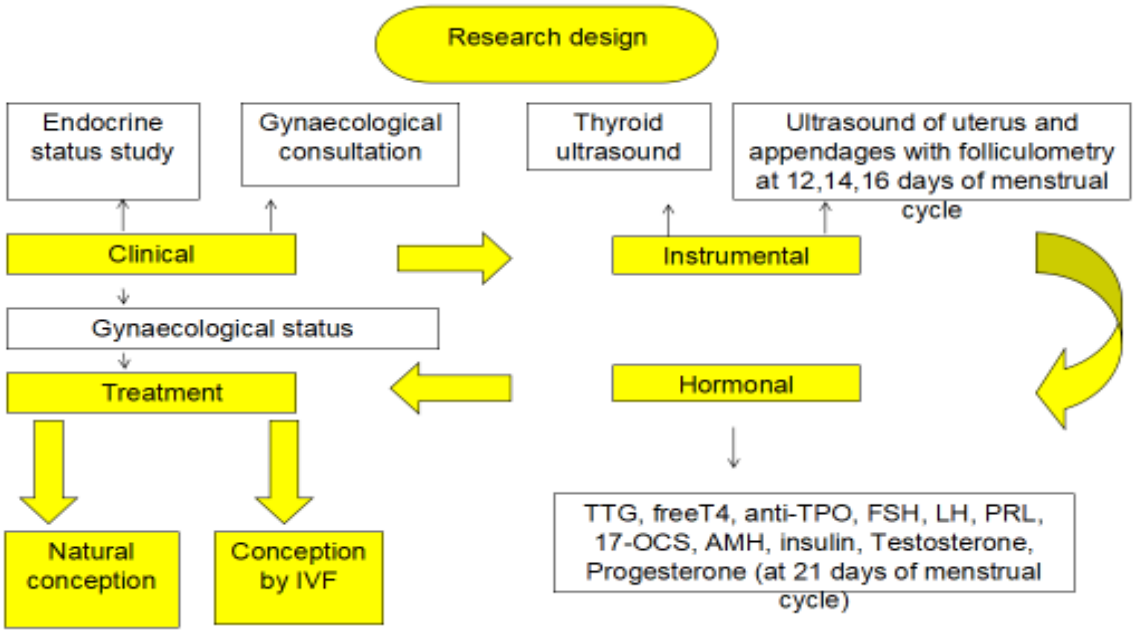
To evaluate the effectiveness of in vitro fertilisation programmes in women with endocrine infertility in hypothyroidism

III. Materials and metods

The study was performed at Mediofarm ECO fertility centre from September 2023 to August 2024. There were 270 subfertile female patients aged between 20 and 45 years. All patients underwent a complete clinical and hormonal and imaging examination, after which 98 hypothyroid (HT) patients were selected among them. After achieving euthyroidism, out of 98 patients, 22 patients became pregnant naturally and 32 patients conceived by IVF procedure. Pregnancy was confirmed by measuring human chorionic gonadotropin (hCG) blood levels. In this paper, the patients are divided into the following groups: Group 1–32 patients with a history of female infertility with hypothyroidism conceived by IVF, Group 2–22 patients with a history of female infertility with hypothyroidism conceived naturally. Women residing in the city were selected. The mean age category for group 1 was 35.03±7 years and for group 2 31.14±8.7 years. Follow-up time during treatment was 3–6–9 months, dura-

tion of infertility in group 1 was 5.69±3.46 years and in group 2 2.82±3.65 years. The mean BMI in group 1 was 24.10±4.71 and in group 2 23.86±4.67. Oocyte retrieval took place in a natural cycle or a short stimulation protocol was used. Preparation for IVF procedure took from 3 to 6 months depending on the causes of infertility.

Figure 1. *Study design of female patients with endocrine infertility in hypothyroidism*



The inclusion criteria for the study were women aged 20 to 45 experiencing infertility due to endocrine factors, specifically those with thyroid dysfunction. Exclusion criteria included women with severe medical conditions such as ischemic heart disease, chronic renal failure, diabetes mellitus in the decompensated stage, serious thyroid disorders, thyrotoxicosis, and diseases affecting the hypothalamic-pituitary system, as well as cases of absolute male infertility (such as aspermia or azoospermia).

Clinical methods included general examination, anthropometry, palpation of the thyroid and mammary glands, and gynecological examination. During the examination of women, the degree of hair loss and the presence of hirsutism were assessed using the Ferriman-Galvey scale. The patients' height and weight were recorded, focusing on their physique, the development of adipose tissue, and its distribution patterns. The body mass index (BMI) was calculated based on the WHO classification (2014) using anthropometric measurements. All women underwent palpation of the thyroid gland. The degree of its enlargement was assessed according to the WHO classification (2001). To assess the endocrine status, hormonal studies of thyroid, gonadotropic hormones, ovarian reserve, prolactin (PRL), 17-oxyprogesterone (17-OX), progesterone on the 21st day of the menstrual cycle, testosterone, and insulin were performed.

The gynecological status of women was assessed together with a gynecologist. The obstetric and gynecological history was gathered, including details on menarche onset and the potential impact of menstrual irregularities due to underlying conditions, stress, relocations, medications, or past surgeries. Information on marital history, pregnancies, and their outcomes was also considered. When assessing reproductive status, the following menstrual cycle disorders were identified: hypomenstrual syndrome (amenorrhea, opsomenorrhea, oligomenorrhea), hypermenstrual syndrome (menorrhagia, metrorrhagia).

The examination of the mammary glands was conducted in both standing and lying positions, with sequential palpation of the external and internal quadrants. Particular attention was given to glandular structure, size variations (hypoplasia, hypertrophy, trophic changes), and other notable characteristics. The presence or absence of nipple discharge was

assessed, including its color, consistency, and nature, along with the pigmentation state of the nipple-areolar complex. If necessary, a consultation with a mammologist was arranged.

Among instrumental diagnostic methods, ultrasound was performed on the thyroid gland, uterus, appendages, and mammary glands. Hysteroscopy was conducted when clinically indicated. Ovarian and uterine ultrasound with folliculometry was carried out using a vaginal transducer on days 12, 14, and 16 of the menstrual cycle, following standard protocols. Measurements included endometrial thickness, antral follicle count (AFC), and the dominant follicle's growth, tracking its progression to ovulation, anovulation, persistence, or atresia. Folliculometry findings were correlated with hormonal data for a comprehensive assessment. Breast ultrasound was performed with BI-RADS classification.

IV. Results

Frequent complaints in women of both groups were ectodermal disorders such as dry skin, hair loss, and brittle nails, which occurred in half of all patients. Hyperprolactinemia was significantly more common in women of the first group 10 (31.3%), increased blood pressure was observed in 5 (16.1%) patients of the first group and 1 (4.5%) of the second group.

Table 1. *Clinical and Anamnestic data of the Studied Women With Endocrine Infertility in Hypothyroidism*

		1st group (n=32)		2nd group (n=22)		Total (n=54)	
		abs	%	abs	%	abs	%
Age (years)	20–35	17	53,1	17	77,3	34	63
	36–45	15	46,9	5	22,7	20	37
BMI	Normal weight	20	62,5	15	68,2	35	64,8
	Overweight	8	25	5	22,7	13	24,1
	Obesity stage I	3	9,4	2	9,1	5	9,3
	Obesity II stage	1	5	0	0	1	1,8
Amenorrhea		2	6,3	0	0	2	3,7
Opsomenorrhea		2	6,3	1	4,5	3	5,5
Oligomenorrhea		4	12,5	4	18,2	8	14,8
Menorrhagia		17	53,1	9	40,9	26	48,1
Metrorrhagia		1	5	0	0	1	1,8
Miscarriages		1	5	2	9,1	3	5,5
Undeveloped pregnancy		3	9,4	4	18,2	4	7,4
Medical abortion		0	0	1	4,5	1	1,8
Ectopic pregnancy		8	25	0	0	8	14,8
Neonatal fetal death		2	6,3	0	0	2	3,7

Clinical and anamnestic data are presented in Table 1. Overweight was found in 13 (24.1%) patients, 1st degree obesity in 5 (9.3%) and 2nd degree obesity in 1 (1.9%) woman. Menstrual disorders in the form of menorrhagia were observed in 48%, oligomenorrhea in 14.8%, while 21% of the patients had normal menstrual cycle. The history in each group was intrauterine intervention after spontaneous miscarriage and undeveloped pregnancy. Termination of pregnancy due to ectopic pregnancies was in 9 (28%) women and neonatal fetal death in 2 (6.3%) patients from the first group.

The gynecological status was assessed (Table 2), of 54 patients, 37 (68.5%) had primary infertility and 17 (31.5%) secondary infertility. The following pathologies were detected in the subjects: uterine myoma (18,5%), endometriosis (13%), endometri-

al polyp (14,8), polycystic ovary syndrome (PCOS) (13%), for which treatment was carried out. And tubal-peritoneal factor of infertility was diagnosed in 9 (28.1%) women of first group. We evaluated the thyroid gland, and the diagnosis of hypothyroidism was confirmed by laboratory parameters and ultrasound (Table 3).

Table 2. *Gynaecological Status of Examined Women With Endocrine Infertility In Hypothyroidism*

		1st group (n=32)		2nd group (n=22)		Total (n=54)	
		abs	%	abs	%	abs	%
Duration of infertility (years)		5,69±3,46		2,82±3,65		–	
Primary infertility		18	58,3	19	86,4	37	68,5
Secondary infertility		14	43,8	3	13,6	17	31,5
Number of IVF attempts	**1**	17	53,1	–	–	17	31,5
	2–3	13	40,6	–	–	13	24,1
	4 and more	2	6,3	–	–	2	3,7
Uterine myoma		7	21,9	3	13,6	10	18,5
Endometriosis (adenomyosis)		6	18,7	1	4,5	7	13
Polyp		5	15,6	3	13,6	8	14,8
Mastopathy		7	21,9	5	22,7	13	24,1
Tubal infertility		9	28,1	–	–	9	16,7
PCOS		4	12,5	3	13,6	7	13

Table 3. *Thyroid Ultrasound Of Women With Endocrine Infertility In Hypothyroidism*

Ultrasound of the thyroid	1st group (n=32)		2nd group (n=22)		Total (n=54)	
	abs	%	abs	%	abs	%
Nodular goiter	5	15,6	4	18,2	9	16,7
Hypoplasia of the thyroid gland	4	12,5	3	13,6	7	13
TAI	16	50	9	41	25	46,3
Diffuse goiter	13	40,6	8	36,4	21	38,9

Table 4. *Ultrasound of Uterus and Appendages of Women With Endocrine Infertility in Hypothyroidism*

Ultrasound of the uterus and ovaries		1st group (n=32)		2nd group (n=22)		Total (n=54)	
		abs	%	%	abs	%	abs
Multifollicular ovaries		6	18,7	5	22,7	11	20,4
DOR		9	28,1	2	9,1	11	20,4
Ovulatory dysfunction		17	53,1	7	31,8	24	44,4
Endometriosis		5	15,6	1	4,5	6	11,1
Myoma		7	21,8	3	13,6	10	18,5
Polyp		5	15,6	3	13,6	8	14,8
AFC	**Up to 4**	20	62,5	2	9,1	22	40,7
	More than 4	12	37,5	20	90,9	32	59,3

Ultrasound was performed to detect uterine and appendage pathology (Table 4), where anovulatory cycle was observed in 17 (54.8%) women of group 1 and 7 (31.8%) of group 2. Diminished ovarian reserve (DOR) was found in 9 (29%) of group 1 and 2 (9.1%) patients of group 2. Diminished antral follicles count (AFC) was observed in 40.7% of cases, which is one of the indicators of reduced ovarian reserve.

To make a final diagnosis, the hormonal profile of the women was studied, which showed the following results (Table 5). In the women of the first group TTG was higher than normal and the hypothyroid state lasted longer, due to this there was an increase in the level of PRL in the blood. The increase in LH and FSH in the same group indicates more pronounced menstrual disorders and an increase in anovulatory cycles.

Table 5. *Hormonal Profile of women with Endocrine Infertility in Hypothyroidism*

	1st group (n=32)	2nd group (n=22)	P
TSH (mIU/ml)	8,91±3,1	7,54±2,9	0.1
T4 (pmol/l)	10,8±0,8*	11,5±1,1	0.015
TPOAb (IU/L)	60,3±8,9**	54,1±6,2	0.004
PRL (ng/ml)	40,9±25,4*	30,7±9,3	0.04
FSH (mIU/ml)	14,9±6,98***	3,86±0,8	0.001
LH (mIU/ml)	14,4±5,8**	4,1±0,6	0.001
Progesterone (ng/ml)	2,45±2,3**	8,6±2,2	0.006
17-OX (nmol/l)	2,23±0,6	6,55±4,06	0.3
Testosterone (nmol/l)	0,84±0,23	0,96±0,59	0.1
AMH (ng/ml)	1,05±0,69***	3,2±0,48	0.001
Insulin (mIU/ml)	11,1±1,64	13,4±2,5	0.6

*Note: *– $p < 0.05$, ** – $p < 0.01$, ***– $p < 0.001$ statistically significant differences compared to the second group*

In preparation for conception, the hormonal background of the thyroid was corrected according to the recommendations of the European Thyroid Association Guideline 2021. After treatment in accordance with the diagnosis, 22 women conceived naturally and the rest by IVF. Positive result from the first IVF attempt was in 17 (53.1%), from the second and/or third in 13 (40.6%) and from the fourth and more – in 2 (6.3%) patients from the first group.

Discussion & Analysis

In the second group (natural conception), T4 levels were significantly higher than in the IVF group ($p < 0.05$). This supports existing data indicating that optimal thyroid hormone levels are essential for normal follicular growth and ovulation. Accordingly, low T4 levels in the IVF group may indicate impaired thyroid function, which can contribute to infertility.

Significantly higher levels of thyroid peroxidase antibodies (TPOAb) in the IVF group further confirm the link between autoimmune thyroid disorders and fertility issues ($p < 0.05$). Studies have shown that autoimmune thyroiditis increases the risk of implantation failure and miscarriage.

The elevated prolactin (PRL) levels observed in the IVF group may suggest hyperprolactinemia, which can disrupt gonadotropin secretion and inhibit ovulation ($p < 0.05$). Hyperprolactinemia is commonly seen in patients with hypothyroidism due to feedback mechanisms affecting dopamine regulation.

The most significant difference was observed in follicle-stimulating hormone (FSH) levels ($p < 0.001$). Substantially higher FSH levels in the IVF group indicate diminished ovarian reserve (DOR). Elevated FSH is a marker of ovarian aging and is associated with poor response to stimulation in assisted reproductive technologies.

Additionally, LH levels were significantly higher in the IVF group, which may indicate disrupted ovulatory processes and hormonal instability ($p < 0.001$).

A significantly lower level of AMH ($p < <0.001$) was observed in women who underwent IVF, confirming the presence of diminished ovarian reserve (DOR) in this group.

While this study provides valuable insights, certain limitations must be acknowledged: the sample size was relatively small, which may limit the generalizability of findings. The observational nature of the study does not establish a direct causal relationship between thyroid dysfunction and infertility outcomes. Further research should focus on longitudinal studies assessing the impact of thyroid hormone optimization on IVF success rates.

Conclusion

The analysis of studies has shown that the change of endocrine status of women with thyroid hypofunction is unfavourably reflected on menstrual cycle of women of fertile age manifested more often by menorrhagia and oligomenorrhoea that proves the necessity of correction of all hormones in a complex for improvement of reproductive function in women.

The study of ovarian reserve in women showed that the patients of the first group have low values of AFC and AMH in comparison with the second group, which is one of the indications for IVF.

In conditions of thyroid hormone imbalance, a change in prolactin concentration in women from the first group was revealed. As well as higher levels of FSH, LH and low levels of Progesterone in relation to the second group, which dictates the need for correction of hormonal status for the effectiveness of IVF.

References

Boivin, Jacky & Bunting, L. & Collins, J.A. & Nygren, Karl-Gösta. (2007). International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Human Reproduction. 22. 10.1093/humrep/dem299.

Cox C. M., Thoma M. E., Tchangalova N., Mburu G., Bornstein M. J., Johnson C. L., Kiarie J. Infertility prevalence and the methods of estimation from 1990 to 2021: a systematic review and meta-analysis. Hum Reprod Open 2022;4: hoac051.

ESHRE ART Fact Sheet 2018. [(accessed on 20 January 2019)]. – Text: electronic. https://www.eshre.eu/Press-Room/Resources.

Fertility problems: assessment and treatment. – London: National Institute for Health and Care Excellence (NICE); 2017 Sep. PMID: 32134604.

Infertility prevalence estimates, 1990–2021. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.

Koyyada A., Orsu P. Role of hypothyroidism and associated pathways in pregnancy and infertility: Clinical insights. Tzu Chi Med J. 2020 Apr 10; 32(4): 312–317. Doi: 10.4103/tcmj.tcmj_255_19. PMID: 33163375; PMCID: PMC7605301.

Mascarenhas M. N., Flaxman S. R., Boerma T., Vanderpoel S., Stevens G. A. (2012.) National, Regional, and Global Trends in Infertility Prevalence Since 1990: A Systematic Analysis of 277 Health Surveys. PLOS Medicine 9(12): e1001356. URL: https://doi.org/10.1371/journal.pmed.1001356

Poppe K., Velkeniers B., Glinoer D. Thyroid disease and female reproduction. Clin Endocrinol (Oxf) 2007; 66: 3: 309–321

Purity Njagi, Wim Groot, Jelena Arsenijevic, Silke Dyer, Gitau Mburu, James Kiarie, Financial costs of assisted reproductive technology for patients in low- and middle-income countries: a

Systematic review, Human Reproduction Open, – Volume 2023, – Issue 2, 2023, hoad007. URL: https://doi.org/10.1093/hropen/hoad007

Vander Borght M., Wyns C. Fertility and infertility: Definition and epidemiology. Clin Biochem. 2018 Dec; 62:2–10. Doi: 10.1016/j.clinbiochem.2018.03.012. Epub 2018 Mar 16. PMID: 29555319.

submitted 14.06.2025;
accepted for publication 30.06.2025;
published 29.09.2025

Contact: zilonovazizbek@gmail.com