УДК 618.177:616.441-002:618.11-008.64
https://doi.org/10.20538/1682-0363-2026-1-61-68

Assessment of Ovarian Function in Infertile Women with Compensated Autoimmune Thyroiditis and Premature Ovarian Insufficiency without Clinical Definitions

Dmitrieva M.L., Tikhonovskaya O.A., Petrov I.A., Logvinov S.V., Timofeeva O.S., Lasukova T.V., Akbasheva O.E., Mikheenko G.A.

Siberian State Medical University (SibSMU)
2 Moskovsky trakt, 634050 Tomsk, Russian Federation

ABSTRACT

Aim. To assess the ovarian reserve and ovarian response to controlled ovarian hyperstimulation (COS) in patients in assisted reproductive technology (ART) programs with compensated chronic autoimmune thyroiditis (CAIT) and with predicted premature ovarian insufficiency (POI).

Materials and methods. We performed a retrospective study of 166 patients with infertility and compensated CAIT (group I, $n = 44$), predicted signs of POI (group II, $n = 62$), tubal infertility factor (group III, $n = 66$), including a comparative analysis of clinical and patient history data, indicators of ovarian reserve, and the effectiveness of COS (number of oocytes retrieved). The groups were divided by age into subgroups: patients younger than 35 years of age and 35 years and older (Ia, Ib, IIb, IIb, IIIa, and IIIb, respectively).

Results. Significant differences in the values of follicle-stimulating hormone (FSH) anti-mullerian hormone (AMH) were revealed in the study groups under 35 years of age: FSH (7.24 (6.0–9.63) mIU/l and 10.35 (10.13–11.01) mIU/L, respectively; $p < 0.001$) and AMH (3,2 (1.48–6.80) ng/ml and 0.68 (0.44–2.91 ng/ml), respectively; $p = 0.015$). The poor ovarian response in COS programs is most often obtained in patients under of 35 years of age with infertility with occult POI. In the age groups 35 years and older, the poor ovarian response to COS was equally common in groups I and II. Estradiol levels in the groups of 35 years of age and older were lower in patients with occult POI.

Conclusion. In groups of patients under 35 years of age with compensated CAIT and with tubal infertility factor, higher rates of ovarian reserve and the effectiveness of COS were recorded than in the groups with occult POI. A decrease in estradiol in patients aged 35 years and older with occult POI and older indirectly indicates a lesion of the ovarian somatic cells, probably as a result of autoimmune aggression.

Keywords: chronic autoimmune thyroiditis, autoimmune oophoritis, premature ovarian insufficiency, "poor ovarian response", assisted reproductive technologies, ovarian reserve

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

Source of financing. The project was supported by the SibSMU Competition Commission (Minutes dated June 27, 2022) in accordance with Regulation No. 51 dated May 16, 2022 “On Support of Research Projects carried out by Young Scientists SibMed.Scholar”.

For citation: Dmitrieva M.L., Tikhonovskaya O.A., Petrov I.A., Logvinov S.V., Timofeeva O.S., Lasukova T.V., Akbasheva O.E., Mikheenko G.A. Assessment of Ovarian Function in Infertile Women with Compensated Autoimmune Thyroiditis and Premature Ovarian Insufficiency without Clinical Definitions. *Bulletin of Siberian Medicine.* 2026;26(1):61–68. https://doi.org/10.20538/1682-0363-2026-1-61-68.

✉ *Dmitrieva Margarita L.,* dmitrieva.ml@ssmu.ru

Оценка функции яичников у женщин с бесплодием при компенсированном аутоиммунном тиреоидите и преждевременной недостаточности яичников без клинических дефиниций

Дмитриева М.Л., Тихоновская О.А., Петров И.А., Логвинов С.В., Тимофеева О.С., Ласукова Т.В., Акбашева О.Е., Михеенко Г.А.

Сибирский государственный медицинский университет (СибГМУ), Россия, 634050, г. Томск, ул. Московский тракт, 2

РЕЗЮМЕ

Цель. Оценка овариального резерва и ответа яичников на контролируемую индукцию суперовуляции (КИСО) у пациентов в программах вспомогательных репродуктивных технологий (ВРТ) с компенсированным хроническим аутоиммунным тиреоидитом (ХАИТ) и при прогнозируемой преждевременной недостаточности яичников (ПНЯ).

Материалы и методы. Ретроспективное исследование 166 пациентов с бесплодием и компенсированным ХАИТ (группа I, n = 44), «оккультной» формой ПНЯ (группа II, n = 62), трубным фактором бесплодия (группа III, n = 66), включающее сравнительный анализ клинико-анамнестических данных, показателей овариального резерва, результативности КИСО (количество полученных ооцитов). Группы разделены по возрасту на подгруппы: до 35 лет и 35 лет и старше (Ia, Ib, IIb, IIb, IIIa, IIIb соответственно).

Результаты. Выявлены достоверные отличия в значениях фолликулостимулирующего (ФСГ) и антимюллерового (АМГ) гормонов в группах исследования до 35 лет: ФСГ (7,24 (6,0–9,63) мМЕ/л и 10,35 (10,13–11,01) мМЕ/л соответственно; p < 0,001) и АМГ (3,2 (1,48–6,80) нг/мл и 0,68 (0,44–2,91 нг/мл) соответственно; p = 0,015). «Бедный ответ» в программах КИСО наиболее часто получен у пациенток до 35 лет при бесплодии с «оккультной» формой ПНЯ. В возрастных группах 35 лет и старше «бедный ответ» КИСО встречался одинаково часто в I и II группах. Эстрадиол у пациентов 35 лет и старше был ниже у пациентов с формирующимся ПНЯ.

Заключение. В группах пациентов до 35 лет с компенсированным ХАИТ и с трубным фактором бесплодия зафиксированы более высокие показатели овариального резерва и эффективность КИСО, чем в группе женщин с «оккультной» формой ПНЯ. Снижение эстрадиола у пациентов 35 лет с «оккультной» формой ПНЯ и старше косвенно свидетельствует о поражении овосоматического гистиона, вероятно, в результате аутоиммунной агрессии.

Ключевые слова: хронический аутоиммунный тиреоидит, аутоиммунный оофорит, преждевременная недостаточность яичников, «бедный ответ» яичников, вспомогательные репродуктивные технологии, овариальный резерв

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источники финансирования. Проект поддержан конкурсной комиссией СибГМУ (протокол заседания от 27.06.2022) в соответствии с положением от 16.05.2022 № 51 «О поддержке научно-исследовательских проектов, выполняемых молодыми учеными SibMed.Scholar».

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследование одобрено локальным этическим комитетом СибГМУ (протокол № 9308 от 15.12.2022).

Для цитирования: Дмитриева М.Л., Тихоновская О.А., Петров И.А., Логвинов С.В., Тимофеева О.С., Ласукова Т.В., Акбашева О.Е., Михеенко Г.А. Оценка функции яичников у женщин с бесплодием при компенсированном аутоиммунном тиреоидите и преждевременной недостаточности яичников без клинических дефиниций. *Бюллетень сибирской медицины.* 2026;26(1):61–68. https://doi.org/10.20538/1682-0363-2026-1-61-68.

INTRODUCTION

The outcome of the autoimmune inflammatory process in the gonads is endocrine and reproductive dysfunction of the ovarian follicles and premature ovarian insufficiency (POI), which leads to infertility and complications associated with hormone deficiency. Autoimmune POI in the population is much more common in women with other autoimmune diseases [1], including autoimmune thyroid diseases (14–32.7%) [2–4].

Chronic autoimmune thyroiditis (CAIT) is the most common cause of thyroid dysfunction in women of reproductive age [5]. It is known that thyroid dysfunction can exacerbate a decrease in ovarian reserve [3], which reduces the effectiveness of assisted reproductive technology (ART) programs. Y.T. Hsieh and J.Y.T.Ho published data on a high risk of POI development in patients with autoimmune thyroiditis [6]. A condition for overcoming infertility is a hormone-compensated CAIT. Euthyroidism in the absence of other detectable causes of infertility is not a guarantee of successful controlled ovarian hyperstimulation (COH) in ART programs. Since 2006–2008, Nelson and Welt have proposed to use the term occult (i.e. latent) form without clinical definitions. Currently, signs of early onset of POI without typical clinical manifestations have not been established. The problems of idiopathic infertility and poor ovarian response to COH remain very relevant in reproductive medicine, in which autoimmune gonadal damage is possible.

The aim of the study was to assess ovarian reserve and ovarian response to COH in patients in assisted reproductive technology (ART) programs with compensated CAIT and with occult POI.

MATERIALS AND METHODS

The present work is a retrospective study. The medical records of patients with infertility who were treated at the ART center of Siberian State Medical University from 2017 to 2022 were studied. The research work was approved by the local Ethics Committee of Siberian State Medical University (Minutes No. 9308 dated December 15, 2022).

The study included 166 patients. Main group I consisted of patients aged 18–40 years with infertility with a history of CAIT compensated with hormone therapy (n = 44), who were divided into 2 age-adjusted subgroups: IA – patients under 35 years of age (n = 22), IB – patients 35 years of age and older (n = 44). Main group II consisted of patients with infertility, in whom hormonal examination revealed signs of occult POI (concentration of follicle-stimulating hormone (FSH) in blood serum was 10–12 mIU/l) without established thyroid pathology (n = 62) (IIA is a subgroup of patients under aged 35 years (n = 28), IIB is a subgroup of patients 35 years of age and older (n = 34)) [6]. The comparison group consisted of patients with tubal infertility (bilateral salpingectomy) (n = 60) (IIIA is a subgroup of patients younger than 35 years of age (n = 33), IIIB is a subgroup of patients aged 35 years and older (n = 27)). The division by age was performed to make the study groups uniform, taking into account the age-related features of the hormonal functioning of the ovaries, which are described in the POSEIDON stratification [7].

Inclusion criteria for the study were as follows: 1) age from 18 to 40 years; 2) tubal factor infertility. Exclusion criteria were: 1) non-compliance with the inclusion criteria; 2) CAIT without hormonal compensation; 3) uterine factor infertility; 4) history of ovarian surgery; 5) endocrine diseases (hyperprolactinemia, diabetes mellitus, and obesity of any degree); 6) gynecological diseases requiring surgical treatment; 7) endometriosis of any localization; 8) precancerous and malignant diseases; 9) any extragenital pathology associated with immune and endocrine manifestations; 10) the presence of contraindications for treatment as part of *in vitro* fertilization (IVF) (Order of the Ministry of Health of the Russian Federation dated July 31, 2020 No. 803n “On the Procedure for the Use of Assisted Reproductive Technologies, Contraindications and Restrictions to Their Use”). According to the patient management protocols, superovulation was stimulated in a fixed gonadotropin-releasing hormone antagonist protocol (recombinant and menopausal gonadotropins).

Statistical processing was performed using the computer program SPSS® 26.0. The normality of the data distribution in each of the groups was checked using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Quantitative data that did not obey the law of normal distribution were presented as the median and the interquartile range Me (Q_1–Q_3). The significance of the differences was calculated using a nonparametric method for three or more independent groups using the Kruskal–Wallis test (H-test), and post hoc comparison was performed using the Mann–Whitney test. To solve the problem of multiple comparisons, the Bonferroni correction was applied, the significance level was set according to the formula $p = 1–0.95^{1/n}$», where n is the number of comparisons. Qualitative variables were analyzed using Pearson's chi-squared test, and the results were described using the criterion value, significance level, relative risk (RR), and confidence interval (CI).

RESULTS

The clinical and patient history characteristics of the analyzed parameters of patients with infertility of the main groups and the comparison group are presented in Table 1. In statistical calculations, the body mass index (BMI) and age of menarche did not differ between the groups (Table 1). The average age of women in the main group I was 34.5 (30.0–38.0) years, in the main group II–36.0 (33.0–38,0) years old, and in the comparison group – 33.5 (29.0–36.0) years. When patients were divided into subgroups, their age distribution remained uniform across all subgroups..

The duration of infertility was longer in main group II than in the comparison group (p = 0.011). The number of IVF attempts in the history of women in main group I and main group II was higher than in the comparison group.

Table 1

Comparative Analysis of Clinical and Patient History Data of the Main Groups and Comparison Group, *Me* (Q_1–Q_3), Mann–Whitney Test

Parameters	Main group I	p, main group I and comparison group	Main group II	p, main group II and comparison group	Comparison group	p, main group I and comparison group
Age, years	34.5 (30.0–38.0)	0.774	36.0 (33.0–38.0)	0.024	33.5 (29.0–36.0)	0.827
BMI	21.60 (20.06–25.96)	0.589	23.10 (20.08–25.65)	0.402	23.70 (20.28–27.30)	0.286
Age at menarche, years	13.0 (13.0–14.0)	0.776	14.0 (12.0–14.0)	0.294	13.0 (12.0–14.0)	0.477
Duration of infertility, years	4.5 (2.0–9.3)	0.118	8.0 (2.0–13.0)	0.011	4.0 (2.0–7.0)	0.510
IVF in the anamnesis	1.0 (1.0–1.25)	0.052	2.0 (1.0–3.0)	<0.001	0	<0.001

Note. BMI is body mass index; IVF is *in vitro* fertilization.

The analysis revealed the following infertility profile: 9.6% of patients (16 out of 166) with combined infertility (male factor) and 7.2% of patients (12 out of 166) with combined infertility (anovulation). Primary and secondary infertility was recorded in 45.8% of patients (76 out of 166) and 54.2% of patients (90 out of 166), respectively. In the statistical analysis, the main groups and the comparison group were uniform according to the above criteria.

We compared the average concentrations of FSH, estradiol, anti-Müllerian hormone (AMH), the antral follicles count (AFC), as well as the number of oocytes obtained to calculate the poor ovarian response. The results are presented in Tables 2 and 3.

Table 2

Hormonal and Ultrasound Status of Women in the Main Groups and Comparison Group, the Number of Oocytes Obtained after Ovarian Puncture in the ART Program, *Me* (Q_1–Q_3)

Parameters	Main group I		Main group II		Comparison group	
	IA	IB	IIA	IIB	IIIA	IIIB
FSH, mME/ml	7.24 (6.0–9.63)	8.28 (6.7–15.7)	10.35 (10.13–11.01)	11.1 (10.29–11.63)	8.1 (5.49–11.15	7.57 (3.93–12.6)
Estradiol, pmol/l	108.0 (50.0–190.0)	118.5 (68.25–234.4)	132.5 (89.51–195.09)	119.0 (65.78–218.89)	140 (85.0–200,0)	215.0 (138.0–275.0)
AMH, ng/ml	3.2 (1.48–6.80)	1.19 (0.72–2.23)	0.68 (0.44–2.91)	1.14 (0.65–1.84)	4.07 (1.56–5.10)	2.41 (0.83–3.91)
AFC	14.0 (11.0–17.0)	9.0 (5.0–14.0)	9.0 (4.5–13.5)	6.0 (5.0–16.0)	11.0 (9.0–17.5)	9.0 (6.0–15.0)
Oocytes	10.0 (4.0–15.0)	4.0 (2.0–8.0)	1.0 (2.5–10.0)	3.0 (2.0–5.0)	5.0 (4.5–9.0)	5.0 (4.0–8.0)

Note. Here and in Table 3: FSH – follicle-stimulating hormone, AMH – anti-Müllerian hormone, AFC – antral follicle count.

Table 3

Post Hoc Comparisons of Hormonal and Ultrasound Status of Patients in the Main Groups and Comparison Group, the Number of Oocytes Obtained after Ovarian Puncture in the ART Program Using the Mann–Whitney Test

	FSH, mME/ml	Estradiol, pmol/l	AMH, ng/ml	AFC	Oocytes
p, IA and IB	0.243	0.654	0.023	0.193	0.116
p, IIA and IIB	0.118	0.728	0.544	0.934	1.0
p, IIIA and IIIB	0.672	0.009	0.025	0.248	0.231
p, IA and IIA	<0.001	0.501	0.015	0.072	0.044
p, IA and IIIA	0.380	0.641	0.946	0.063	0.450
p, IB and IIB	0.091	1.0	0.711	0.926	0.329
p, IIA and IIIA	0.010	0.968	0.002	0.056	0.137
p, IB and IIIB	0.293	0.068	0.123	0.465	0.546
p, IIB and IIIB	0.099	0.025	0.014	0.270	0.031

The concentration of FSH in patients of the IA subgroup was within the limits of the reference laboratory values for the follicular phase in women of reproductive age. This indicator was significantly higher in patients of subgroup IIA ($p < 0.001$) (Tables 2, 3). Also, in patients of the IIA subgroup with occult POI, it was significantly higher than in the comparison group of IIIA patients with tubal factor infertility ($p = 0.010$). There were no statistically significant differences in FSH in patients aged 35 and older in the main groups and the comparison group (Table 3).

The concentration of estradiol was comparable between the subgroups of main group 1 with CAIT and main group 2 with occult POI. In the comparison group, significant differences were found between the subgroups in patients after salpingectomy, estradiol prevailed in patients aged 35 years and older ($p = 0.009$). It was noted that the level of estradiol in group IIB with an occult POI tended to decrease compared to group IIIB with tubal infertility factor ($p = 0.024$) (Tables 2, 3).

The median AMH of the IB subgroup was lower than in the IA subgroup, probably due to age characteristics ($p = 0.023$) (Table 2). In the main group of patients with occult POI, this indicator had equally low values both in patients under the age of 35 and in those aged 35 years and older, which indicates a small ovarian reserve. The level of AMH in patients under 35 in the comparison group with occult POI (subgroup IIA) was significantly lower than that in patients in the main group with compensated hypertension (subgroup IA) ($p = 0.015$), whereas in patients aged 35 and older with compensated CAIT (subgroup IB) and with occult POI (subgroup IIB), there were no significant differences ($p = 0.711$). It was noted that in patients under 35 and those aged 35 years and older, the level of AMH in the main group with an occult POI was significantly lower than in the comparison group with tubal infertility factor.

Thus, the greatest decrease in the level of AMH was determined in the main group of patients with occult POI. Post hoc comparisons for AFC are provided for review, as the Kruskal–Wallis test showed insignificant results (Table 3). However, the highest value of AFC was noted in patients under 35 years of age in the main group with compensated CAIT.

The analysis of the effectiveness of COH in the main group with CAIT between the subgroups did not reveal statistically significant differences in the number of oocytes obtained, as well as between the subgroups in the main group with the occult POI and the comparison group (Tables 2, 3). In the main group with CAIT, the number of oocytes obtained tended to increase compared with the main group with occult POI ($p = 0.044$). In addition, there was a trend towards a decrease in the number of oocytes obtained in patients aged 35 and older in the main group with an occult POI, in contrast to the comparison group with tubal factor infertility ($p = 0.031$).

The proportion of poor ovarian response, as measured by the number of oocytes obtained after puncture in the main group with CAIT was 32% (14 out of 44), in the main group with occult POI – 58% (36 out of 62), in the comparison group with tubal factor infertility – only 10% (6 out of 60).

The proportion of poor ovarian response in women under 35 years of age in the main group (IA subgroup) was 18.2% (4 out of 22), in the comparison group with occult POI (IIA subgroup) – 57% (16 out of 28), (3.896, $p = 0.048$ with the main group; RR = 0.32, 95% CI: 0.12–0.82) and in the comparison group with tubal factor infertility (IIIA subgroup) – 6% (2 out of 33) (1.995, $p = 0.158$

with the main group; RR = 3.0 95% CI: 0.6–15.0). In patients aged 35 and older, the proportion of poor ovarian response in the main group (IB subgroup) was 46% (10 out of 22), in the comparison group with occult POI (IIB subgroup) – 59% (20 out of 34) (0.480, p = 0.700 with the main group; RR = 0.773, 95% CI: 0.45–1.32), and in the comparison group with tubal factor infertility (IIIB subgroup) – 15% (4 out of 27) (5.576, p = 0.018 with the main group; RR = 3.07 95% CI: 1.11–8.46). Thus, our data indicate a decrease in the effectiveness of superovulation stimulation in patients under 35 years with occult POI, whereas the most effective COH was in the comparison group with tubal factor infertility.

DISCUSSION

The question of the effect of CAIT on the ovarian reserve and reproductive function remains open. The relationship between thyroid and ovarian function is complex and interrelated [8]. Thyroid hormones are involved in the functioning of granulosa cells and the growth of follicles. With inflammatory changes in the thyroid gland of a low degree of activity, as in CAIT, the microenvironment of the ovarian somatic cells is disrupted, which leads to a decrease in ovarian function. Unambiguous studies indicating a close relationship between CAIT and ovarian insufficiency have not been published, however, there is evidence indicating lower AMH values in subclinical hypothyroidism and CAIT [9] and a decrease in ovarian reserve in CAIT [10–13].

A limitation in the work is the fact that the ART program does not include patients without thyroid function compensation. Thus, the main group consisted of patients receiving hormone replacement therapy and having an euthyroid condition at the time of the COH. Not all patients had medical history data on the duration of CAIT and hormone therapy, which did not allow us to assess the duration of the inflammatory process in the thyroid gland. However, compensation of thyroid function does not affect the activity of the autoimmune process.

The results of a comparative analysis of ovarian reserve and ovarian response to COH are of interest in groups of patients under 35 years of age. The ovarian reserve in the main group of patients with compensated CAIT was higher than in the main group with occult POI and did not differ from that in the comparison group with tubal factor infertility. The ovarian response to COH was lower in the main group with occult POI compared to the main group with compensated CAIT and the comparison group with tubal infertility.

Thus, the most significant indicator for predicting the ovarian response to stimulation according to the results of this study is not the presence of antibodies to thyroid tissue, but transitional FSH values (10–12 mIU/ml). It can be assumed that under the age of 35, the compensation of CAIT and the short-term effect of the autoimmune process of low activity do not achieve a significant effect on ovarian function.

It was found that the presence of CAIT compensated by hormonal therapy or occult POI in patients aged 35 years and older was not associated with diminished ovarian reserve. The decrease in ovarian reserve at the age of 35 years and older is due to the age-related features of folliculogenesis. Also, in the group of patients aged 35 years and older, no significant differences were found in the indicators of ovarian reserve in the main group with CAIT and the comparison group with tubal factor infertility. The most interesting fact was the differences in hormonal profile indicators in patients of main group II and the comparison group aged 35 years and older. The levels of estradiol and AMH were significantly higher in the comparison group with tubal factor infertility. At the same time, the number of oocytes obtained was smaller in patients with occult POI (main group I). Thus, in patients with occult POI aged 35 years and older with FSH levels of 10–12 mIU/l, the ovarian response to stimulation was diminished due to a decrease in ovarian reserve, which was indirectly confirmed by a decrease in estradiol levels compared to the group of patients after salpingectomy. The median estradiol index in the main group with CAIT is comparable to that in the main group in patients with occult POI. Estradiol is not a reliable marker of the assessment of ovarian reserve; however, its relative decrease may be an early marker of impaired functioning of ovarian somatic cells in autoimmune ovarian damage.

According to the two-cell theory of ovarian steroidogenesis, the synthesis of androgens and estrogens is compartmentalized. It is known that in autoimmune oophoritis, the aggression of immunocompetent cells in the early stages is aimed at damaging the theca cells. So, subsequently, the destruction of the internal theca leads to a decrease in the synthesis of estradiol in granulosa cells. According to the data of this study, the trend towards a decrease in the level of estradiol in main group I aged 35 years and older may be a consequence of the described pathogenetic mechanism, while an increase in FSH concentration is secondary. Further prospective clinical studies are needed to confirm the data.

The results of this study are the closest to the results of a single-center cross-sectional study conducted in 2024 by M. Pan et al. (China), which studied the association of thyroid peroxidase autoantibodies and antithyroglobulin autoantibodies with infertility and AMH levels. Thus, the authors identified the association of a high titer of thyroid peroxidase autoantibodies with anovulatory infertility, but did not establish a significant correlation with the level of AMH. On the contrary, a high titer of antithyroglobulin autoantibodies was not associated with anovulatory infertility and with the level of AMH [14].

Analyzing the results of this study and the existing understanding of ovarian function in women with CAIT, it can be concluded that compromised ovarian function of unclear etiology with FSH values above the reference reduces the results of COH. It is of interest to study markers of autoimmune oophoritis in patients with occult POI, since the preservation of estradiol synthesis in women under 35 and a decrease in estradiol levels in women aged 35 years and older may be the basis for the hypothesis of gradual destruction of follicles as a result of partial damage to the internal theca, as is possible with autoimmune oophoritis. It is possible to confirm the hypothesis in a prospective clinical trial with the study of markers of autoimmune oophoritis both in blood serum and in histological examination of ovarian biopsies as a more reliable diagnostic method.

CONCLUSION

In the group of patients under 35 years of age with compensated CAIT and with tubal factor infertility, higher rates of ovarian reserve and the effectiveness of COH were recorded than in the group of women with occult POI. In patients aged 35 years and older with compensated CAIT and occult POI, in the absence of significant differences in FSH, there was a downward trend in the concentration of estradiol, which may indicate damage to ovarian somatic cells, probably as a result of autoimmune aggression. The data obtained will have an applied value in reproductology, but require further research.

REFERENCES

1. Hoek A., van Kasteren Y., de Haan-Meulman M., Hooijkaas H., Schoemaker J., Drexhage H.A. Analysis of peripheral blood lymphocyte subsets, NK cells, and delayed type hypersensitivity skin test in patients with premature ovarian failure. *Am. J. Reprod. Immunol.* 1995;33(6):495–502. DOI: 10.1111/j.1600-0897.1995.tb00912.x.
2. Grossmann B., Saur S., Rall K., Pecher A.C., Hübner S., Henes J. et al. Prevalence of autoimmune disease in women with premature ovarian failure. *Eur. J. Contracept Reprod. Health Care.* 2020;25(1):72–75. DOI: 10.1080/13625187.2019.1702638.
3. Osuka S., Iwase A., Goto M., Takikawa S., Nakamura T., Murase T. et al. Thyroid Autoantibodies do not Impair the Ovarian Reserve in Euthyroid Infertile Women: A Cross-Sectional Study. *Horm. Metab. Res.* 2018;50(7):537–542. DOI: 10.1055/a-0637-9430.
4. Domniz N., Meirow D. Premature ovarian insufficiency and autoimmune diseases. *Best Pract. Res. Clin. Obstet. Gynaecol.* 2019;60:42–55. DOI: 10.1016/j.bpobgyn.2019.07.008.
5. Vissenberg R., Manders V.D., Mastenbroek S., Fliers E., Afink G.B., Ris-Stalpers C. et al. Pathophysiological aspects of thyroid hormone disorders/thyroid peroxidase autoantibodies and reproduction. *Hum. Reprod. Update.* 2015;21(3):378–387. DOI: 10.1093/humupd/dmv004.
6. Hsieh Y.T., Ho J.Y.P. Thyroid autoimmunity is associated with higher risk of premature ovarian insufficiency-a nationwide Health Insurance Research Database study. *Hum. Reprod.* 2021;36(6):1621–1629. DOI: 10.1093/humrep/deab025.
7. Alviggi C., Andersen C.Y., Buehler K., Conforti A., De Placido G., Esteves S.C. et al. A new more detailed stratification of low responders to ovarian stimulation: from a poor ovarian response to a low prognosis concept. *Fertil. Steril.* 2016;105(6):1452–1453. DOI: 10.1016/j.fertnstert.2016.02.005.
8. Popa E.C., Maghiar L., Maghiar T.A., Brihan I., Georgescu L.M., Toderaș B.A. et al. Hashimoto's Thyroiditis and Female Fertility: Endocrine, Immune, and Microbiota Perspectives in Assisted Reproduction-A Narrative Review. *Biomedicines.* 2025;13(6):1495. DOI: 10.3390/biomedicines13061495.
9. Shi C.-J., Shao T.-R., Zhao X., Wang B. Evaluation of the Ovarian Reserve in Women and Adolescent Girls with Hashimoto's Thyroiditis by Serum Anti-Müllerian Hormone Level: A Systematic Review and Meta-Analysis. *Heliyon.* 2023;9:e19204. DOI: 10.1016/j.heliyon.2023.e19204.
10. Safarian G.K., Niauri D.A., Kogan I.Y., Bespalova O.N., Dzhemlikhanova L.K., Lesik E.A. et al. Impact of antithyroperoxidase antibodies (Anti-TPO) on ovarian reserve and early embryo development in assisted reproductive technology cycles. *Int. J. Mol. Sci*. 2023;24(5):4705. DOI: 10.3390/ijms24054705.
11. Samsami A., Ghasmpour L., Moradi Alamdarloo S., Davoodi S., Rahmati J., Karimian A. et al. Women with Autoimmune Thyroiditis have Lower Reproductive Life Span or Not? A Cross- Sectional Study. *Int. J. Community Based Nurs Midwifery.* 2020;8(4):305–310. DOI: 10.30476/ijcbnm.2020.84255.1207.
12. Huang N., Chen L., Lian Y., Wang H., Li R., Qiao J. et al. Impact of thyroid autoimmunity on *in vitro* fertilization/intracytoplasmic sperm injection outcomes and fetal weight. *Front. Endocrinol. (Lausanne).* 2021;12:698579. DOI: 10.3389/fendo.2021.698579.
13. Li N., Lu Y., Si P., Li Z., Qin Y., Jiao X. The impact of moderately high preconception thyrotropin levels on ovarian re-

serve among euthyroid infertile women undergoing assisted reproductive technology. *Thyroid.* 2022;32(7):841–848. DOI: 10.1089/thy.2021.0534.
14. Pan M., Qi Q., Li C., Wang J., Pan X., Zhou J. et al. Effect and mechanism of Hashimoto thyroiditis on female infertility: A clinical trial, bioinformatics analysis, and experiments-based study. *Biosci. Trends.* 2024;18(4):356–369. DOI: 10.5582/bst.2024.01120.

Author Contribution

Dmitrieva M.L., Tikhonovskaya O.A., and Petrov I.A. – conception and design. Dmitrieva M.L., Petrov I.A., Timofeeva O.S., Lasukova T.V., Akbasheva O.E., and Mikheenko G.A. – analysis and interpretation of data. Dmitrieva M.L., Tikhonovskaya O.A., Petrov I.A., and Logvinov S.V. – justification of the manuscript. Tikhonovskaya O.A. and Logvinov S.V. – final approval of the manuscript for publication.

Author Information

Dmitrieva Margarita L. – Cand. Sci. (Med.), Associate Professor, Associate Professor of the Obstetrics and Gynecology Division, Siberian State Medical University, Tomsk, dmitrieva.ml@ssmu.ru; https://orcid.org/0000-0002-2958-9424

Tikhonovskaya Olga A. – Dr. Sci. (Med.), Professor, Professor of the Obstetrics and Gynecology Division, Siberian State Medical University, Tomsk, tikhonovskaya2012@mail.ru; https://orcid.org/0000-0003-4309-5831

Petrov Ilya A. – Dr. Sci. (Med.), Head of the Center for Assisted Reproductive Technologies, Professor of the Obstetrics and Gynecology Division, Siberian State Medical University, Tomsk, obgynsib@gmail.com; https://orcid.org/0000-0002-0697-3896

Logvinov Sergey V. – Dr. Sci. (Med.), Professor, Head of the Histology, Embryology and Cytology Division, Siberian State Medical University, Tomsk, s_logvinov@mail.ru; https://orcid.org/0000-0002-9876-6957

Timofeeva Oksana S. – Obstetrician-Gynecologist, the Center for Assisted Reproductive Technologies; Assistant,Obstetrics and Gynecology Division, Siberian State Medical University; Tomsk, oksi91@bk.ru, https://orcid.org/0000-0002-5768-4031

Lasukova Tatyana V. – Dr. Sci. (Biol.), Professor, Professor of the Normal Physiology Division, Siberian State Medical University, Tomsk, tlasukova@mail.ru, https://orcid.org/0000-0003-3274-6010

Akbasheva Olga E. – Dr. Sci. (Med.), Associate Professor, Professor of the Division of Biochemistry and Molecular Biology with Clinical Laboratory Diagnostics Course, Siberian State Medical University, Tomsk, akbasheva.oe@ssmu.ru, https://orcid.org/0000-0003-0680-8249

Mikheenko Galina A. – Dr. Sci. (Med.), Associate Professor, Professor of the Obstetrics and Gynecology Division, Siberian State Medical University, Toms, miheenko.ga@ssmu.ru, https://orcid.org/0000-0002-3869-1906

(🖂) **Dmitrieva Margarita L.,** dmitrieva.ml@ssmu.ru

Received on August 27, 2025;
approved after peer review on September 23, 2025;
accepted on October 16, 2025