

# AUTOIMMUNE THYROIDITIS AND ASSISTED REPRODUCTIVE TECHNOLOGIES: MODERN CONTROVERSIES

## LITERATURE REVIEW

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## INTRODUCTION

Thyroid autoimmunity (TAI) is a persistent inflammatory disorder of the thyroid, recognized by medical science for over a century. Despite decades of research, the exact etiopathogenesis of TAI remains unclear. The hypothyroid form of TAI is known to adversely affect reproductive potential in females [1–4]. Even in its mild or silent forms, TAI frequently escapes detection, which may lead to immune dysfunction and impaired tolerance mechanisms within both the reproductive tract and the broader immune system [5, 6].

Before the end of puberty, the female endocrine, immune, and reproductive systems become closely interconnected, a relationship that, in the presence of TAI, leads to considerable clinical challenges [7]. Given the rate of TAI in women experiencing infertility and its association with impaired reproductive potential, it is crucial to explore how TAI affects the outcomes of assisted reproductive technologies (ART). These connected processes support the need for regular TAI screening in women with infertility, due to its influence on therapeutic decisions, reproductive prognosis, and overall outcomes.

This bibliographic review explores TAI, with special attention to euthyroid stage of autoimmune thyroiditis (AT), also known as Hashimoto's thyroiditis.

**Objective of the review:** to explain the theory behind the complex relationship between TAI and ART. It also aims to analyze the effectiveness and limitations of different ART techniques in women with TAI, highlighting potential blind spots with the need for further research.

## MATERIALS AND METHODS

Although this work does not represent a full systematic review, it follows several key principles of the PRISMA guidelines [8]. The following databases were searched for the last 5 years: MEDLINE (PubMed), Embase, Scopus, Lilacs, Web of Science, Clinical Trials, and SciELO. The keywords used were: thyroid autoimmunity, autoimmune thyroiditis or Hashimoto disease, female reproductive health and thyroid autoimmunity, infertility and thyroid autoimmunity, assisted reproductive technologies and thyroid autoimmunity, ovarian stimulation and thyroid

autoimmunity, pregnancy risks and thyroid autoimmunity as well as similar terms. Articles were selected based on titles and abstracts.

Inclusion criteria were as follows: 1) original research articles, reviews, and meta-analyses; 2) studies involving women of reproductive age with TAI in the context of fertility, ART, or reproductive outcomes; 3) availability of full text. No restrictions were placed on publication date or language. Articles not directly addressing the clinical or biological interaction between TAI and reproduction were excluded.

Due to the narrative nature of this review, we did not conduct formal risk of bias assessments or perform a meta-analytic synthesis. Nevertheless, methodological transparency and reproducibility were prioritized throughout the literature selection and analysis process.

## ANALYSIS OF LITERARY DATA

### *Epidemiological and reproductive impact of TAI*

AT is considered the most widespread autoimmune condition [9] and the most frequently diagnosed endocrine disorder [10]. It is also the primary global cause of hypothyroidism [11, 12], with up to 30% of individuals with TAI progressing to hypothyroid states [13].

Females are affected by this condition 4 to 10 times more frequently than males [14–16]. Among women of reproductive age, subclinical hypothyroidism has a prevalence of 4–10%, compared to 2–4% for clinical hypothyroidism [17, 18]. Approximately 8–14% of women of the same age gap test positive for thyroid peroxidase antibodies (TPOAb) [19]. This serological marker is associated with a higher likelihood of progressing to hypothyroidism compared to women without TPOAb. Moreover, recent studies groups of researchers with the participation of the author of our article indicate that TAI is present in 13–19% of women experiencing infertility [20].

Analysis of two large randomized controlled trials revealed TPOAb positivity in 8.6% of infertile women, suggesting a possible role in fertility impairment [21].

Also, unexplained subfertility, recurrent miscarriage, polycystic ovary syndrome, lower antral follicular count, reduced ovarian reserve and

embryo quality were observed with greater incidence among TPOAb-positive women [22–30]. TAI is considered an indicator of underlying immune dysregulation that may contribute to implantation failure [31]. Moreover, studies have shown that women with TAI more frequently present with antiphospholipid antibodies, which have been implicated in compromised implantation outcomes [32, 33].

These findings support the implementation of routine thyroid screening in infertile women prior to ART as a tool for diagnosis, prognosis, and improving pregnancy outcomes.

**ART outcomes in TAI-positive women**

Numerous investigations over the last several decades have examined the relationship between TAI and ART success, but their conclusions have been inconsistent.

**Controversies in the impact of TAI on ART outcomes**

The effect of TAI on ART outcomes in euthyroid women continues to be under discussion. Evidence suggests that TAI is linked to adverse pregnancy outcomes, such as a higher risk of miscarriage and preterm birth, both in spontaneous conceptions and those achieved through ART [16].

Unuane et al. [34] found that in euthyroid women undergoing intrauterine insemination treatment, the presence of TAI had no significant impact on clinical pregnancy or live birth rates. In contrast, a retrospective cohort study found a connection between TAI and poorer reproductive outcomes in women treated with intrauterine insemination for unexplained infertility [35]. However, when combined with other studies in a meta-analysis, the association was not statistically significant [35].

Table illustrates that the majority of studies found no association between TAI and adverse pregnancy outcomes [36]. In contrast, Zhong et al. [37] found that women with TAI undergoing in vitro fertilisation (IVF) had significantly reduced fertilization, implantation, and pregnancy rates (64.3%, 17.8%, and 33.3%,

respectively) compared to controls, as well as an increased miscarriage rate (26.9% vs. 11.8%).

In the latest meta-analysis (Table), studies reporting an effect on pregnancy outcomes were noted by Unuane et al. [36], who advised caution due to considerable heterogeneity. This included differences in cohort size, causes of infertility, and laboratory methods used to evaluate thyroid-stimulating hormone (TSH), free thyroxine (FT4), and TPOAb.

In addition, several studies listed in Table failed to show a clear adverse effect of TAI on ART outcomes. For instance, a retrospective analysis by Lukaszuk et al. involving 114 TAI-positive and 495 TAI-negative infertile women revealed no significant variation in key reproductive outcomes, including fertilization, implantation, pregnancy, live birth, or miscarriage rates [38]. Similarly, Sakar et al. [39] conducted a prospective study showed no difference in pregnancy or miscarriage rates between TAI-positive and TAI-negative IVF patients, though delivery rates were not assessed.

Furthermore, evidence from two meta-analyses suggests that TAI-positive women undergoing ART face an elevated risk of miscarriage [40–42]. According to the first meta-analysis, which included four prospective studies, the likelihood of miscarriage after IVF was doubled in TAI-positive women [41]. Despite the increased miscarriage risk, the absolute difference between euthyroid TAI-positive women and controls was minor, with limited influence on clinical pregnancy and delivery rates. The second meta-analysis, based on data from 12 studies, also supported the association between TAI and both a higher risk of miscarriage and decreased live birth rates. However, the presence of TAI did not seem to impact the number of retrieved oocytes, fertilization rates or overall pregnancy rates [42].

Again, in a recent study, among women with various underlying causes of infertility, the presence of TAI did not significantly impact the likelihood of achieving a live birth within a complete controlled ovarian stimulation cycle [43]. To further explore

**Table.** Main characteristics of studies on the association between TAI and IVF/ICSI outcomes (adapted from Unuane et al. [36])

Author	Year	Study design	Antibodies tested	Number TAI+	Nº TAI	Thyroid function status	Main conclusion
Poppe et al.	2003	Prospective cohort study	TPOAbs	32	202	Euthyroid	Lower LBR; increased MR
Negro et al.	2005	Prospective cohort study	TPOAbs	43	576	Euthyroid	Lower LBR; no effect on CPR
Negro et al.	2007	Retrospective cohort study	TPOAbs	42	374	Euthyroid	No effect on pregnancy outcome
Kilic et al.	2008	Prospective cohort study	TPOAbs; Tg Abs	23	31	Euthyroid	Lower CPR
Zhong et al.	2012	Retrospective cohort study	TPOAbs; Tg Abs	90	676	Not specified	Lower CPR, FR, IR and higher MR
Karacan et al.	2013	Prospective cohort study	TPOAbs; Tg Abs	34	219	Euthyroid	No effect on pregnancy outcome
Mintziori et al.	2014	Retrospective cohort study	TPOAbs; Tg Abs	15	67	Euthyroid	No effect on pregnancy outcome
Tan et al.	2014	Retrospective cohort study	TPOAbs; Tg Abs	110	725	Euthyroid	No effect on pregnancy outcome
Chai et al.	2014	Retrospective cohort study	TPOAbs; Tg Abs	89	419	Euthyroid	No effect on pregnancy outcome
Lukaszuk et al.	2015	Retrospective cohort study	TPOAbs	114	551	Euthyroid	No effect on pregnancy outcome
Litwicka et al.	2015	Prospective cohort study	TPOAbs; Tg Abs	60	134	Euthyroid	Lower LBR; increased MR
Sakar et al.	2016	Prospective cohort study	Not specified	49	202	Not specified	No effect on pregnancy outcome
Unuane et al.	2016	Retrospective cohort study	TPOAbs	333	2019	Euthyroid	No effect on pregnancy outcome
Huang et al.	2024	Retrospective cohort study	TPOAbs; Tg Abs	2603	10193	Euthyroid	No difference in LBR

Abbreviation: LBR – life birth rate; CPR – clinical pregnancy rate; OPR – ongoing pregnancy rate; MR – miscarriage rate; IR – implantation rate; NOR – number of oocytes retrieved; FR – fertilization rate, Tg Abs – thyroglobulin antibodies.

this, the researchers analyzed subgroups based on the cause of infertility and found that TAI did not significantly affect the overall live birth rate, regardless of the specific diagnosis. The types and the titers of thyroid antibodies were also taken into account. Notably, this was the first study to show that neither the type nor the concentration of thyroid antibodies made a significant difference in the cumulative live birth rate. This suggests that simply having TAI might not be a key factor affecting ART success in this case [43].

The other systematic review investigated the association between TAI and IVF/ICSI outcomes, with a particular focus on euthyroid females of known age, applying rigorous criteria for categorizing pregnancy outcomes found no effect of TAI on pregnancy outcomes in euthyroid women alone or in euthyroid women and women with subclinical hypothyroidism [44]. Similarly, Hamad et al. [45] found no significant impact of TAI on IVF outcomes in euthyroid women.

At the same time a major meta-analysis by Zhang et al. [46] indicates that in euthyroid patients, elevated levels of TPOAb (above 100 IU/mL) may negatively affect ART pregnancy outcomes such as miscarriage and delivery rates, even in the absence of overt thyroid dysfunction.

These findings suggest that antibody concentration, rather than just presence alone, may be the critical determinant of reproductive success in TAI-positive women undergoing ART [46].

### *Potential benefits of ICSI in ART*

Interestingly, the diminished effect of TAI on ART outcomes reported in more recent studies has been attributed by some authors to the increased utilization of ICSI [15, 36, 38, 47].

As initial evidence for this hypothesis, Lee et al. [48] reported the detection of antithyroid antibodies on preimplantation embryo surfaces. According to the authors, antithyroid antibodies may interfere with early developmental processes, leading to impaired implantation and diminished fertility outcomes [48]. In addition, a study by Kelkar et al. [49] showed that antibodies targeting the zona pellucida can also recognize antigens expressed in mouse thyroid tissue. This suggests that antigenic overlap between thyroid and zona pellucida tissues may cause antibodies formed in TAI to affect reproductive components like the zona pellucida [49].

Finally, the study by Monteleone et al. [50] demonstrated the presence of antithyroid antibodies in follicular fluid. Among women undergoing ART, those with TAI had lower fertilization rates and a smaller percentage of grade A embryos compared to antibody-negative counterparts. Moreover, the authors observed that all positive pregnancy tests in TAI-positive women coincided with the use of ICSI. This technique bypasses the interaction between sperm and the zona pellucida, although further investigations were needed to confirm its protective role [50].

Additionally, one recent study found that women with TAI had a higher incidence of suboptimal ovarian response to stimulation, along with reduced fertilization rates and fewer high-quality embryos. A follicular fluid anti-thyroid peroxidase antibody level of 105.0 IU/mL was identified as the threshold negatively impacting these outcomes [51].

Also, in one study the ICSI outcome data were derived from a cohort of 835 euthyroid women and the study indicates that TAI alone does not appear to affect any ICSI outcome parameters [52]. This supports the idea of ICSI as a preferable technique as the influence of TAI on the outcomes was refuted. Additionally, a recent meta-analysis focusing solely on ICSI-treated women concluded that TAI-positive women undergoing ICSI did not have a higher risk of first-trimester miscarriage compared to TAI-negative women [53]. These data also support ICSI, as it minimizes the impact of antithyroid antibodies on oocytes at the moment of fertilization. Although, the addition of another group of women with TAI who did not undergo ICSI could have made the conclusions more robust, this comparison was not included.

Continuing the analysis, another study, identified a significant gap in pregnancy rates between TAI-positive and TAI-negative groups when measured per initiated and per embryo transfer (ET) cycle [54]. Conversely, the study's oocyte count results led the authors to suggest that thyroid autoantibodies, even when detected in follicular fluid, do not influence oocyte development, maturation, or quality [55]. As a result, the authors rejected the hypothesis that thyroid autoantibodies impair the zona pellucida via molecular mimicry [48]. They also did not consider ICSI the method of choice for TAI-positive women despite its ability to bypass sperm–zona pellucida interaction [50, 54].

One of the primary limitations of the study was a low number of participants, comprising 52 participants divided equally between the two groups [54]. However, the same limitation can also be applied to the study conducted by Monteleone et al. [50] which involved only 31 participants (14 and 17 in each group), further weakening the interpretative power of the findings.

In conclusion, it remains controversial whether TAI affects intrauterine insemination outcomes. It also remains unclear whether the variation in outcomes associated with TAI in ART cycles is linked to the more widespread use of ICSI (Figure 1). Thus, studies that directly compare IVF and ICSI outcomes are needed to determine whether ICSI should be systematically preferred in this patient population.

### *Postpartum thyroiditis in ART patients*

In certain cases, TAI can present with transient hyperthyroid phases caused by the destruction of thyroid cells, leading to the release of stored hormones into the bloodstream and subsequent suppression of TSH. Known as the thyrotoxic phase, this transient period is characterized by symptoms of hyperthyroidism such as palpitations, anxiety, heat intolerance, and weight loss [55].

In conditions such as postpartum thyroiditis (PT), this phase often marks the earliest detectable sign of immune activation against the thyroid gland. Almost half of the women known with TAI prior to pregnancy will also develop PT [56]. Despite its name, postpartum thyroiditis includes thyroid dysfunction not only after childbirth but also following miscarriage or medical termination of pregnancy [57]. The hyperthyroid phase typically develops within the first six months after delivery and lasts for about one to two months [58]. Following this, transient or permanent hypothyroidism may develop due to exhaustion of hormone reserves and injury to thyroid hormone-secreting cells.

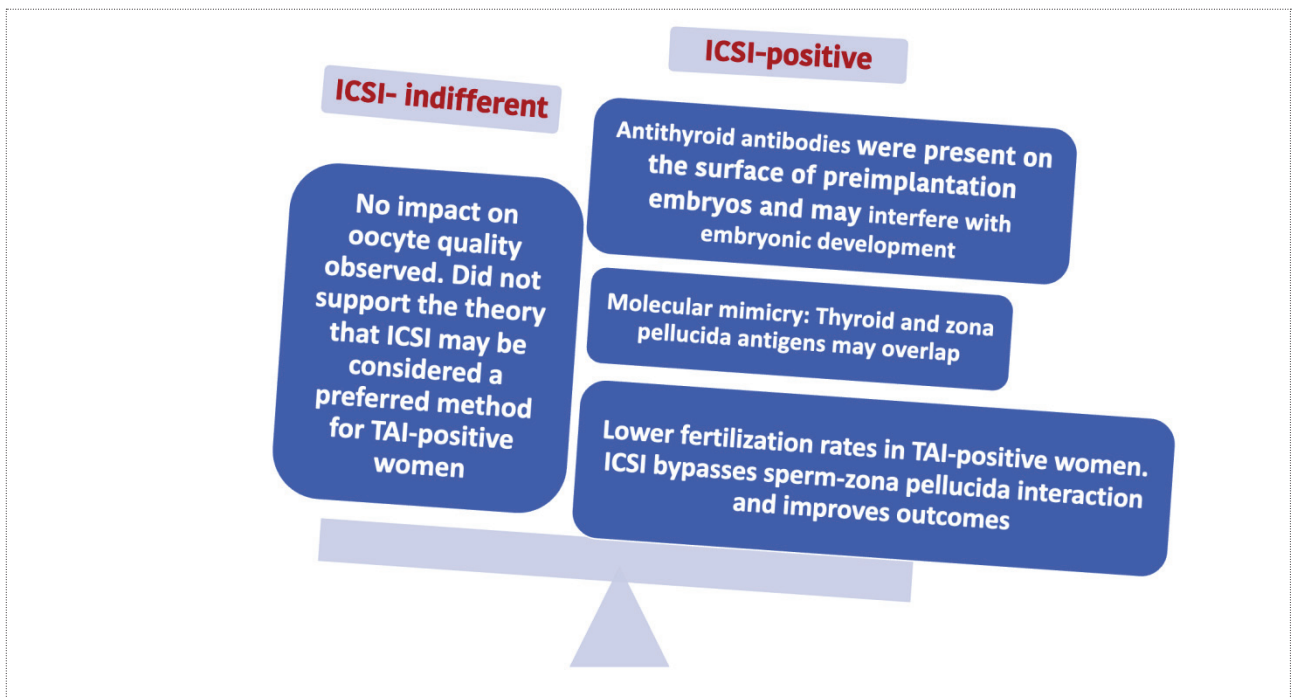


Figure 1. Conflicting evidence on the impact of ICSI in improving ART outcomes [48-50, 54]

While hyperthyroid symptoms in this phase can mimic those of Graves' disease, they are typically less severe. In contrast, findings such as exophthalmos, an increased free T3 (triiodothyronine) to free T4 ratio, and positive TSH receptor antibodies point toward Graves' disease [56], which is outside the scope of this review. During the course of this bibliographic review, several factors drew attention to this particular phase (Figure 2).

Firstly, research specifically addressing the relationship between PT development after miscarriage and ART outcomes, particularly its thyrotoxic stage, remains scarce. Secondly, as indicated by the previously cited data, recurrent miscarriage

was observed more often in women who tested positive for antithyroid antibodies [23]. This raises the possibility that some infertile women, particularly those with TAI, may begin ART treatment within one year after miscarriage placing them at risk of developing PT. Therefore, careful evaluation of early thyroid function tests, especially when thyrotoxicosis is present, could be essential for appropriate diagnosis and follow-up.

Finally, awareness of this transitional period helps clinicians anticipate the risk of hypothyroidism, which is especially important after spontaneous pregnancy or assisted reproductive procedures. With PT prevalence in the U.S. ranging from 1.1% to 9% [59],

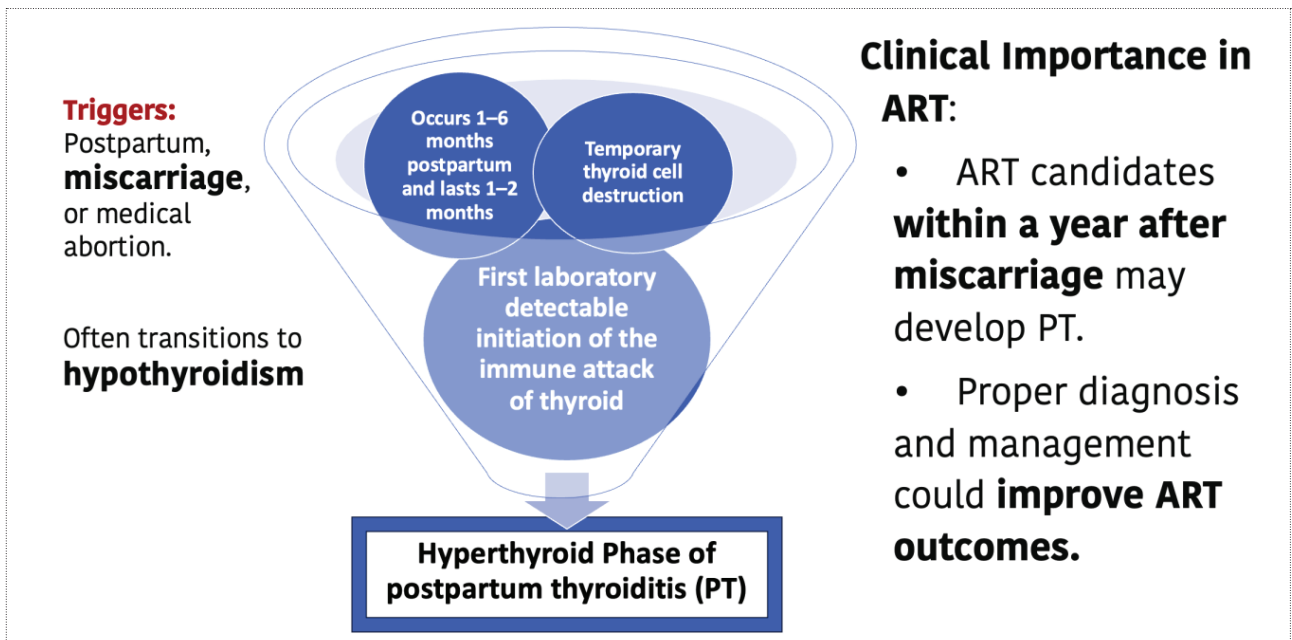


Figure 2. Clinical detection of the early hyperthyroid phase in PT

we suggest that this condition be explored further within the context of ART. A better understanding of how to manage affected patients may lead to higher treatment success rates.

### Managing TAI in ART

Owing to its structural similarity to TSH, human chorionic gonadotropin (hCG) promotes thyroid hormone synthesis by stimulating the thyroid during early pregnancy [60].

In one population-based prospective study, a positive correlation between hCG and free T4 levels, as well as a negative correlation between hCG and TSH levels, were identified in TPOAb-negative women [61]. This inverse relationship is attributed to the feedback mechanism in which hCG-induced thyroid hormone production suppresses pituitary TSH secretion.

However, this association was absent in women with positive TPOAb status in early pregnancy [61]. One possible reason is that the damaged thyroid tissue in TPOAb-positive women cannot adequately respond to hCG stimulation, leading to disrupted interactions among hCG, T4, and TSH [61, 62] (Figure 3). Notably, according to the same study, TPOAb-positive women with suboptimal free T4 levels faced a greater likelihood of preterm delivery [61].

In ART, hCG-triggered ovarian stimulation can increase thyroid hormone requirements earlier than in spontaneous conception, where this usually happens after implantation. Therefore, women with TAI may not experience the full stimulatory benefit of hCG [20].

Determining the ideal hCG dose for inducing ovulation remains an open question, highlighting the need for continued research. According to a recent study, thyroglobulin antibodies may interfere with how the thyroid responds to hCG. In 822 pregnant women between 7 and 20 weeks of gestation, despite normal TSH levels, high concentrations of TPOAb and thyroglobulin antibodies were shown to limit the usual thyroxine elevation and TSH suppression prompted by hCG. The impact

was greater when both TPOAb and thyroglobulin antibodies were detected [6]. The results indicate that hCG dosage could potentially be personalized based on antithyroid antibody profiles, highlighting the importance of future research into personalized strategies to minimize the risk of hypothyroidism-related complications [47].

Furthermore, poor thyroid responsiveness to hCG in women with TAI may signal early functional impairment and contribute to TSH rising above 2.5 mIU/L during ovarian stimulation or within the first month thereafter. This, in turn, elevates the risk of progression to subclinical or overt hypothyroidism [63, 64]. Because thyroid hormones play a role in oocyte development and implantation, reduced thyroid function due to stimulation protocols in TAI-positive women may contribute to poorer ART outcomes [36].

Finally, it is important to note that there is a lack of research focused on how TAI specifically affects ovarian stimulation when using alternative triggers such as gonadotropin releasing hormone (GnRH) agonists. More studies are necessary to establish which ovulation induction strategies are most effective for women with TAI, with a focus on the potential benefits of GnRH agonists in preserving thyroid function.

Clinicians working with women who have infertility and TAI should be aware of the complexities and limitations of the current evidence in this area. Although findings on ART outcomes remain inconsistent, the 2021 European Thyroid Association Guideline reflects a growing consensus that routine TAI screening in women from subfertile couples may help identify individuals at increased risk of fertilization failure [47]. However, according to the guideline of American Society for Reproductive Medicine (2024) TSH and T4 levels should be tested in patients with signs or symptoms of hypothyroidism (including irregular menstrual cycles) rather than in all patients with infertility (strength of evidence: B; strength of recommendation: moderate) [23]. Also, in the study by Hamad et al. [45] screening for TAI

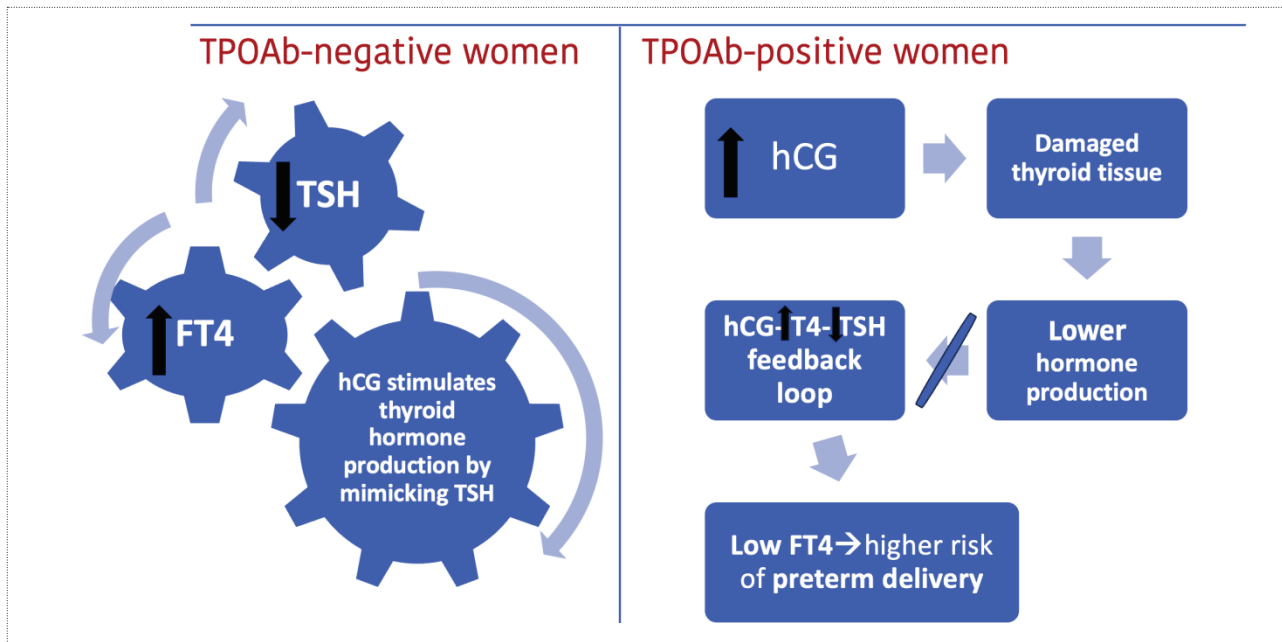


Figure 3. Use of hCG for ovulation induction in ART cycles with TAI

was considered a greater financial burden on patients than the potential clinical benefits it provides.

From the treatment perspective, to address fertility issues, it is common in clinical practice to prescribe a combination of prednisone and aspirin (P + A) to women with anti-thyroid antibodies, although the effectiveness of this approach remains debated. In the study by Zhou et al. [65] administering adjunctive therapy with P + A after embryo transfer proved to be unnecessary for euthyroid women with TAI undergoing their first IVF cycle, regardless of whether fresh or frozen embryos are used. On the contrary, in the other study glucocorticoid treatment enhanced pregnancy outcomes in ART of TAI-positive patients, however, it did not significantly decrease the risk of miscarriage [66]. Thus, the use of glucocorticoid as an adjuvant therapy should await further confirmation through randomized controlled trials.

In summary, hCG-triggered ovarian stimulation appears to exacerbate thyroidal demand and may impair thyroid response in antibody-positive women. These findings underscore the importance of personalized approaches, including careful monitoring of thyroid function and potential adjustments to hCG dosing. Exploring alternative triggers like GnRH agonists may present a more thyroid-friendly option for ovulation induction. Moreover, conflicting recommendations from the leading professional societies and cost-benefit concerns highlight the need for individualized, evidence-based approaches.

**CONCLUSIONS**

The relationship between TAI and ART remains complex and not fully understood. While many studies have found no significant differences in outcomes between TAI-positive and TAI-negative women, others suggest that TAI may be linked to lower fertilization, implantation, and pregnancy rates, along with a higher risk of miscarriage. These inconsistencies could be due to variations in study designs, differences in patient populations or discrepancies in lab protocols.

One possible explanation for improved outcomes in some cases is the increasing use of ICSI, which bypasses the zona pel-

lucida. This structure thought to be a target of cross-reactive antithyroid antibodies. However, current evidence is conflicting and, while ICSI may offer theoretical benefits in TAI-positive patients, its routine application as a preferred method in this group warrants further investigation and a direct comparison to conventional IVF.

Regarding ovulation triggering, hCG remains the standard agent, but in TAI-positive women, it may exacerbate thyroidal demand and reveal subclinical dysfunction due to impaired thyroid responsiveness. These effects could contribute to adverse pregnancy outcomes. GnRH agonists, often used as a gentler alternative in patients at risk of ovarian hyperstimulation syndrome, were offered as a more thyroid-neutral approach to final oocyte maturation. However, evidence on their specific role in TAI-positive women remains scarce. Altogether, these observations emphasize the need for personalized ART protocols, including careful selection of fertilization methods and ovulation triggers, guided by the endocrine and immunological profile of each patient.

Furthermore, special attention should be given to the transient hyperthyroid phase of PT, particularly in ART patients who may initiate treatment within one year after a miscarriage or pregnancy. Early recognition of this phase is crucial, as it may be the first sign of thyroid dysfunction and a predictor of subsequent hypothyroidism. Proper interpretation of thyroid function tests during this period can improve diagnostic accuracy, guide follow-up, and potentially enhance ART outcomes in TAI-positive women.

Considering TAI's possible impact on ART success, thyroid autoantibody screening may be advisable, particularly in cases of unexplained infertility or recurrent pregnancy loss.

In conclusion, further research into diagnostic criteria, personalized care, and the underlying mechanisms of TAI may enhance fertility outcomes for women undergoing ART.

**Conflict of interests**

No declared.

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# ТЕРЖИНАН

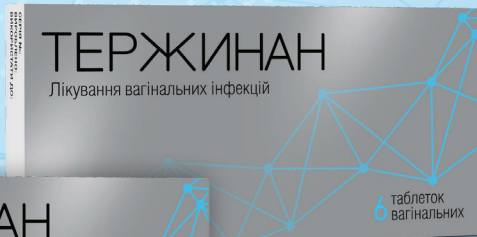
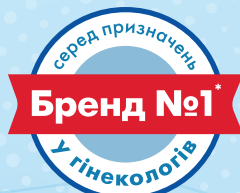
На захисті здоров'я жінки

## КОМПЛЕКСНЕ ЛІКУВАННЯ:<sup>1</sup>

- ✓ Бактеріального вагінозу<sup>2</sup>
- ✓ Аеробного вагініту
- ✓ Вагініту, асоційованого з цервіцитом<sup>3</sup>
- ✓ Кандидозного вагініту у вагітних



Препарат  
з Франції



\* Дані Pharmexplorer Q2 2023.

1. Родзинський В.Е. Емпірична терапія вульвовагінітів у жінок репродуктивного віку в рутинній практиці. «Репродуктивне здоров'я, Восточная Европа», 2020, том 10, № 4. 2. Наказ МОЗ України №286 Про удосконалення дерматовенерологічної допомоги населенню України та методичні рекомендації: «Діагностика і лікування невиношування вагітності та антенатальна профілактика респіраторного дистрес-синдрому у новонароджених» та «Діагностика і лікування інфекцій статевих органів у вагітних». 3. Згідно Інструкції для медичного застосування лікарського засобу Тержинан є активним проти мікроорганізмів, збудників захворювання, а також чинить протизапальну дію. 4. Носенко О.М. Сучасний погляд на цервіковагінальний дисбіоз, викликаний сполученням бактеріальних вагіноз-асоційованих бактерій та дріжджоподібних грибів роду Candida. ЗДОРОВ'Я ЖЕНЩИНИ №7 (153)/2020 ISSN 1992-5921. 5. В.І. Пирогова та співавтори. Порівняльне дослідження ефективності топічної терапії комбінованими препаратами змішаних вагінітів, асоційованих з цервіцитами // «ЗДОРОВ'Я ЖЕНЩИНИ» №6 (132)/2018.

Інформація про лікарські засоби для професіоналів сфери охорони здоров'я. Тержинан, таблетки вагінальні. Рп. в Україні НРUA/8116/01/01, термін дії необмежений. Характеристика і лікувальні властивості. Тержинан застосовується для лікування вагінітів, спричинених чутливими до препарату мікроорганізмами, у тому числі: бактеріальних вагінітів, спричинених банальною піогенною мікрофлорою; неспецифічних вагінітів, що супроводжуються десквамативними виділеннями; трихомоназу піхви; вагінітів, спричинених грибами роду *Candida*; вагінітів, спричинених змішаною інфекцією (трихомонадами, аеробною інфекцією та дріжджоподібними грибами). Тержинан чинить трихомонацидну дію, активний відносно анаеробних бактерій, у т.ч. гарднерел, Неомицину сульфат – антибіотик широкого спектра дії з групи аміноглікозидів. Нестатин – протрихібковий антибіотик з групи поліенив, активний відносно грибів роду *Candida*. Преднізолон – глюкокортикоїд, має виразну протизапальну дію. Склад ексципієнтів дозволяє забезпечити цілісність слизової оболонки піхви та постійне рН. Можлива побічна дія: гіперчутливість, алергічний дерматит, висип, свербіж, кропив'янка, подразнення у місці застосування, ерозії, набряк піхви, вульвовагінальний еритема, вульвовагінальний біль або свербіж. Для докладної інформації ознайомтесь з інструкцією для медичного застосування лікарського засобу. Категорія відпуску лікарського засобу. За рецептом. Власник реєстраційного посвідчення: Лабораторії Бушара Рекордати, Франція. Виробник: Софартекс, Франція.

Затверджено до друку: серпень 2023 р.

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RECORDATI



## THYROID AUTOIMMUNITY AND ASSISTED REPRODUCTIVE TECHNOLOGIES: MODERN CONTROVERSIES

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**Background.** Thyroid autoimmunity (TAI) affects approximately 13–19% of those experiencing infertility and is often associated with unexplained infertility, recurrent miscarriage, polycystic ovary syndrome, lower antral follicular count, reduced ovarian reserve and embryo quality.

**Objective of the review:** to consolidate and interpret recent studies investigating the role of TAI in ART success.

**Materials and methods.** Following several key principles of the PRISMA guidelines the following databases were searched for the last 5 years: MEDLINE (PubMed), Embase, Scopus, Lilacs, Web of Science, Clinical Trials, and SciELO.

**Analysis of literary data.** While some evidence links TAI with impaired reproductive outcomes, such as reduced fertilization and implantation rates and increased miscarriage, other studies propose that intracytoplasmic sperm injection may alleviate these issues by avoiding immune interference during fertilization. TAI-positive women tend to develop hypothyroidism during ovarian stimulation with human chorionic gonadotropin trigger, which may further compromise pregnancy outcomes. Data supporting the same risk under alternative stimulation protocols are currently not well established. Lastly, transitional hyperthyroidism in cases of postpartum thyroiditis, presents an added challenge for women initiating ART soon after miscarriage.

**Conclusions.** Early identification of TAI in women undergoing ART is crucial. Screening programs and personalized treatment strategies play a key role in improving fertility outcomes.

Existing data highlights potential areas for further study. These involve the influence of postpartum thyroiditis on ART results, as well as the role of alternative ovulation triggers in TAI-positive patients in order to get better obstetric outcomes. In addition, upcoming research should concentrate on optimizing diagnostic models and developing personalized treatment plans.

**Keywords:** thyroid autoimmunity, fertility, assisted reproductive technologies, recurrent miscarriage, postpartum thyroiditis, transitional hyperthyroidisms, alternative ovulation triggers, intracytoplasmic sperm injection.

## АУТОІМУННИЙ ТИРЕОЇДИТ ТА ДОПОМІЖНІ РЕПРОДУКТИВНІ ТЕХНОЛОГІЇ: СУЧАСНІ ПОГЛЯДИ

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**Обґрунтування.** Аутоімунний тиреоїдит (АТ) спостерігається у 13–19% безплідних жінок, частіше поєднуючись із безпліддям невизначеного генезу, невиношуванням, синдромом полікістозних яєчників, малою кількістю антральних фолікулів, зниженням оваріального резерву та якості ембріона.

**Мета дослідження:** об'єднати та інтерпретувати результати актуальних досліджень, які вивчають вплив АТ на результати допоміжних репродуктивних технологій (ДРТ).

**Матеріали та методи.** Відповідно до ключових принципів настанови PRISMA було проведено літературний пошук у таких базах даних, як MEDLINE (PubMed), Embase, Scopus, Lilacs, Web of Science, Clinical Trial та SciELO, серед публікацій за останні 5 років.

**Аналіз даних літератури.** Хоча деякі дослідження пов'язують АТ із порушеннями репродуктивних результатів, як-от зниження рівня запліднення та імплантації, а також збільшення кількості викиднів, інші дослідження припускають, що інтрацитоплазматична ін'єкція сперматозоїдів може зменшити ці проблеми, оминаючи імунологічно залежні бар'єри під час запліднення. Під час стимуляції яєчників за допомогою хоріонічного гонадотропіну жінки з АТ мають вищу ймовірність переходу до гіпотиреоїдного стану, що ще більше ускладнює процес настання вагітності. Докази, які свідчать про такий ризик у разі використання альтернативних протоколів стимулювання, залишаються обмеженими. Також додатковим викликом для жінок із невиношуванням, які планують скористатися ДРТ, є транзиторний гіпертиреоз, який спостерігається за наявності післяпологового тиреоїдиту.

**Висновки.** Доведено важливість раннього виявлення, скринінгових програм та модифікованих втручань для поліпшення фертильності, успішного настання та виношування вагітності в жінок з АТ у програмах ДРТ.

Наявні дані дають змогу визначити потенційні області для подальшого вивчення. Це стосується впливу післяпологового тиреоїдиту на результати ДРТ, а також ролі альтернативних тригерів овуляції в пацієнок із позитивним АТ для досягнення кращих акушерських результатів. Майбутні дослідження мають зосередитись на вдосконаленні діагностичних моделей, персоналізації протоколів лікування та дослідженні альтернативних тригерів овуляції для оптимізації результатів лікування.

**Ключові слова:** аутоімунний тиреоїдит, фертильність, допоміжні репродуктивні технології, невиношування, безпліддя невизначеного генезу, післяпологовий тиреоїдит, транзиторний гіпертиреоз, альтернативні тригери овуляції, інтрацитоплазматична ін'єкція сперматозоїда.