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The Overlooked Role of Autoimmune Thyroiditis in Female Infertility: Evidence from Global and Uzbek Populations

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Abstract Female infertility is a widespread global health issue, affecting around 17.5% of adults worldwide. In Uzbekistan, infertility rates are even higher up to 25% of marriages are affected, highlighting it as a national concern. While causes are multifactorial, growing evidence points to autoimmune thyroid disorders, particularly autoimmune thyroiditis (Hashimoto's disease), as a significant yet underrecognized contributor. A literature review was conducted (2020–2025) using PubMed and Uzbek national platforms (ZiyoNET, Natlib.uz) to gather data on infertility prevalence and its association with autoimmune thyroid conditions. Autoimmune thyroiditis affects ~10% of women of reproductive age and is more common among infertile women. Even when thyroid hormone levels are normal (euthyroid state), the presence of thyroid autoantibodies is linked to reduced fertility, increased miscarriage risk, and poorer pregnancy outcomes. Autoimmune thyroid disease is a modifiable risk factor for female infertility. Routine thyroid screening in infertility workups is advisable. In Uzbekistan, where infertility rates are high, addressing thyroid autoimmunity could improve outcomes. Continued research and improved access to reproductive care are essential to support affected women.

Keywords Female Infertility, Uzbekistan, Autoimmune Thyroiditis, Hashimoto's Disease, Global Health

1. Introduction

Infertility is defined as the inability to achieve a clinical pregnancy after 12 months or more of regular unprotected intercourse [1]. It is a global health concern that affects a significant fraction of couples. According to a 2023 World Health Organization (WHO) report, roughly 1 in 6 people worldwide (17.5% of the adult population) experience infertility during their lifetime [1]. Notably, the prevalence of infertility shows limited variation across regions and income levels, indicating that this challenge is universal: lifetime prevalence is ~17–18% in high-income countries and ~16% in low- and middle-income countries [1].

Infertility carries profound personal and social implications. In many cultures, including Uzbekistan, childbearing is highly valued and central to family life. Consequently, inability to conceive can lead to stigma, psychological distress, and marital strain. Uzbekistan, a country in Central Asia, has identified infertility as a problem of national importance, given the high proportion of affected couples [5]. Recent local data suggest that about 20% of Uzbek marriages face infertility, and some experts estimate this figure could be as high as 24–25% [5]. These rates appear elevated compared to the global average, underlining the need for focused attention. In response, the Uzbek government enacted the Law "On the protection of reproductive health of citizens" in 2019 to improve access to infertility treatment and provide social support to affected families [5].

The causes of female infertility are diverse, spanning anatomical, hormonal, genetic, and immunological factors. Among the female-related causes (which account for roughly 35% of infertility cases [2]), common conditions include:

- Ovulation disorders: e.g. polycystic ovary syndrome (PCOS) leading to anovulation.
- Tubal factor infertility: often due to fallopian tube blockage or adhesions (e.g. from pelvic inflammatory disease or prior infections).
- Endometriosis: ectopic endometrial tissue causing pelvic inflammation and impaired fertility.
- Uterine or cervical abnormalities: fibroids, congenital anomalies, or cervical mucus issues.
- Hyperprolactinemia and other hormonal imbalances: interfering with ovulation.
- Unexplained infertility: no definitive cause identified (accounts for ~15% of cases [2]).

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Increasingly, research is shedding light on autoimmune and endocrine factors that can contribute to infertility. In particular, disorders of the thyroid gland have emerged as important contributors to female reproductive dysfunction [4]. Adequate thyroid hormone levels are essential for normal menstrual cycles, ovulation, and maintaining pregnancy [4]. Thyroid disorders – whether overt (clinical hypothyroidism or hyperthyroidism) or subclinical – can disrupt these processes and reduce fertility. Autoimmune thyroid disease, predominantly Hashimoto's thyroiditis (autoimmune hypothyroidism), is the most common cause of thyroid dysfunction in women of childbearing age [4]. There is growing evidence that even in women with normal thyroid hormone levels, the presence of thyroid autoantibodies (a hallmark of autoimmune thyroiditis) may negatively affect their fertility and pregnancy outcomes [3, 4].

This review will therefore pay special attention to autoimmune thyroid disorders as a contributing factor to female infertility. We will present a comparative overview of female infertility prevalence globally versus in Uzbekistan, discuss the role of autoimmune thyroiditis in infertility, and summarize recent findings and implications for clinical practice in this context.

2. Background

Global Prevalence of Female Infertility: Infertility is a widespread issue, impacting couples in every region of the world. Traditional estimates indicated that about 8–12% of couples of reproductive age are infertile at any given time [2]. Newer lifetime estimates by WHO put the figure at 17.5% of adults who will experience infertility, highlighting that many individuals encounter infertility at some point in their lives [1]. Importantly, infertility affects high-income and low-income regions relatively equally [1]. This contrasts with some other reproductive health indicators and underscores that infertility is not confined to specific socio-economic settings – it is a universal reproductive health challenge.

Infertility can be categorized as primary (no prior pregnancies) or secondary (infertility after a previous successful pregnancy). In many developing countries, secondary infertility due to untreated infections or childbirth complications has historically been common. Central Asian and other post-Soviet countries have reported relatively high rates of secondary infertility, likely owing to factors such as past inadequate obstetric care or high rates of sexually transmitted infections in previous decades. Today, with improving healthcare, attention is turning to both primary and secondary infertility as significant public health concerns.

Female Infertility in Uzbekistan: Uzbekistan has a young population and strong cultural emphasis on family-building, which means infertility is acutely felt as a social problem. Recent local analyses estimate that roughly one in five marriages in Uzbekistan is affected by infertility [5]. By some accounts, the prevalence could approach one in four in the near future [5]. These figures suggest that infertility in Uzbekistan may be higher than the global average, though differences in measurement (lifetime prevalence vs. point prevalence) should be considered. The high rate in Uzbekistan includes both female and male factors; however, female infertility is often highlighted in local research and media. For instance, a 2021 study in Tashkent noted that many infertility cases were linked to gynecological conditions and that the issue had reached "crisis" levels nationally [5]. Primary infertility (inability to ever conceive) and secondary infertility (inability to conceive again after a prior birth or pregnancy loss) both contribute to the overall burden. Some regional data within Uzbekistan have identified polycystic ovary syndrome (PCOS) as a leading cause of female infertility, reflecting global trends, while tubal blockage from past infections is also a concern in certain populations. These local patterns align with global causes, though the exact contribution of each factor in Uzbekistan needs further research. The government's recognition of the problem, via legislation and public health programs [5], indicates a commitment to improving reproductive health services, including infertility diagnostics and treatment (such as assisted reproductive technologies).

Autoimmune Thyroid Disorders and Fertility: Among endocrine factors affecting fertility, thyroid disorders stand out because of the thyroid's integral role in reproductive physiology. Both hypothyroidism and hyperthyroidism can cause menstrual disturbances, anovulation, and complications in pregnancy. Autoimmune thyroiditis – also known as Hashimoto's thyroiditis – is of special interest because it is common in women of reproductive age and often presents with subtle or subclinical dysfunction. Autoimmune thyroiditis (AIT) is characterized by the immune system's production of antibodies against the thyroid (typically anti-thyroid peroxidase (TPO) and anti-thyroglobulin antibodies), which can gradually destroy thyroid tissue. It affects nearly 10% of women of childbearing age [3], making it a prevalent condition in the general population. Many women with autoimmune thyroiditis are euthyroid (normal thyroid levels) or only mildly hypothyroid, especially in early phases of the disease. Traditionally, clinicians have focused on overt thyroid disease in infertility; however, evidence now suggests that thyroid autoimmunity itself — even with normal hormone levels — may interfere with fertility and pregnancy. Thyroid autoimmunity has been linked to:

- Increased infertility risk: Multiple studies report a higher prevalence of thyroid antibodies in women with infertility compared to fertile controls [3, 2]. A recent meta-analysis (2024) found that worldwide about 20% of women with infertility test positive for thyroid autoantibodies, significantly higher than the rate in women without infertility [2]. In other words, infertile women are about 1.5 times as likely to have thyroid autoimmunity as fertile women [2].
- Unexplained infertility and ovarian reserve: Thyroid autoimmunity is particularly over-represented in certain infertility subsets, such as unexplained infertility and premature ovarian insufficiency. Women with

unexplained infertility, endometriosis, or ovulatory disorders have higher odds of being TPO/Tg antibody positive than fertile women [2]. This suggests a potential link between AIT and diminished ovarian reserve or egg quality, although causality is not yet established.

- Miscarriage and obstetric complications: Perhaps the most well-documented impact of thyroid autoimmunity is on pregnancy loss. Women who are euthyroid but TPO-antibody positive have an increased risk of early miscarriage and recurrent pregnancy loss [3]. A comprehensive analysis noted that presence of thyroid antibodies was associated with more than tripled odds of miscarriage in euthyroid women [2]. Additionally, thyroid autoimmunity has been associated with a higher risk of preterm birth and other complications in pregnancy [2]. The mechanisms are still under investigation, but one hypothesis is that thyroid antibodies or related immune imbalances may affect the endometrium and early embryo implantation. Indeed, recent research found that the thyroid peroxidase enzyme (target of TPO antibodies) is expressed in endometrial and placental tissues, offering a possible explanation for the antibody-mediated interference in pregnancy establishment [2].
- Outcomes of infertility treatment: Thyroid autoimmunity can also affect assisted reproduction outcomes. Studies including large meta-analyses have shown that women with autoimmune thyroiditis undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) have lower live birth rates compared to antibody-negative women [2]. In one analysis, the live birth rate was roughly 30–35% lower in thyroid antibody–positive women despite normal thyroid function, mainly attributable to a higher miscarriage rate in early pregnancy [9]. Notably, in these studies, the response to ovarian stimulation (number of eggs retrieved, fertilization rates, etc.) was similar between women with or without thyroid autoimmunity [9]. This suggests that the embryos can be created at similar rates, but women with thyroid autoimmunity are less likely to carry the pregnancy to term, reinforcing the link to implantation failure or miscarriage.

Researchers have proposed several pathophysiological mechanisms by which autoimmune thyroid disease may impact female fertility:

- Direct effect on reproductive organs: Autoimmune processes may not be limited to the thyroid; autoantibodies or immune cells could potentially cross-react with ovarian or placental tissue, impairing their function [3].
- Coexisting autoimmune disorders: Women with one autoimmune condition (like Hashimoto's) may be more prone to other autoimmune diseases (e.g. subtle ovarian autoimmunity or systemic autoimmune conditions) that can affect fertility [3].
- Immune system dysregulation: Thyroid autoimmunity reflects an imbalance in immune tolerance. The same heightened immune reactivity might hinder the immune adaptation needed for pregnancy (which requires tolerance to the semi-allogeneic fetus) [3]. This could lead to implantation failures or early rejections of the embryo.
- Thyroid hormone deficiency in critical periods: Even a relative deficiency of thyroid hormones – for instance, a high-normal thyroid-stimulating hormone (TSH) or slight drop in T4 – in thyroid antibody-positive women might disturb ovulatory cycles or the luteal phase, affecting fertility [3]. Autoimmune thyroiditis often progresses to subclinical hypothyroidism under stress (such as ovarian stimulation or early pregnancy), which may then impact pregnancy maintenance [3, 3].

Overall, the presence of thyroid autoimmunity serves as a red flag in infertility evaluations. It is increasingly recommended that women struggling to conceive be screened for thyroid function and thyroid antibodies [2]. If abnormalities are found, appropriate interventions (like thyroid hormone therapy if TSH is elevated) can be implemented to optimize chances of conception and healthy pregnancy.

3. Materials and Methods

Literature Search and Data Sources: A comprehensive literature search was performed to gather information for this review. International scientific databases including PubMed, Scopus, and Google Scholar were queried for articles published in the last 5 years (2020–2025) using keywords such as female infertility, prevalence, Uzbekistan infertility, thyroid autoimmunity, Hashimoto's thyroiditis, and infertility causes. Particular emphasis was placed on review articles, meta-analyses, and guidelines to obtain up-to-date synthesized evidence. To incorporate Uzbekistan-specific data, we accessed national information portals: ZiyoNET (an educational and scientific network of Uzbekistan) and the National Library of Uzbekistan (Natlib.uz) digital collections. These repositories were searched (in English, Uzbek) for statistics, government reports, and medical dissertations related to infertility and thyroid disorders. For example, dissertations and articles published by local researchers on infertility rates in Uzbekistan and on autoimmune thyroiditis were identified through these platforms.

Data Extraction: Key data points were extracted from the selected sources, including: global infertility prevalence rates; infertility prevalence or incidence in Uzbekistan; breakdown of infertility causes (female vs male factors, and specific female etiologies); prevalence of autoimmune thyroid antibodies in various populations (infertile women vs general population); and outcomes (pregnancy rates, miscarriage rates) in relation to thyroid autoimmunity. When multiple sources provided overlapping information, preference was given to the most recent and/or comprehensive source (for instance, a 2023 WHO report for global prevalence, or a 2024 meta-analysis for the impact of thyroid antibodies).

All data and claims in this review are supported by in-text citations to the relevant sources.

4. Results

Infertility Prevalence: Global Perspective Analysis of recent global data confirms that infertility remains a common challenge worldwide. The WHO's 2023 report on infertility, which pooled data from 133 studies across 1990–2021, found a lifetime infertility prevalence of 17.5% in the adult population [1]. This means roughly one out of every six adults of reproductive age has experienced infertility at some point. The similarity of rates across regions was a notable finding: high-income countries had a lifetime prevalence of 17.8%, whereas low- and middle-income countries had 16.5% [1]. These figures dispel the misconception that infertility is predominantly an issue of either the "developed" or "developing" world – in reality, it is a global health issue cutting across socio-economic and geographic boundaries.

It is important to distinguish between lifetime prevalence and current infertility rates. Lifetime prevalence (as above) captures the proportion of individuals who have ever experienced a year or more of infertility. Period prevalence (or point prevalence) looks at how many couples are infertile at a given time. Earlier estimates for current infertility (which often focused on women 15–49 years who are trying to conceive) tended to be in the range of 9–12% globally [2]. The new WHO analysis suggests that when considering the entire reproductive lifespan, the probability of experiencing infertility is higher (closer to 17%). Regardless of the metric, the numbers illustrate a substantial burden.

From a clinical standpoint, female and male partners contribute to infertility in roughly equal measure overall. Female factors alone account for ~35% of infertility cases, male factors for ~30%, and combined male-female factors for ~20%; the remaining ~15% are unexplained [2]. However, these proportions can vary by population. In regions with high rates of untreated infections, female tubal factor infertility can be more prominent; in areas with prevalent lifestyle factors affecting men (e.g. smoking, environmental toxins), male infertility might be higher. The WHO report emphasized not only prevalence but also the lack of accessible infertility care in many parts of the world [1, 1]. Many couples, especially in low-resource settings, cannot obtain advanced fertility treatments (like IVF) due to cost and limited availability, which means the true burden of involuntary childlessness can translate into unresolved health and social issues.

Infertility in Uzbekistan: Prevalence and Characteristics Uzbekistan has limited nationwide published data on infertility, but available evidence indicates a higher-than-average prevalence. According to recent reports summarized in a 2024 publication, approximately 20% of marriages in Uzbekistan are affected by infertility, and experts warn the number could reach 24–25% [5]. This suggests that up to one in four couples in the country may struggle to conceive – a striking figure that has drawn concern from public health officials. Indeed, the phrase "exceeds crisis levels" has been used to describe the infertility frequency in Uzbekistan, underscoring its significance as a national health priority [5].

It is worth noting how "infertility" is defined in local contexts. The Uzbek data often refer to "infertile marriages," which implies couples who have not had a child after a certain period of cohabitation. Cultural factors come into play: couples typically expect to conceive soon after marriage, and if a marriage remains childless for a few years, it is likely to be labeled infertile and come under social scrutiny. The reported 20–25% figure likely encompasses both primary and secondary infertility. There is evidence that secondary infertility (inability to have another child after a prior birth) is relatively common in Central Asia, possibly due to complications from prior deliveries or untreated infections. However, primary infertility (no prior pregnancies) is also widely reported and may relate to issues like PCOS, ovulatory dysfunction, or tubal problems in young women.

A regional study from Uzbekistan's Fergana Valley (though a bit older) had found an infertility incidence of ~16.8% among women of reproductive age, with polycystic ovary syndrome (PCOS) identified as the most frequent cause of female infertility in that area [8]. This aligns with global observations that PCOS – an endocrine disorder causing irregular ovulation – is a leading cause of infertility in women worldwide. Other gynecological issues noted in Uzbek clinical practice include uterine fibroids and chronic pelvic inflammatory disease leading to blocked tubes. Socio-demographic correlates specific to Uzbekistan have also been documented: fr example, a case-control study in Samarkand found that infertile women were more likely to report high stress and poorer quality of life, and that infertility was sometimes linked with marital instability (higher remarriage rates) in the local setting [8, 8]. These social dimensions reflect how infertility in Uzbekistan is not only a medical condition but also a deeply personal and societal challenge.

The response of the Uzbek health system has been to improve reproductive health services. The 2019 law on reproductive health laid the groundwork for better access to infertility evaluation and treatment, including assisted reproductive technologies (ART). As of the past few years, IVF and related services have been expanding in Uzbekistan, with state support or public-private partnerships making them more accessible. The data on how many infertility cases are due to female vs male factors in Uzbekistan remain scarce in published literature, but local reproductive specialists indicate that male infertility (due e.g. to low sperm counts) is also an area of concern. Public awareness campaigns are increasingly addressing both partners when dealing with infertility.

In summary, Uzbekistan's infertility prevalence appears to be comparable to some of the highest rates reported globally, which could be due to a combination of persistent health issues (like complications of reproductive tract infections) and increased detection/reporting. Culturally, the impact of infertility is profound, propelling national efforts to address the problem.

Autoimmune Thyroid Disorders as a Contributing Factor

One of the salient findings emerging from recent research is the role of autoimmune thyroid disorders, particularly Hashimoto's thyroiditis, in female infertility. Autoimmune thyroiditis (AIT) is a common condition in young and middle -aged women, and its overlap with reproductive health has gained attention. Thyroid autoimmunity (TAI) is typically defined by the presence of anti-thyroid antibodies (anti-TPO and/or anti-thyroglobulin) in the blood [3]. TAI affects roughly 1 in 10 women of reproductive age [3], and many of these women may not have obvious thyroid-related symptoms.

Research indicates that infertile women have a higher prevalence of thyroid autoantibodies than fertile women. A systematic review and meta-analysis published in late 2024 quantified this relationship: it found a worldwide pooled prevalence of thyroid autoantibody positivity of 20% in women with infertility, significantly greater than in women without infertility [2]. In that analysis, women with infertility were 51% more likely to test positive for thyroid antibodies compared to healthy controls [2]. Subgroup analyses provided further insight: infertile women who had normal thyroid function (euthyroid) still exhibited higher antibody positivity than controls, and those with a history of recurrent miscarriage or undergoing fertility treatments also had higher rates of TAI [2].

Specifically, certain infertility diagnoses show a strong association with thyroid autoimmunity:

- In **unexplained infertility**, where no overt cause is found, thyroid antibodies are disproportionately found, suggesting an occult factor like subtle autoimmunity might play a role [3].
- In **endometriosis-related infertility**, one study noted higher TPO antibody rates, hinting at a possible immunological link between endometriosis (itself influenced by immune factors) and thyroid autoimmunity [3].
- Women with **polycystic ovary syndrome (PCOS)** – a common endocrine disorder causing infertility – also have higher prevalence of thyroid antibodies than women without PCOS, as reported in several studies [3]. PCOS and autoimmune thyroiditis often coexist, possibly due to shared risk factors like obesity and insulin resistance or a general autoimmune-prone status in some individuals.
- **Premature ovarian insufficiency (POI)**, where ovaries lose function at an early age, has been linked in case studies to autoimmune factors, including thyroid autoimmunity [3]. While POI is relatively rare, the presence of thyroid antibodies in a young woman with unexplained ovarian failure might indicate a broader autoimmune etiology.

The impact of thyroid autoimmunity on fertility outcomes extends into pregnancy if conception occurs. Numerous studies, including meta-analyses, have established that euthyroid women with positive thyroid antibodies have a higher risk of miscarriage than those without antibodies [3]. In fact, thyroid autoimmunity is considered one of the most common treatable factors in recurrent pregnancy loss (after excluding chromosomal or anatomic causes). These women also face a greater risk of *subclinical pregnancy loss* (very early miscarriages that might be mistaken for a late menstrual period).

There is evidence that treating overt hypothyroidism dramatically reduces miscarriage risk; however, in antibody-positive women who are euthyroid, it has been debated whether prophylactic levothyroxine (thyroid hormone) could improve outcomes. Two recent randomized trials (including the large UK "TABLET" trial) addressed this by giving levothyroxine to euthyroid, thyroid-antibody-positive women trying to conceive or in early pregnancy. The consensus of these trials was that levothyroxine did not significantly improve live birth rates or reduce miscarriage in this specific group [3]. This was a somewhat unexpected finding, as many clinicians hoped that normalizing TSH to low-normal ranges might mitigate the risk.

The results suggest that the mere presence of autoantibodies – rather than mild thyroid hormone deficiency – could be the key detrimental factor. Therefore, attention is turning to the autoimmune aspect itself. Some researchers have speculated about using immunomodulatory therapies (e.g. selenium supplementation to reduce antibody levels, or even immune suppressants in certain cases) for women with high thyroid antibody titers who suffer recurrent reproductive failure [3]. However, such approaches remain experimental at this stage.

From a clinical management perspective, current recommendations include:

- **Screening:** Women with infertility or recurrent miscarriage should be screened with at least a serum TSH test, and if TSH is abnormal or there is clinical suspicion, tested for TPO antibodies [2].
- **Thyroid function optimization:** If an infertile woman has subclinical hypothyroidism (e.g. TSH >4 mIU/L or >2.5–3 mIU/L in context of fertility) and/or positive antibodies, most specialists will treat with levothyroxine to bring TSH to an optimal range (around 1–2 mIU/L) before and during pregnancy.
- **Monitoring:** Pregnant women with thyroid autoimmunity should be monitored closely. TSH is often checked each trimester because women with TAI have a higher chance of developing hypothyroidism during pregnancy due to increased thyroid hormone demands [3].
- **Other interventions:** For women with coexisting conditions like PCOS, managing those (e.g. weight loss, ovulation induction) remains crucial. Selenium supplementation may reduce TPO antibody levels and slow progression to hypothyroidism, though its fertility effects remain unclear.

In Uzbekistan, the link between thyroid disorders and infertility is an important area for future research. Salt iodization has improved iodine status, but autoimmune thyroiditis has become more visible as a cause of dysfunction. Local experts, such as Dilaram Jaqsimuratova et al. [7],

highlight that women with AIT frequently suffer from menstrual disorders, infertility, and miscarriage. They recommend **active management** rather than observation alone, including thyroid therapy and lifestyle adjustments (e.g. weight reduction) [9, 10].

5. Discussion

This review highlights the burden of female infertility globally and in Uzbekistan, and examines the emerging evidence implicating autoimmune thyroiditis as a contributing factor. Several important points emerge from the findings:

High Prevalence and Global Comparability: Infertility affects a sizeable portion of the population worldwide (around 17.5% on a lifetime basis) [1]. The new WHO data emphasize that no region is untouched – infertility is truly a global issue that warrants attention akin to other major health concerns. For Uzbekistan, the reported infertility rates (20–25% of couples) are notably high [5]. While these figures might be influenced by local diagnostic practices or definitions, they undeniably signal that infertility is a common challenge in Uzbek society. The fact that Uzbekistan's rates may exceed the global average could be due to persisting factors such as secondary infertility from past infections or insufficient reproductive health services in earlier decades. It could also reflect greater awareness and reporting in recent years. Regardless, the country-specific context underscores that national strategies are needed. The 2019 reproductive health law is a positive step, indicating political will to tackle issues like infertility by improving healthcare access. The findings in this review support that continued investment in fertility clinics, public education, and possibly insurance coverage for infertility treatments would be beneficial in Uzbekistan.

Social and Health Implications: In both global and Uzbek contexts, infertility carries social stigma and personal trauma. Particularly in cultures where childbearing is closely tied to a woman's role and marital stability, infertility can lead to serious psychosocial consequences [8]. Women may face blame or ostracism, even when male factors are equally at play. The discussion of social correlates in the Uzbek setting reveals that infertile women often experience higher stress and marital discord [8, 8]. This suggests that infertility is not just a medical condition to treat, but also a social issue requiring counseling and community support. Globally, there's a growing movement to recognize infertility as a disease and a human rights issue – meaning that affordable fertility care should be part of universal health coverage. WHO's call to reduce the financial burden of infertility care resonates with the experience in Uzbekistan, where many couples historically could not afford IVF and would remain childless or seek risky alternatives. With new government support, hopefully more couples can pursue safe and effective treatments.

Autoimmune Thyroiditis – from Association to Action: The role of autoimmune thyroid disorders in infertility, as highlighted, represents a convergence of endocrinology and reproductive medicine. The evidence reviewed confirms a clear association: women with infertility (especially those with unexplained infertility or certain conditions like PCOS) have higher rates of thyroid autoantibodies [2, 3], and these antibodies are linked to poorer reproductive outcomes (increased miscarriage, etc.) [2, 3]. However, association does not automatically mean causation. One discussion point in the scientific community is to what extent does treating thyroid autoimmunity improve fertility? Thus far, treating overt hypothyroidism is proven to improve fertility – for example, a woman with untreated hypothyroidism often has anovulatory cycles, and starting levothyroxine can restore ovulation and enable pregnancy. The contentious question is about euthyroid women with thyroid autoimmunity (normal TSH but positive antibodies). The lack of benefit from levothyroxine in large trials [3] suggests that simply correcting subclinical shifts in thyroid hormone may not resolve the issue. This directs attention to potential immunological therapies. Some small studies have tried therapies like glucocorticoids or IV immunoglobulin in women with recurrent miscarriage and thyroid antibodies, but results are inconclusive and such treatments carry side effects. Another area of interest is whether selenium supplementation (which can reduce thyroid antibodies) could improve pregnancy outcomes – a 2019 trial in Italy showed that selenium reduced the rise of TSH and antibody levels in TPO-positive pregnant women, correlating with a slight reduction in miscarriage, but the sample was small [3]. Future research, possibly some of it emerging from infertility centers in Uzbekistan and similar settings, may explore adjunct immunomodulation for women with high thyroid antibody titers who have failed other interventions.

Relevance for Uzbekistan: The intersection of infertility and thyroid health has particular resonance in Uzbekistan. The country historically had iodine deficiency pockets; now, with more iodine sufficiency, autoimmune thyroiditis is frequently diagnosed. It would not be surprising if a considerable subset of Uzbek women with infertility have underlying thyroid issues. Currently, we lack published Uzbek data quantifying this subset. It would be valuable for local researchers to conduct studies measuring how many infertile women in Uzbekistan have positive TPO/Tg antibodies and to follow their pregnancy outcomes. Such local evidence could drive guidelines on screening: for instance, making TSH and TPO tests routine in the work-up of every infertile woman in Uzbekistan. Given that these tests are relatively inexpensive, this is a feasible step. Moreover, thyroid hormone replacement (if needed) is simple and cost-effective compared to advanced fertility treatments. Identifying even subclinical hypothyroidism or mild thyroid imbalances in an infertile woman can lead to a straightforward intervention that might save the couple from more invasive procedures. For example, if anovulation is partly due to high-normal TSH, a low dose of levothyroxine could restore ovulatory cycles [9, 10].

Multi-Factorial Nature of Infertility: Despite focusing on autoimmune thyroiditis, it is crucial to remember that infertility is usually multi-factorial. A woman with thyroid antibodies may also have other issues (age-related egg

decline, slight tubal scarring, etc.). In Uzbekistan, many women with infertility present late, after years of trying, which can compound factors (age + untreated conditions). Therefore, tackling infertility successfully often requires a comprehensive approach: treating any thyroid dysfunction, improving ovulation through medications if needed, performing surgical corrections for anatomical issues, and addressing male partner factors concurrently. The presence of thyroid autoimmunity should be seen as one piece of the puzzle – an important piece, but one that should be addressed alongside other factors.

Need for Data and Research: One theme in both global and Uzbek contexts is the lack of data. WHO highlighted the paucity of infertility data in many countries [1]. Uzbekistan is one such case; aside from Demographic and Health Surveys or small clinic-based studies, there isn't a recent nationwide survey on infertility prevalence and causes. Establishing a registry or incorporating infertility indicators into national health statistics would greatly help in monitoring trends and evaluating interventions (like the impact of the 2019 law or new IVF clinics). On the thyroid aspect, research could delve into the cost-benefit of universal thyroid screening in prenatal care, or trials of interventions (like selenium or vitamin D supplementation in women with thyroid autoimmunity, since vitamin D deficiency has also been linked with autoimmunity and is common in Central Asia).

Public Health and Clinical Recommendations: In light of the findings, several recommendations can be made. For public health officials in Uzbekistan: strengthen reproductive health education so that women (and men) seek help for infertility earlier, and destigmatize the issue so couples feel supported rather than shamed. Ensure that basic evaluations (including hormone tests like TSH) are available even at primary care or regional clinics, not just specialized centers. For clinicians: adopt a multidisciplinary approach – an infertile woman with any symptoms of thyroid disturbance (or a positive family history of thyroid disease) should be thoroughly evaluated by an endocrinologist. Conversely, endocrinologists treating women with autoimmune thyroiditis should inquire about their reproductive plans; if a patient with AIT is planning pregnancy, proactive management and preconception counseling should be offered. This might include adjusting thyroid medication to achieve optimal TSH (<2.5 mIU/L) before conception and advising on timely obstetric care once pregnant.

In conclusion, this discussion reinforces that addressing infertility requires both broad strategies (making fertility care accessible and affordable, as WHO advocates) and targeted medical interventions (identifying specific factors like thyroid autoimmunity). Uzbekistan's case exemplifies how a country can begin to tackle a traditionally "silent" problem by bringing it into the spotlight through policy and research. Continued international support and knowledge exchange will help Uzbekistan and other countries reduce the burden of infertility. The connection with autoimmune thyroid disorders adds a layer of complexity but also offers an actionable target, as thyroid conditions are diagnosable and often treatable. As evidence evolves, guidelines will likely be refined on how to manage thyroid autoimmunity in women seeking to conceive. The ultimate goal is to improve the chances for women to achieve a healthy pregnancy – turning the tide on the infertility statistics, both globally and in Uzbekistan.

6. Conclusions

Infertility is a prevalent condition worldwide, affecting millions of couples and showing that no region or socio-economic group is immune to the problem. In Uzbekistan, infertility rates are alarmingly high, with roughly 20–25% of couples experiencing difficulties in conceiving, highlighting an urgent need for continued public health interventions and resource allocation [5]. This review has underscored that while infertility has multiple causes, autoimmune thyroid disorders (especially Hashimoto's thyroiditis) stand out as a significant contributing factor that is often under-recognized. Autoimmune thyroiditis, marked by the presence of anti-thyroid antibodies, is common in women of reproductive age and has been linked to decreased fertility, increased miscarriage risk, and potentially poorer outcomes of fertility treatments [3, 2].

For healthcare providers and researchers, these findings call for a few clear actions: • Integrate Thyroid Screening: Incorporate thyroid function tests and antibody screening as a routine part of infertility evaluations. Given that thyroid autoimmunity is more prevalent among infertile women [2], identifying and managing thyroid-related issues could improve reproductive outcomes. In Uzbekistan, where such screening may not yet be universal, training and protocols can be updated to ensure every woman with infertility is checked for TSH and TPO antibodies. • Optimize Thyroid Health: Ensure that women who are found to have hypothyroidism (even subclinical) receive appropriate treatment before and during attempts to conceive. Maintaining a euthyroid state is known to facilitate regular ovulation and reduce miscarriage risk. Although treating euthyroid women with positive antibodies remains controversial, a personalized approach is warranted – at minimum, those women should be closely monitored throughout pregnancy if they do conceive [3]. • Holistic Management: Address all relevant factors in parallel. For example, if an infertile woman in Uzbekistan has both PCOS and autoimmune thyroiditis (not an uncommon scenario), both conditions should be managed (weight loss, ovulation induction for PCOS, plus thyroid hormone for elevated TSH or selenium if appropriate for thyroid antibodies). A multidisciplinary team including gynecologists, endocrinologists, and immunologists (when needed) will provide the best care for complex cases. • Research and Surveillance: Close the data gaps by conducting local research on infertility causes and outcomes in Uzbekistan. Establishing registries or including infertility in national health surveys will help track progress. Moreover, investigating interventions like immunotherapy or nutritional supplementation

for thyroid antibody–positive women could contribute valuable knowledge to the global discourse. Uzbekistan's medical universities and research institutes, possibly with international collaboration, should be encouraged to focus on these topics. • Patient Education and Support: Educate patients that factors like thyroid health can impact fertility. In Uzbekistan, disseminating information through ZiyoNET or public health campaigns about the importance of preconception health (controlling chronic diseases, including thyroid conditions) could empower couples. Additionally, support groups or counseling for those experiencing infertility can alleviate the psychosocial burden, as the journey can be stressful and isolating.

In closing, female infertility is a multifaceted challenge that requires both broad societal efforts and precision medical solutions. Autoimmune thyroid disorders exemplify a modifiable medical factor – by paying attention to the thyroid, we may improve the chances of conception and successful pregnancy for many women. The global comparison provided in this review shows that while the magnitude of infertility in Uzbekistan is high, it is part of a worldwide pattern that warrants solidarity and shared strategies. Tackling infertility will involve advancing medical care (like making IVF more accessible, which Uzbekistan has begun working on) and also addressing underlying health issues such as untreated endocrine disorders. There is reason for optimism: with heightened awareness, supportive policies, and ongoing research, outcomes can improve. Women in Uzbekistan and around the world who aspire to motherhood stand to benefit from these concerted efforts – turning what is often a heartbreaking struggle into, hopefully, a success story with the right interventions.

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