ISSN NO: 2770-2936
May 2026

Endocrine and Genetic Mechanisms of the Influence of Subclinical Thyroid Dysfunction on Women's Reproductive Health

Zokirova D.D., Yusupova Sh.Q.
Department of Hospital Therapy and Endocrinology
Andijan State Medical Institute

Abstract
Subclinical thyroid dysfunction is one of the most common endocrine disorders among women of reproductive age and represents an important medical and social problem due to its impact on fertility, menstrual function, pregnancy outcomes, and hormonal balance. Subclinical hypothyroidism and subclinical hyperthyroidism are characterized by altered thyroid-stimulating hormone levels with normal circulating thyroid hormone concentrations. Despite the absence of pronounced clinical manifestations, these conditions may significantly affect reproductive health through complex endocrine and genetic mechanisms. Thyroid hormones regulate ovarian function, folliculogenesis, ovulation, implantation, and placental development. Disturbances in thyroid homeostasis can lead to menstrual irregularities, infertility, miscarriage, polycystic ovary syndrome, and adverse obstetric outcomes. In recent years, increasing attention has been paid to the genetic and molecular mechanisms underlying the relationship between thyroid dysfunction and reproductive disorders. Genetic polymorphisms involving thyroid hormone receptors, deiodinases, autoimmune susceptibility genes, and reproductive hormone receptors may contribute to impaired fertility and hormonal imbalance in affected women. This article reviews current scientific evidence regarding the endocrine and genetic pathways linking subclinical thyroid dysfunction with female reproductive health and highlights the importance of early diagnosis and personalized therapeutic strategies.
Keywords: subclinical thyroid dysfunction, reproductive health, infertility, thyroid hormones, endocrine mechanisms, genetic polymorphism, women's health, fertility.

Introduction

The thyroid gland plays a central role in maintaining metabolic, endocrine, and reproductive homeostasis. Thyroid hormones influence nearly every organ system and are particularly important for normal reproductive functioning in women. Subclinical thyroid dysfunction is defined as an abnormal serum thyroid-stimulating hormone (TSH) concentration accompanied by normal free thyroxine (fT4) and triiodothyronine (fT3) levels. Subclinical hypothyroidism is characterized by elevated TSH levels, whereas subclinical hyperthyroidism presents with suppressed TSH concentrations[1,5].

The prevalence of subclinical thyroid disorders among women of reproductive age ranges from 4% to 15%, depending on iodine status, geographic region, and diagnostic criteria. Women are affected significantly more frequently than men due to hormonal and autoimmune factors. Although clinical symptoms may be absent or mild, subclinical thyroid dysfunction can negatively influence reproductive capacity and pregnancy outcomes. Reproductive health depends on the coordinated interaction between the hypothalamic-pituitary-ovarian axis and thyroid endocrine regulation. Thyroid hormones interact with gonadotropins, prolactin, estrogen, and progesterone, thereby influencing ovulation, implantation, and fetal development. Even subtle thyroid dysfunction may disturb these mechanisms and contribute to infertility and obstetric complications.

Recent molecular and genetic studies have demonstrated that reproductive impairment associated with thyroid dysfunction may also involve genetic susceptibility factors, autoimmune pathways, and receptor-mediated alterations in endocrine signaling. Understanding these mechanisms is essential for improving diagnostic and therapeutic approaches in women with reproductive disorders[8].

Physiological Role of Thyroid Hormones in Female Reproduction

Thyroid hormones are essential regulators of ovarian physiology and reproductive function. Receptors for thyroid hormones are present in ovarian tissue, granulosa cells, endometrium, placenta, and the hypothalamus.

ISSN NO: 2770-2936
May 2026

Through these receptors, thyroid hormones influence follicular development, steroidogenesis, oocyte maturation, and endometrial receptivity.

The hypothalamic-pituitary-thyroid axis is closely connected with the hypothalamic-pituitary-ovarian axis. Thyrotropin-releasing hormone stimulates not only TSH secretion but also prolactin production. Elevated prolactin levels may inhibit gonadotropin-releasing hormone secretion, leading to anovulation and menstrual dysfunction.

Thyroid hormones also regulate sex hormone-binding globulin synthesis in the liver. Altered thyroid status can therefore modify the bioavailability of estrogen and androgen hormones. In hypothyroid states, decreased sex hormone-binding globulin levels increase free estrogen concentrations and contribute to hormonal imbalance.

Normal thyroid function is especially important during pregnancy. During the first trimester, the developing fetus depends almost entirely on maternal thyroid hormones. Impaired thyroid hormone availability during early gestation may lead to miscarriage, placental insufficiency, preeclampsia, premature delivery, and fetal neurodevelopmental disorders[3].

Endocrine Mechanisms Linking Subclinical Thyroid Dysfunction and Reproductive Disorders

Subclinical Hypothyroidism and Reproductive Dysfunction

Subclinical hypothyroidism is associated with elevated TSH levels despite normal thyroid hormone concentrations. Even mild thyroid insufficiency can disturb reproductive physiology through several endocrine mechanisms.

One of the major mechanisms involves hyperprolactinemia. Increased thyrotropin-releasing hormone secretion stimulates prolactin release from the pituitary gland. Elevated prolactin inhibits pulsatile gonadotropin-releasing hormone secretion and suppresses luteinizing hormone release, resulting in impaired ovulation.

Subclinical hypothyroidism may also reduce ovarian sensitivity to gonadotropins. Thyroid hormones are required for normal granulosa cell proliferation and follicular maturation. Their deficiency can impair folliculogenesis and contribute to infertility.

Menstrual irregularities including oligomenorrhea, menorrhagia, and amenorrhea are frequently observed in women with thyroid dysfunction. Endometrial abnormalities associated with altered estrogen metabolism may additionally impair implantation and pregnancy maintenance[4].

Several studies have shown that elevated TSH levels are associated with increased miscarriage rates and decreased success of assisted reproductive technologies. Women undergoing in vitro fertilization with untreated subclinical hypothyroidism demonstrate lower implantation and pregnancy rates compared with euthyroid women.

Subclinical Hyperthyroidism and Reproductive Disturbances

Subclinical hyperthyroidism is characterized by suppressed TSH levels and relatively normal thyroid hormone concentrations. Although often asymptomatic, excessive thyroid stimulation may affect reproductive function.

Elevated thyroid activity accelerates estrogen metabolism and alters gonadotropin secretion. Increased sex hormone-binding globulin production reduces biologically active steroid hormone concentrations, leading to menstrual disturbances and impaired ovulatory cycles[2].

Women with subclinical hyperthyroidism may experience oligomenorrhea, decreased fertility, and pregnancy complications. Excess thyroid hormone activity may also increase oxidative stress within ovarian tissue and negatively affect oocyte quality.

Cardiovascular and metabolic effects associated with hyperthyroid states may indirectly impair placental circulation and fetal development during pregnancy.

Autoimmune Mechanisms and Reproductive Health

Autoimmune thyroid disease represents one of the leading causes of subclinical thyroid dysfunction in women. Autoimmune thyroiditis is characterized by the production of antithyroid antibodies, including thyroid peroxidase antibodies and thyroglobulin antibodies.

Thyroid autoimmunity has been strongly associated with infertility, recurrent miscarriage, premature ovarian insufficiency, and adverse pregnancy outcomes even in euthyroid women. The exact mechanisms remain incompletely understood, but several theories have been proposed[1].

ISSN NO: 2770-2936
May 2026

One hypothesis suggests that thyroid autoantibodies reflect generalized immune dysregulation that affects implantation and placental development. Increased inflammatory cytokine production and altered T-helper cell balance may impair maternal immune tolerance toward the embryo.

Another possible mechanism involves direct antibody-mediated ovarian damage. Some studies indicate cross-reactivity between thyroid and ovarian antigens, contributing to follicular destruction and decreased ovarian reserve.

Women with autoimmune thyroid disease frequently exhibit other autoimmune disorders, including type 1 diabetes mellitus and autoimmune ovarian insufficiency, which may further impair fertility[4].

Genetic Mechanisms of Reproductive Disorders in Subclinical Thyroid Dysfunction

Recent advances in molecular genetics have identified several genetic factors involved in thyroid-related reproductive dysfunction.

Thyroid Hormone Receptor Gene Polymorphisms

Thyroid hormone receptors mediate cellular responses to thyroid hormones. Polymorphisms in thyroid hormone receptor genes may alter receptor sensitivity and intracellular signaling pathways. Such variations can influence ovarian responsiveness and endometrial receptivity.

Abnormal receptor activity may impair follicular maturation and embryonic implantation despite normal circulating thyroid hormone levels[3].

Deiodinase Enzyme Gene Variants

Deiodinases are enzymes responsible for the activation and inactivation of thyroid hormones at the tissue level. Genetic polymorphisms affecting deiodinase enzymes can modify local thyroid hormone availability within reproductive tissues.

Altered intracellular thyroid hormone metabolism may contribute to ovarian dysfunction, poor oocyte quality, and implantation failure.

Autoimmune Susceptibility Genes

Certain human leukocyte antigen haplotypes and immune-regulatory gene polymorphisms are associated with autoimmune thyroid disease. Genes involving cytotoxic T-lymphocyte-associated protein 4, protein tyrosine phosphatase non-receptor type 22, and interleukin signaling pathways have been implicated.

These genetic variants may predispose women to both thyroid autoimmunity and reproductive immune dysfunction[6].

Gonadotropin and Estrogen Receptor Gene Variants

Interactions between thyroid hormones and reproductive hormone receptors are essential for normal ovarian physiology. Genetic polymorphisms affecting follicle-stimulating hormone receptors, luteinizing hormone receptors, and estrogen receptors may increase susceptibility to reproductive complications in women with thyroid dysfunction.

Combined endocrine and genetic abnormalities may therefore produce more severe reproductive disturbances.

Clinical Implications and Diagnostic Approaches

Early identification of subclinical thyroid dysfunction is essential for preserving reproductive health. Screening for thyroid dysfunction is recommended in women with infertility, recurrent miscarriage, menstrual disorders, polycystic ovary syndrome, and adverse obstetric history.

Laboratory evaluation should include measurement of serum TSH, free thyroxine, thyroid autoantibodies, and reproductive hormone profiles. In selected patients, genetic testing may provide additional information regarding susceptibility and prognosis[7].

Ultrasonographic evaluation of the thyroid gland and reproductive organs may also assist in diagnosis and treatment planning.

Management strategies depend on the severity of endocrine abnormalities, reproductive goals, and presence of autoimmunity. Levothyroxine therapy has demonstrated beneficial effects on fertility and pregnancy outcomes in women with subclinical hypothyroidism. Careful endocrine monitoring during pregnancy is particularly important.

Personalized medicine approaches integrating endocrine, immunological, and genetic information may improve therapeutic effectiveness and reproductive outcomes[1].

Future Perspectives

ISSN NO: 2770-2936
May 2026

Current evidence highlights the importance of multidisciplinary research investigating endocrine-genetic interactions in reproductive disorders. Future studies should focus on identifying molecular biomarkers for early detection and risk stratification.

Advances in genomics, proteomics, and reproductive endocrinology may facilitate the development of individualized therapeutic strategies targeting specific molecular pathways.

Artificial intelligence and predictive modeling may further improve diagnosis and management of reproductive complications associated with thyroid dysfunction.

Conclusion

Subclinical thyroid dysfunction significantly affects women's reproductive health through complex endocrine, autoimmune, and genetic mechanisms. Even mild disturbances in thyroid homeostasis may impair ovulation, fertility, implantation, and pregnancy outcomes. Thyroid hormones interact closely with reproductive endocrine pathways and immune regulation, while genetic susceptibility factors further contribute to reproductive dysfunction[5,10].

Early diagnosis, comprehensive hormonal evaluation, and individualized treatment strategies are essential for improving reproductive outcomes in affected women. Further research into molecular and genetic mechanisms will enhance understanding of disease pathogenesis and support the development of precision medicine approaches in reproductive endocrinology.

References

1. Alexander EK, Pearce EN, Brent GA, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2017;27(3):315–389.
2. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. *Endocrine Reviews*. 2010;31(5):702–755.
3. Poppe K, Velkeniers B. Thyroid disorders in infertile women. *Annals of Endocrinology*. 2003;64(1):45–50.
4. Unuane D, Velkeniers B, Deridder S, et al. Impact of thyroid autoimmunity in euthyroid women on live birth rate after IVF. *Human Reproduction*. 2017;32(4):915–922.
5. Rao M, Zeng Z, Zhou F, et al. Effect of thyroid dysfunction on female infertility and pregnancy outcomes. *Frontiers in Endocrinology*. 2021;12:743.
6. Korevaar TIM, Medici M, Visser TJ, Peeters RP. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. *Nature Reviews Endocrinology*. 2017;13(10):610–622.
7. Doufas AG, Mastorakos G. The hypothalamic-pituitary-thyroid axis and the female reproductive system. *Annals of the New York Academy of Sciences*. 2000;900:65–76.
8. Medenica S, Garalejic E, Arsic B, et al. Follicular fluid thyroid hormones and reproductive outcome in women undergoing assisted reproductive technology. *Gynecological Endocrinology*. 2018;34(8):703–706.
9. Weetman AP. Autoimmune thyroid disease and female reproduction. *Clinical Endocrinology*. 2019;90(1):13–20.
10. Lazarus JH. Thyroid disorders associated with infertility and pregnancy loss. *Endocrine*. 2012;42(1):45–50.