Adverse Effects of Hypothyroidism on Fertility and Pregnancy: A Mini Review

Akhtar Seifi (Doctor of pharmacy)Department of Pharmacology. Gorgan medical school.Golestan University of medical sciences-Gorgan, IRAN
Negarsadat Taheri (MD)Department of Gynecology, Mashhad Medical School.Mashhad University of Medical Sciences-Mashhad, IRAN
Hanieh Kia (MD)Department of Clinical Research.Clinical Science Institute, Santa Monica, CA 90404, USA-Department of Clinical Research.Clinical Science Institute, Santa Monica, CA 90404, USA
Hady Reza Mansourian (MD)Department of Emergency. Hakim Jorjani Hospital.Gorgan, IRAN
Azad Reza Mansourian (PhD)Metabolic disorders research center. Department of biochemistry.Gorgan medical school.Golestan University of medical sciences-Gorgan, IRAN

Corresponding Author: Azad reza Mansourian
Tel: +9111758010
Email: azad_r_mansourian@yahoo.com
Address: Department of biochemistry.Gorgan medical school.Golestan University of medical sciences-Gorgan, IRAN

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ABSTRACT
The prevalence of hypothyroidism is much higher among women than in men. Hypothyroidism is also one of the most prevalent thyroid disorders among women of reproductive age. The disease exerts its effect on female sex hormones by manipulating the production of luteinizing hormone and follicle-stimulating hormone that are crucial for the production of estrogen by the ovaries. Various studies demonstrated the adverse effect of overt hypothyroidism on ovulation, menstrual cycle, and fertility. This review surveys the adverse effects of hypothyroidism on fertility and pregnancy.

Keywords: Hypothyroidism, Thyroid hormones, Women, Infertility, Pregnancy.
INTRODUCTION

Hypothyroidism is characterized by elevated thyroid-stimulating hormone (TSH) and reduced tetraiodothyronine (T4) levels. The main cause of hypothyroidism is Hashimoto's disease, an autoimmune disorder that targets thyroid peroxidase, the enzyme responsible for iodine oxidation as the initial step for thyroid hormone synthesis. In this disease, autoantibodies are also produced against thyroglobuline, a macro-protein containing 5000 amino acids and 115 tyrosine residues (1-3). In this mini-review, we provide the latest findings on the role of hypothyroidism in infertility in women regardless of the types of hypothyroidism. For this purpose, we studied the published papers from 2000 to 2021 on various databases including PubMed, Web of Science, and Google Scholar.

Different types of hypothyroidism

Primary and secondary hypothyroidism

Primary hypothyroidism occurs either due to thyroid disruption due to insufficient iodine intake, iodine malabsorption, autoimmune thyroid diseases, or the adverse effects of medical procedures including thyroid operation and radiotherapy (4-6). Hypothyroidism can be divided into overt and subclinical types. Hypothyroidism can have metabolic, neurologic, dermatologic, ocular, gastrointestinal, gynecologic, and cardiovascular manifestations. Hoarseness of voice and slow speech are some common features of overt hypothyroidism. Hypothyroidism mostly affects women. If undiagnosed or left untreated, the condition may lead to myxedema coma, which is associated with a high risk of morbidity and mortality. Secondary hypothyroidism is caused by the disruption in the hypothalamus–pituitary axis (7-9). Thyrotropin-releasing hormone (TRH) is a peptide hormone produced by the hypothalamus that stimulates TSH release by the pituitary gland, which ultimately leads to production of T4 and triiodothyronine (T3). Extrathyroidal deiodination of T4 can also result in T3 production (10-13).

Subclinical hypothyroidism

Subclinical hypothyroidism usually presents with normal thyroid hormones but elevated TSH level. The incidence of subclinical hypothyroidism is estimated to be about 5%. The interference of subclinical hypothyroidism with fertility is still under investigation (14-20). Subclinical hypothyroidism may be asymptomatic and can be misdiagnosed in clinical examination. The definite diagnosis relay on thyroid function tests with elevated serum TSH and normal T4 (21-27).

Laboratory investigation of hypothyroidism

Based on the biochemical pathways of thyroid hormone production, TSH plays a critical role in the biosynthesis of T4 and T3. The circulating T4 concentration controls TSH release from the pituitary gland, and T3 does not seem to play an important role in this regard. In hypothyroidism, T4 suppression leads to elevation of TSH level, which is the first indicator of primary hypothyroidism (9, 28). In secondary hypothyroidism, TSH and T4 are both suppressed. In some rare conditions, the thyroid hormones concentration decrease due to a disorder in production of thyroxine-binding globulin, a protein biosynthesized in the liver that transports thyroid hormones (29-38). Therefore, TSH, T4, T3, and thyroxine-binding globulin in some cases can be considered as valuable laboratory factors in diagnosing hypothyroidism (39-48).

Hypothyroidism and infertility

The overall prevalence of hypothyroidism is much higher among women than in men. Hypothyroidism is one of the most common thyroid abnormalities among women of reproductive age. Thus, the level of T4, T3, and TSH should be monitored closely in pregnant women (49, 50). Thyroid abnormalities that lead to hypothyroidism during pregnancy may be accompanied with some pregnancy complications including miscarriage, cardiovascular disorders, high blood pressure, and metabolic abnormalities such as gestational diabetes. Low birth weight, fetal death, and abortion are other consequences of hypothyroidism during pregnancy. Other pregnancy complications associated with hypothyroidism include cretinism, a neurocognitive disorder, preterm delivery, and stillbirth due to undeveloped placenta (51-59). Measurement of antibodies against thyroid peroxidase and thyroglobulin is crucial for determining the origin of thyroid
abnormalities. Various studies from different parts of the world indicate that overt hypothyroidism can eventually lead to gestational hypertension and diabetes in pregnant women. Some other studies indicate that even subclinical hypothyroidism can result in some pregnancy complications (60-69).

Numerous studies demonstrated the direct relationship between infertility and hypothyroidism (70). Thyroid abnormality may eventually lead to ovulatory dysfunction, which is accompanied with endocrine reproductive disorders. It has been reported that hypothyroidism-related infertility can be resolved following the treatment of hypothyroidism (71). The prevalence of thyroid disorders is considerably higher among infertile women (72). It has been reported that following treatment of hypothyroidism, hypothyroidism-related side effects and pregnancy complications are reduced significantly (73). Thyroid autoantibodies are among factors that may cause pregnancy complications (74,75). The hypothalamic-pituitary-ovarian axis tightly controls female reproduction, the dysfunction of which leads to ovulation disorders (76-78). In this regard, serum levels of prolactin may also contribute to infertility (79). The high level of TSH in hypothyroidism is directly correlated with prolactin levels, which contributes to infertility (80). Accurate assessment of thyroid function during pregnancy is critical, for both the initiation of thyroid hormone therapy, and for the adjustment of thyroid hormone dose in those already receiving thyroid hormone (81,82).

Epidemiological studies have shown a high prevalence of thyroid disorders (dysfunction and autoimmunity) in women of reproductive age (83,84). Hypothyroidism also leads to changes in the menstrual cycle (85-88).

The roles of hypothalamus and pituitary hormones in infertility

Thyroid hormones act through binding to their receptor in ovary and the subsequent stimulation of follicles. Therefore, hypothyroidism can directly affect the function of ovary, menstrual cycle, fertility, and pregnancy outcome. One of the major characteristics of hypothyroidism is the suppression of the thyroid hormones, which results in increased production of TRH. This will in turn trigger the biosynthesis of TSH. Some reports indicate that TRH can also induce the production of prolactin, which is thought to have adverse effects on the biosynthesis of sex hormones, thereby leading to infertility. Insufficient production of gonadotropin-releasing hormone (GnRH) is accompanied with suppressed production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

All the mentioned abnormalities eventually lead to loss of estrogen and progesterone biosynthesis in ovary, the essential hormones required for fertility and pregnancy (89-92).

Interference of thyroid hormones with female sex hormones

Various studies demonstrated the adverse effect of overt hypothyroidism on infertility. In severe cases, hypothyroidism can cause ovulation and menstrual disorders. Interference of hypothyroidism with women sex hormones is the basis of infertility in women (93-99).

Such disruption consequently exerts its effect on the production of female sex hormones and prolactin levels. Hypothyroidism affects the level of female sex hormones by manipulating the production of LH. On the other hand, GnRH, LH, and FSH are the main hypothalamus-pituitary hormones crucial for estrogen production in ovaries (100-104). These studies clearly indicate the role played by thyroid hormones on women’s fertility and reproductive physiology. As mentioned earlier, Hashimoto’s disease is one of main causes of hypothyroidism. Studies demonstrate that the incidence of autoimmunity-related hypothyroidism is higher among females compared to males. There is also a significant correlation between autoimmunity and reproductive disorders among women of childbearing age (105-109).

CONCLUSION

Hypothyroidism can have adverse effects on reproductive physiology and some metabolic functions, which are impaired due to sex hormones disorders following the thyroid hormones suppression.
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REFERENCES


Maternal hypothyroxinaemia

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Pak J Biol View PubMed Google

Int J Gynecol Endocrinol. View


46. WF Simons, PW Fuggle, DB Grant, I Smith. Intellectual development at 10 years in early treated congenital hypothyroidism. Arch Dis Child. 1994; 71(3): 232-234 [View at Publisher] [DOI:10.1136/adc.71.3.232] [PubMed] [Google Scholar]


79. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. JAMA. 2004;291:228-38. [View at Publisher] [DOI:10.1001/jama.291.2.228] [PubMed] [Google Scholar]


88. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. JAMA. 2004;291:228-38. [View at Publisher] [DOI:10.1001/jama.291.2.228] [PubMed] [Google Scholar]


93. Petta CA, Arruda MS, Zantut-Wittmann DE, Benetti-Pinto CL. Thyroid autoimmunity and thyroid dysfunction in women with endometriosis. Hum Reprod. 2007;22(10):2693-7. [View at Publisher] [DOI:10.1093/humrep/dem267] [PubMed] [Google Scholar]

94. Krassas GE, Poppe K, Ginoer D. Thyroid function and human reproductive health. Endocr Rev. 2010; 31(5): 702-55. [View at Publisher] [DOI] [PubMed] [Google Scholar]


96. Samantha Anandappaa, Manta Joshi, Lukasz Polanski, Paul V. Carroll , Thyroid disorders in subfertility and early pregnancyTherAdvEndocrinolMetab. 2020; 11 [DOI:10.1177/2042018820945855] [PubMed] [Google Scholar]


100. Mansourian AR, Sifi A, Mansourian HR. Serum thyroid level during the first trimester of pregnancy. J Clin Diagn Res. 2011; 5: 733-736. [View at Publisher] [Google Scholar]


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