Medical Laboratory Journal
Online ISSN: 2538-4449
Golestan University of Medical Sciences

Review Article

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 Emegency. Hakim JorjaniHospital.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

Received: 2021/06/27
Revised: 2021/08/12
Accepted: 2021/08/30

DOI: 10.29252/mlj.16.4.1

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.

ACKNOWLEDGMENTS
None.

DECLARATIONS
Funding
Not applicable.

Ethics approvals and consent to participate
Not applicable.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest regarding publication of this article.

REFERENCES
1. Beynon ME, Pinneri K. *An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist.* Acad Forensic Pathol. 2016; 6(2): 217-236. [View at Publisher] [DOI:10.23907/2016.024] [PubMed] [Google Scholar]

2. Colin IM, Denef JF, Lengelé B, Many MC, Gérard AC. *Recent insights into the cell biology of thyroid angiofollicular units.* Endocr Rev. 2013; 34(2): 209-38. [View at Publisher] [DOI:10.1210/er.2012-1015] [PubMed] [Google Scholar]

3. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al. *American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement*. Thyroid. 2014; 24(12): 1670-751. [View at Publisher] [DOI] [PubMed] [Google Scholar]

4. Wang C, Crapo LM. *The epidemiology of thyroid disease and implications for screening.* Endocrinol Metab Clin North Am. 1997; 26(1): 189-218. [DOI:10.1016/S0889-8529(05)70240-1] [PubMed] [Google Scholar]

5. Mansourian AR. *Metabolic pathways of tetraidothyronine and triidothyronine production by thyroid gland: a review of articles*. Pak J Biol Sci. 2011; 14(1): 1-12. [View at Publisher] [DOI:10.3923/pjbs.2011.1.12] [PubMed] [Google Scholar]

6. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, et al. *The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey.* Clin Endocrinol (Oxf). 1995; 43(1): 55-68. [View at Publisher] [DOI:10.1111/j.1365-2265.1995.tb01894.x] [PubMed] [Google Scholar]

7. Mansourian AR. *A review on post-puberty hypothyroidism: a glance at myxedema*. Pak J Biol Sci. 2010; 13(18): 866-76. [View at Publisher] [DOI:10.3923/pjbs.2010.866.876] [PubMed] [Google Scholar]

8. Mansourian AR. *The immune system which adversely alter thyroid functions: a review on the concept of autoimmunity.* Pak J Biol Sci. 2010; 13(16): 765-74. [View at Publisher] [DOI:10.3923/pjbs.2010.765.774] [PubMed] [Google Scholar]

9. Mansourian AR *Abnormal serum thyroid hormones concentration with healthy functional gland: a review on the metabolic role of thyroid hormones transporter proteins Pakistan* Journal of Biological Sciences. 2011; 14(5): 313-326. [View at Publisher] [DOI:10.3923/pjbs.2011.313.326] [PubMed] [Google Scholar]

10. Kiran Z, Sheikh A, Malik S, Meraj A, Masood M, Ismail S, et al. *Maternal characteristics and outcomes affected by hypothyroidism during pregnancy (maternal hypothyroidism on pregnancy outcomes, MHPO-1).* BMC Pregnancy Childbirth. 2019; 19(1): 476. [View at Publisher] [DOI:10.1186/s12884-019-2596-9] [PubMed] [Google Scholar]

11. Chaker L, Bianco AC, Jonklaas J, Peeters RP. *Hypothyroidism.* Lancet. 2017; 390(10101): 1550-1562. [View at Publisher] [DOI:10.1016/S0140-6736(17)30703-1] [PubMed]

12. Schoenmakers N, Alatzoglou KS, Chatterjee VK, Dattani MT. *Recent advances in central congenital hypothyroidism.* J Endocrinol. 2015; 227(3): R51-71. [DOI:10.1530/JOE-15-0341] [PubMed] [Google Scholar]

13. Donaldson M, Jones J. *Optimising outcome in congenital hypothyroidism; current opinions on best practice in initial assessment and subsequent management.* J Clin Res Pediatr Endocrinol. 2013;Suppl 1(Suppl 1):13-22. [View at Publisher] [DOI] [PubMed] [Google Scholar]

14. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. *Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome.* Arch Gynecol Obstet. 2010;281(2):215-20. [View at Publisher] [DOI:10.1007/s00404-009-1105-1] [PubMed] [Google Scholar]

15. Sharmeen M, Shamsunnahar PA, Laita TR, Chowdhury SB. *Overt and subclinical hypothyroidism among Bangladeshi pregnant women and its effect on fetomaternal outcome.* Bangladesh Med Res Counc Bull. 2014; 40(2): 52-7. [DOI:10.3329/bmrcb.v40i2.25183] [PubMed] [Google Scholar]

16. Maraka S, Ospina NM, O'Keeffe DT, Espinosa De Ycaza AE, Gionfriddo MR, Erwin PJ, et al. *Subclinical Hypothyroidism in Pregnancy: A Systematic Review and Meta-Analysis.* Thyroid. 2016; 26(4): 580-90. [View at Publisher] [DOI:10.1089/thy.2015.0418] [PubMed] [Google Scholar]

17. Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients *with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systematic review and meta-analysis*. PLoS One. 2017; 12(4): e0175708. [DOI:10.1371/journal.pone.0175708] [PubMed] [Google Scholar]

18. Abalovich M, Mitelberg L, Allami C, Gutierrez S, Alcaraz G, Otero P, et al. *Subclinical hypothyroidism and thyroid autoimmunity in women with infertlity*. GynecolEndocrinol. 2007; 23(5): 279-83. [View at Publisher] [DOI:10.1080/09513590701259542] [PubMed] [Google Scholar]

19. Eldar-Geva T, Shoham M, Rosler A, Margalioth EJ, Livne K, Meirow D. *Subclinical hypothyroidism in infertile women: the importance of continuous monitoring and the role of the thyrotropin-releasing hormone stimulation test*. GynecolEndocrinol. 2007;23(6):332-7. [View at Publisher] [DOI:10.1080/09513590701267651] [PubMed] [Google Scholar]

20. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG. *Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol.* 2005; 105(2): 239-45. [DOI:10.1097/01.AOG.0000152345.99421.22] [PubMed] [Google Scholar]

21. Reid SM, Middleton P, Cossich MC, Crowther CA, Bain E. *Interventions for clinical and subclinical hypothyroidism pre-pregnancy and during pregnancy*. Cochrane Database Syst Rev. 2013;5:CD007752. [View at Publisher] [DOI:10.1002/14651858.CD007752.pub3] [PubMed] [Google Scholar]

22. Yibing Zhang, Haoyu Wang, Xifeng Pan, WeipingTeng, Zhongyan Shan , *Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systematic review and meta-analysis*, PLoS One. 2017; 12(4): e0175708. [View at Publisher] [DOI:10.1371/journal.pone.0175708] [PubMed] [Google Scholar]

23. Woeber KA. *Subclinical thyroid dysfunction.* Arch Intern Med. 1997;157(10):1065-8. [DOI:10.1001/archinte.1997.00440310023002] [PubMed] [Google Scholar]

24. Abalovich M, Mitelberg L, Allami C, Gutierrez S, Alcaraz G, Otero P, Levalle O. *Subclinical hypothyroidism and thyroid autoimmunity in women with infertility*. Gynecol Endocrinol. 2007; 23(5): 279-83. [View at Publisher] [DOI:10.1080/09513590701259542] [PubMed] [Google Scholar]

25. Maraka S, Singh Ospina NM, Mastorakos G, O'Keeffe DT. *Subclinical Hypothyroidism in Women Planning Conception and During Pregnancy: Who Should Be Treated and How?* J Endocr Soc. 2018;2(6):533-546. [View at Publisher] [DOI:10.1210/js.2018-00090] [PubMed] [Google Scholar]

26. Mansourian AR. *Thyroid function tests during first-trimester of pregnancy: a review of literature*. Pak J Biol Sci. 2010; 13(14): 664-73. [View at Publisher] [DOI:10.3923/pjbs.2010.664.673] [PubMed] [Google Scholar]

27. ,YunYingCai, LanPingZhong, Jie Guan, RuiJinGuo, Ben Niu, YanPing Ma, Heng Su . *Outcome of in vitro fertilization in women with subclinical hypothyroidismReprodBiolEndocrinol.* 2017; 15: 39 [View at Publisher] [DOI:10.1186/s12958-017-0257-2] [PubMed] [Google Scholar]

28. Raber W, Nowotny P, Vytiska-Binstorfer E, Vierhapper H. *Thyroxine treatment modified in infertile women according to thyroxine-releasing hormone testing: 5 year follow-up of 283 women referred after exclusion of absolute causes of infertility*. Hum Reprod. 2003;18(4):707-14. [View at Publisher] [DOI:10.1093/humrep/deg142] [PubMed] [Google Scholar]

29. Nambiar V, Jagtap VS, Sarathi V, Lila AR, Kamalanathan S, Bandgar TR, et al. *Prevalence and impact of thyroid disorders on maternal outcome in asian-Indian pregnant women*. J Thyroid Res. 2011;2011:429097. [View at Publisher] [DOI:10.4061/2011/429097] [PubMed] [Google Scholar]

30. Dhanwal DK, Bajaj S, Rajput R, Subramaniam KA, Chowdhury S, Bhandari R, et al. *Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India*. Indian J Endocrinol Metab. 2016; 20(3): 387-90. [View at Publisher] [DOI:10.4103/2230-8210.179992] [PubMed] [Google Scholar]

31. Pop VJ, Brouwers EP, Vader HL, Vulsma T, Van Baar AL, De Vijlder JJ. *Maternal hypothyroxinaemia during early pregnancy and subsequent child development: a 3-year follow-up study*. ClinEndocrinol. 2003; 59(3): 282-8. [View at Publisher] [DOI:10.1046/j.1365-2265.2003.01822.x] [PubMed] [Google Scholar]

32. Arojoki M, Jokimaa V, Juuti A, Koskinen P, Irjala K, Anttila L. *Hypothyroidism among infertile women in Finland.* Gynecol Endocrinol. 2000; 14(2): 127-31. [View at Publisher] [DOI:10.3109/09513590009167671] [PubMed] [Google Scholar]

33. Yadav V, Dabar D, Goel AD, Bairwa M, Sood A, Prasad P, et al. *Prevalence of Hypothyroidism in Pregnant Women in India: A Meta-Analysis of Observational Studies.* J Thyroid Res. 2021; 2021: 5515831. [View at Publisher] [DOI:10.1155/2021/5515831] [PubMed] [Google Scholar]

34. Feldthusen AD, Pedersen PL, Larsen J, Toft Kristensen T, Ellervik C, Kvetny J. *Impaired Fertility Associated with Subclinical Hypothyroidism and Thyroid Autoimmunity: The Danish General Suburban Population Study.* J Pregnancy. 2015;2015:132718. [View at Publisher] [DOI:10.1155/2015/132718] [PubMed] [Google Scholar]

35. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. *Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child*. N Engl J Med. 1999; 341(8): 549-55. [View at Publisher] [DOI:10.1056/NEJM199908193410801] [PubMed]

36. Vanes NK, Charlesworth D, Imtiaz R, Cox P, Kilby MD, Chan SY. *Optimal treatment of hypothyroidism associated with live birth in cases of previous recurrent placental abruption and stillbirth*. Int J Gynecol Obstet. 2013;123(3):196-9. [View at Publisher] [DOI:10.1016/j.ijgo.2013.05.025] [PubMed] [Google Scholar]

37. Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. *Perinatal outcome in hypothyroid pregnancies.* Obstet Gynecol. 1993; 81(3): 349-53. [View at Publisher] [PubMed] [Google Scholar]

38. Idris I, Srinivasan R, Simm A, Page RC. *Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome.* ClinEndocrinol. 2005; 63(5): 560-5. [View at Publisher] [DOI:10.1111/j.1365-2265.2005.02382.x] [PubMed] [Google Scholar]

39. Cao XY, Jiang XM, Dou ZH, Rakeman MA, Zhang ML, O'Donnell K, et al. *Timing of vulnerability of the brain to iodine deficiency in endemic cretinism*. N Engl J Med. 1994; 331(26): 1739-44. [View at Publisher] [DOI:10.1056/NEJM199412293312603] [PubMed] [Google Scholar]

40. Salas-Lucia F, Pacheco-Torres J, González-Granero S, García-Verdugo JM, Berbel P. *Transient Hypothyroidism During Lactation Alters the Development of the Corpus Callosum in Rats. An in vivo Magnetic Resonance Image and Electron Microscopy Study*. Front Neuroanat. 2020; 14: 33. [View at Publisher] [DOI:10.3389/fnana.2020.00033] [PubMed] [Google Scholar]

40. Salas-Lucia F, Pacheco-Torres J, González-Granero S, García-Verdugo JM, Berbel P. *Transient Hypothyroidism During Lactation Alters the Development of the Corpus Callosum in Rats. An in vivo Magnetic Resonance Image and Electron Microscopy Study*. Front Neuroanat. 2020; 14: 33. [View at Publisher] [DOI:10.3389/fnana.2020.00033] [PubMed] [Google Scholar]

41. Biondi B, Kahaly GJ, Robertson RP. *Thyroid Dysfunction and Diabetes Mellitus: Two Closely Associated Disorders.* Endocr Rev. 2019; 40(3): 789-824. [View at Publisher] [DOI:10.1210/er.2018-00163] [PubMed] [Google Scholar]

42. Hromadnikova I, Kotlabova K, Dvorakova L, Krofta L, Sirc J. *Substantially Altered Expression Profile of Diabetes/Cardiovascular/Cerebrovascular Disease Associated microRNAs in Children Descending from Pregnancy Complicated by Gestational Diabetes Mellitus-One of Several Possible Reasons for an Increased Cardiovascular Risk.* Cells. 2020; 9(6): 1557. [View at Publisher] [DOI:10.3390/cells9061557] [PubMed] [Google Scholar]

43. Haddow JE, Craig WY, Neveux LM, Palomaki GE, Lambert-Messerlian G, Malone FD, et al. *First and Second Trimester Risk of Aneuploidy (FaSTER) Research Consortium. Free Thyroxine During Early Pregnancy and Risk for Gestational Diabetes*. PLoS One. 2016; 11(2): e0149065. [View at Publisher] [DOI:10.1371/journal.pone.0149065] [PubMed]

44. Panuganti PL, Hinkle SN, Rawal S, Grunnet LG, Lin Y, Liu A, et al. *Lactation Duration and Long-Term Thyroid Function: A Study among Women with Gestational Diabetes.* Nutrients. 2018; 10(7): 938. [View at Publisher] [DOI:10.3390/nu10070938] [PubMed] [Google Scholar]

45. Cherella CE, Wassner AJ. *Congenital hypothyroidism: insights into pathogenesis and treatment. Int J Pediatr Endocrinol.* 2017;2017:11. [View at Publisher] [DOI:10.1186/s13633-017-0051-0] [PubMed] [Google Scholar]

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]

47. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. *The Colorado thyroid disease prevalence study*. Arch Intern Med. 2000; 160(4): 526-34. [View at Publisher] [DOI:10.1001/archinte.160.4.526] [PubMed] [Google Scholar]

48. Barber KJ, Franklyn JA, McCabe CJ, Khanim FL, Bulmer JN, Whitley GS, et al. *The in vitro effects of triiodothyronine on epidermal growth factor-induced trophoblast function.* J Clin Endocrinol Metab. 2005; 90(3): 1655-61. [View at Publisher] [DOI:10.1210/jc.2004-0785] [PubMed] [Google Scholar]

49. Kim YM, Bujold E, Chaiworapongsa T, Gomez R, Yoon BH, Thaler HT, et al. *Failure of physiologic transformation of the spiral arteries in patients with preterm labor and intact membranes*. Am J Obstet Gynecol. 2003;189(4):1063-9. [View at Publisher] [DOI:10.1067/S0002-9378(03)00838-X] [PubMed] [Google Scholar]

50. Stagnaro-Green A, Chen X, Bogden JD, Davies TF, Scholl TO. *The thyroid and pregnancy: a novel risk factor for very preterm delivery.* Thyroid. 2005;15(4):351-7. [View at Publisher] [DOI:10.1089/thy.2005.15.351] [PubMed] [Google Scholar]

51. Yang Y, Hou Y, Wang H, Gao X, Wang X, Li J, Teng W, Shan Z. *Maternal Thyroid Dysfunction and Gestational Anemia Risk: Meta-Analysis and New Data.* Front Endocrinol (Lausanne). 2020; 11: 201. [View at Publisher] [DOI:10.3389/fendo.2020.00201] [PubMed] [Google Scholar]

52. Eschler DC, Kulina G, Garcia-Ocana A, Li J, Kraus T, Levy CJ. *Circulating Levels of Bone and Inflammatory Markers in Gestational Diabetes Mellitus.* Biores Open Access. 2018; 7(1): 123-130. [View at Publisher] [DOI:10.1089/biores.2018.0013] [PubMed] [Google Scholar]

53. Hemati Z, Hashemipour M, Hovsepian S, Mansourian M, Zandieh M, Ahmadian M, et al. *Congenital hypothyroidism in different cities of the Isfahan province: A descriptive retrospective study*. J Educ Health Promot. 2019; 8: 137. [DOI:10.4103/jehp.jehp_219_18] [PubMed] [Google Scholar]

54. Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G,et al. *European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism.* J Clin Endocrinol Metab. 2014; 99(2): 363-84. [View at Publisher] [DOI:10.1210/jc.2013-1891] [PubMed] [Google Scholar]

55. Kalra S, Aggarwal S, Khandelwal D. *Thyroid Dysfunction and Type 2 Diabetes Mellitus: Screening Strategies and Implications for Management*. Diabetes Ther. 2019; 10(6): 2035-2044. [View at Publisher] [DOI:10.1007/s13300-019-00700-4] [PubMed] [Google Scholar]

56. Liu H, Shan Z, Li C, Mao J, Xie X, Wang W, et al. *Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study*. Thyroid. 2014; 24(11): 1642-9. [View at Publisher] [DOI:10.1089/thy.2014.0029] [PubMed] [Google Scholar]

57. Bartáková J, Potluková E, Rogalewicz V, Fait T, Schöndorfová D, Telička Z, et al. *Screening for autoimmune thyroid disorders after spontaneous abortion is cost-saving and it improves the subsequent pregnancy rate.* BMC Pregnancy Childbirth. 2013;13:217. [View at Publisher] [DOI:10.1186/1471-2393-13-217] [PubMed] [Google Scholar]

58. Lata K, Dutta P, Sridhar S, Rohilla M, Srinivasan A, Prashad GR, et al. *Thyroid autoimmunity and obstetric outcomes in women with recurrent miscarriage: a case-control study.* Endocr Connect. 2013; 2(2):118-24. [View at Publisher] [DOI:10.1530/EC-13-0012] [PubMed] [Google Scholar]

59. Kaur R, Gupta K. *Endocrine dysfunction and recurrent spontaneous abortion: An overview*. Int J Appl Basic Med Res. 2016; 6(2): 79-83. [DOI:10.4103/2229-516X.179024] [PubMed] [Google Scholar]

60. Meng L, Rijntjes E, Swarts HJ, Keijer J, Teerds KJ. *Prolonged hypothyroidism severely reduces ovarian follicular reserve in adult rats*. J Ovarian Res. 2017; 10(1):19. [View at Publisher] [DOI:10.1186/s13048-017-0314-7] [PubMed] [Google Scholar]

61. Gracia CR, Morse CB, Chan G, Schilling S, Prewitt M, Sammel MD, et al. *Thyroid function during controlled ovarian hyperstimulation as part of in vitro fertilization.* Fertil Steril. 2012; 97(3): 585-91. [View at Publisher] [DOI:10.1016/j.fertnstert.2011.12.023] [PubMed] [Google Scholar]

62. Rodríguez-Castelán J, Méndez-Tepepa M, Carrillo-Portillo Y, Anaya-Hernández A, Rodríguez-Antolín J, Zambrano E, et al. *Hypothyroidism Reduces the Size of Ovarian Follicles and Promotes Hypertrophy of Periovarian Fat with Infiltration of Macrophages in Adult Rabbits*. Biomed Res Int. 2017;2017:3795950. [View at Publisher] [DOI:10.1155/2017/3795950] [PubMed] [Google Scholar]

63. Kaprara A, Krassas GE. *Thyroid autoimmunity and miscarriage.* Hormones (Athens). 2008; 7(4): 294-302. [View at Publisher] [DOI:10.14310/horm.2002.1210] [PubMed] [Google Scholar]

64. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. *High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome*. Eur J Endocrinol. 2004;150(3):363-9. [DOI:10.1530/eje.0.1500363] [PubMed] [Google Scholar]

65. Mahadik K, Choudhary P, Roy PK. *Study of thyroid function in pregnancy, its feto-maternal outcome; a prospective observational study*. BMC Pregnancy Childbirth. 2020;20(1):769. [View at Publisher] [DOI:10.1186/s12884-020-03448-z] [PubMed] [Google Scholar]

66. Meng L, Rijntjes E, Swarts HJ, Keijer J, Teerds KJ. *Prolonged hypothyroidism severely reduces ovarian follicular reserve in adult rats*. J Ovarian Res. 2017;10(1):19. [View at Publisher] [DOI:10.1186/s13048-017-0314-7] [PubMed] [Google Scholar]

67. Wilson KL, Casey BM, McIntire DD, Halvorson LM, Cunningham FG. *Subclinical thyroid disease and the incidence of hypertension in pregnancy*. Obstet Gynecol. 2012; 119(2 Pt 1): 315-20. [View at Publisher] [DOI:10.1097/AOG.0b013e318240de6a] [PubMed] [Google Scholar]

68. Klein RZ, Haddow JE, Faix JD, Brown RS, Hermos RJ, Pulkkinen A, et al. *Prevalence of thyroid deficiency in pregnant women*. ClinEndocrinol. 1991;35(1):41-6. [View at Publisher] [DOI:10.1111/j.1365-2265.1991.tb03494.x] [PubMed] [Google Scholar]

69. Poppe K, Glinoer D, Tournaye H, Maniewski U, Haentjens P, Velkeniers B. *Is systematic screening for thyroid disorders indicated in subfertile men?* Eur J Endocrinol. 2006;154(3):363-6. [View at Publisher] [DOI:10.1097/AOG.0b013e318240de6a] [Google Scholar]

70. Glinoer D. *The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology*. Endocr Rev. 1997;18:404-33 [View at Publisher] [DOI:10.1210/edrv.18.3.0300] [Google Scholar]

71. Verma I, Sood R, Juneja S, Kaur S. *Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility.* Int J Appl Basic Med Res. 2012;2:17-9. [DOI:10.4103/2229-516X.96795] [PubMed]

72. Poppe K, Glinoer D, Van Steirteghem A, Tournaye H, Devroey P, Schiettecatte J, et al. *Thyroid dysfunction and autoimmunity in infertile women.*Thyroid.2002;12:997-1001. [View at Publisher] [DOI:10.1089/105072502320908330] [PubMed] [Google Scholar]

73. Stagnaro-Green A, Roman SH, Cobin RH, el-Harazy E, Alvarez-Marfany M, Davies TF. *Detection of at-risk pregnancy by means of highly sensitive assays for thyroid autoantibodies.* JAMA. 1990; 264:1422-5. [View at Publisher] [DOI:10.1001/jama.264.11.1422] [PubMed] [Google Scholar]

74. Karbownik-Lewinska M. *Thyroid dysfunction during pregnancy.* Thyroid Res. 2015;8(Suppl 1):A15 [View at Publisher] [DOI:10.1186/1756-6614-8-S1-A15] [PubMed] [Google Scholar]

75. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. *Overt and subclinical hypothyroidism complicating pregnancy*. Thyroid. 2002;12:63-8. [View at Publisher] [DOI:10.1089/105072502753451986] [PubMed] [Google Scholar]

76. Maggi R, Cariboni AM, Marelli MM, Moretti RM, Andrè V, Marzagalli M, et al. *GnRH and GnRH receptors in the pathophysiology of the human female reproductive system.* Hum Reprod Update. 2016;22:358-81. [View at Publisher] [DOI:10.1093/humupd/dmv059] [PubMed] [Google Scholar]

77. Berga SL, Mortola JF, Girton L, Suh B, Laughlin G, Pham P, et al. *Neuroendocrine aberrations in women with functional hypothalamic amenorrhea.* J Clin Endocrinol Metab. 1989;68:301-8 [View at Publisher] [DOI:10.1210/jcem-68-2-301] [PubMed] [Google Scholar]

78. Cramer DW, Sluss PM, Powers RD, McShane P, Ginsburgs ES, Hornstein MD, et al. *Serum prolactin and TSH in an in vitro fertilization population: Is there a link between fertilization and thyroid function?* J Assist Reprod Genet. 2003;20:210-5. [View at Publisher] [DOI] [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]

80. Zollner U, Lanig K, Steck T, Dietl J. *Assessment of endocrine status in patients undergoing in vitro fertilization treatment? Is it necessary.* Arch Gynecol Obstet. 2001;265:16-20. [View at Publisher] [DOI:10.1007/s004040000110] [PubMed] [Google Scholar]

81. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. *2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum.* Thyroid. 2017 Mar;27(3):315-389. doi: 10.1089/thy.2016.0457. Erratum in: Thyroid. 2017;27(9):1212. [View at Publisher] [DOI:10.1089/thy.2016.0457] [PubMed]

82. Maraka S, Mwangi R, McCoy RG, Yao X, Sangaralingham LR, Singh Ospina NM, et al. *Thyroid hormone treatment among pregnant women with subclinical hypothyroidism: US national assessment.* BMJ. 2017; 356: i6865. [DOI:10.1136/bmj.i6865] [PubMed] [Google Scholar]

83. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. *Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III).* J Clin Endocrinol Metab. 2002;87(2):489-99. [View at Publisher] [DOI:10.1210/jcem.87.2.8182] [PubMed]

84. Poppe K, Glinoer D, Van Steirteghem A, Tournaye H, Devroey P, Schiettecatte J, et al. *Thyroid dysfunction and autoimmunity in infertile women*. Thyroid. 2002;12(11):997-1001. [View at Publisher] [DOI:10.1089/105072502320908330] [PubMed] [Google Scholar]

85. Iravani AT, Saeedi MM, Pakravesh J, Hamidi S, Abbasi M. *Thyroid autoimmunity and recurrent spontaneous abortion in Iran: a case-control study.* Endocr Pract. 2008;14(4):458-64. [View at Publisher] [DOI:10.4158/EP.14.4.458] [PubMed] [Google Scholar]

86. Kutteh WH, Schoolcraft WB, Scott RT Jr. *Antithyroid antibodies do not affect pregnancy outcome in women undergoing assisted reproduction.* Hum Reprod. 1999;14(11):2886-90. [View at Publisher] [DOI:10.1093/humrep/14.11.2886] [PubMed] [Google Scholar]

87. Aghajanova L, Lindeberg M, Carlsson IB, Stavreus-Evers A, Zhang P, Scott JE, Hovatta O, Skjöldebrand-Sparre L. *Receptors for thyroid-stimulating hormone and thyroid hormones in human ovarian tissue*. Reprod Biomed Online. 2009 ;18(3):337-47. [View at Publisher] [DOI:10.1016/S1472-6483(10)60091-0] [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]

89. Cramer DW, Sluss PM, Powers RD, McShane P, Ginsburgs ES, Hornstein MD, et al. *Serum prolactin and TSH in an in vitro fertilization population: is there a link between fertilization and thyroid function?* J Assist Reprod Genet. 2003;20(6):210-5. [View at Publisher] [DOI] [PubMed] [Google Scholar]

90. Acharya N, Acharya S, Shukla S, Inamdar SA, Khatri M, Mahajan SN. *Gonadotropin levels in hypothyroid women of reproductive age group.* J Obstet Gynaecol India. 2011;61(5):550-3. [View at Publisher] [DOI:10.1007/s13224-011-0079-7] [PubMed] [Google Scholar]

91. Poppe K, Bisschop P, Fugazzola L, Minziori G, Unuane D, Weghofer A. *2021 European Thyroid Association Guideline on Thyroid Disorders prior to and during Assisted Reproduction*. Eur Thyroid J. 2021;9(6):281-295. [View at Publisher] [DOI] [PubMed] [Google Scholar]

92. Sun J, Hui C, Xia T, Xu M, Deng D, Pan F, Wang Y. *Effect of hypothyroidism on the hypothalamic-pituitary-ovarian axis and reproductive function of pregnant rats.* BMC Endocr Disord. 2018;18(1):30. [View at Publisher] [DOI:10.1186/s12902-018-0258-y] [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, Glinoer D. *Thyroid function and human reproductive health.* Endocr Rev. 2010; 31(5): 702-55. [View at Publisher] [DOI] [PubMed] [Google Scholar]

95. Grassi G, Balsamo A, Ansaldi C, Balbo A, Massobrio M, Benedetto C. *Thyroid autoimmunity and infertility.* Gynecol Endocrinol. 2001;15(5):389-96. PMID: 11727362. [View at Publisher] [DOI:10.1080/gye.15.5.389.396] [PubMed] [Google Scholar]

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

97. Poppe K, Glinoer D, Tournaye H, Devroey P, Schiettecatte J, Haentjens P, Velkeniers B. *Thyroid autoimmunity and female infertility*. Verh K Acad Geneeskd Belg. 2006;68(5-6):357-77. [PubMed] [Google Scholar]

98. Redmond GP. *Thyroid dysfunction and women's reproductive health.* Thyroid. 2004;14 Suppl 1:S5-15. [View at Publisher] [DOI:10.1089/105072504323024543] [PubMed] [Google Scholar]

99. Poppe K, Velkeniers B, Glinoer D. *Thyroid disease and female reproduction.* Clin Endocrinol (Oxf). 2007;66(3):309-21. [View at Publisher] [DOI:10.1111/j.1365-2265.2007.02752.x] [PubMed] [Google Scholar]

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

101. Jiashu Li, Aihua Liu, Haixia Liu, Chenyan Li, Weiwei Wang, Cheng Han, et al. *Maternal TSH levels at first trimester and subsequent spontaneous miscarriage: a nested case-control study.* Endocr Connect. 2019; 8(9): 1288-1293. [DOI:10.1530/EC-19-0316] [PubMed] [Google Scholar]

102. Verma I, Sood R, Juneja S, Kaur S. *Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility.* Int J Appl Basic Med Res. 2012; 2(1): 17-9. [View at Publisher] [DOI:10.4103/2229-516X.96795] [PubMed] [Google Scholar]

103. Akhtar MA, Agrawal R, Brown J, Sajjad Y, Craciunas L. *Thyroxine replacement for subfertile women with euthyroid autoimmune thyroid disease or subclinical hypothyroidism.* Cochrane Database Syst Rev. 2019; 6(6): CD011009. [View at Publisher] [DOI:10.1002/14651858.CD011009.pub2] [PubMed] [Google Scholar]

104. Wadhwa L, Marghret KM, Arora S. *Evaluation of Reproductive Outcome in Infertile Hypothyroid Women on Thyroxine Therapy*. J Hum Reprod Sci. 2020;13(4):272-276. [View at Publisher] [DOI:10.4103/jhrs.JHRS_14_20] [PubMed] [Google Scholar]

105. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, Grobman WA, Laurberg P, Lazarus JH, Mandel SJ, Peeters RP, Sullivan S. *2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum.* Thyroid. 2017;27(3):315-389. [View at Publisher] [DOI:10.4103/2229-516X.96795] [PubMed] [Google Scholar]

106. Allam MM, El-Zawawy HT, Barakat SS, Ahmed SM, Saleh RNM. *A hidden cause of infertility in hypothyroid patients.* Clin Case Rep. 2020; 8(2):374-378. [View at Publisher] [DOI:10.1002/ccr3.2654] [PubMed] [Google Scholar]

107. Reimand K, Talja I, Metsküla K, Kadastik U, Matt K, Uibo R. *Autoantibody studies of female patients with reproductive failure.* J Reprod Immunol. 2001;51(2):167-76. [View at Publisher] [DOI:10.1016/S0165-0378(01)00075-4] [PubMed] [Google Scholar]

108. Priya DM, Akhtar N, Ahmad J. *Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility.* Indian J Endocrinol Metab. 2015;19(4): 504-6. [DOI:10.4103/2230-8210.159058] [PubMed] [Google Scholar]

109. Kiran Z, Sheikh A, Islam N. *Association of thyroid antibodies status on the outcomes of pregnant women with hypothyroidism (maternal hypothyroidism on pregnancy outcomes, MHPO-4).* BMC Pregnancy Childbirth. 2021;21(1):136. [View at Publisher] [DOI:10.1186/s12884-021-03594-y] [PubMed] [Google Scholar]

How to Cite:
Seifi A, Taheri N, Kia H, Mansourian H R, Mansourian AR[Adverse Effects of Hypothyroidism on Fertility and Pregnancy: A Mini Review]. mljgoums. 2022; 16(4): 1-9 DOI: 10.29252/mlj.16.4.1