

# Management and Treatment Protocols in Sociology of Gender: Role of Thyroid Hormone Dysfunctioning in Infertility

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## Abstract

*This study aims to provide an overview of the current understanding of the intricate connections between hypothyroidism and infertility in both males and females. It also highlights the knowledge gap about the involvement of thyroid hormone in infertility or reproductive system failure. It discusses pregnancy abnormalities, including miscarriage and the effects of hypothyroidism on the fetus and mother. The physiology of the human reproductive system and many other organs, including the male and female gonads, may be linked to the thyroid hormone's proper functioning. The likelihood of becoming pregnant is reduced, or the course of the pregnancy may be affected by thyroid hormone dysfunction. Thus, early infertility screening should include measuring PRL (Prolactin level) and TSH (Thyroid-stimulating hormone) rather than immediately pursuing more expensive or invasive tests. For otherwise asymptomatic infertile women, a straightforward, three-month to one-year course of oral hypothyroidism medication can be helpful toward achieving conception. According to the value of TSH, hypothyroidism is sub-classified into two classes. If the TSH value is 4-6  $\mu$ IU/ml, it is called sub-clinical hypothyroidism, and in clinical hypothyroidism, the TSH value is  $>$  six  $\mu$ IU/ml. Our society usually links infertility with women's issues. In terms of the female problem, poor thyroid function has a negative impact on the results of both spontaneous and assisted reproductive technologies (ART) pregnancies. Conversely, the influence of thyroid function on the male reproductive system remains unclear. At the same time, it may play a part by altering the activity of Sertoli and Leydig cells and spermatogenesis. Given that medication is usually immediate and likely to increase chances of success, thyroid function should be closely monitored in both male and female partners attempting spontaneous conception as well as those using assisted reproductive technology.*

**Keywords:** Sociology, Gender, Thyroid Dysfunction, Infertility, Treatment.

## Introduction

Most medical sociologists agree that rather than viewing health and sickness as objectively measurable states, socially produced classes created by medical professionals, patients, and others in a sociocultural context are the best approach to comprehending them. A social context determines what constitutes abnormality, how to describe it, and whether any action should be taken to address its symptoms. Both how sufferers view themselves and how others perceive them are outcomes of social definition processes (Greil et al., 2010). In the case of infertility, the social construction of health and illness may be much more evident than in the case of other disorders (Greil et al., 1988). Trouble to conceive, infertility, or subfertility is a leading social and psychological burden (McQuillan et al., 2003; Kris et al., 2004). Infertility is a problem when an individual is unable to conceive or to establish a clinical pregnancy within twelve months of a regular unprotected sexual relationship. About 8-12 % of couples of reproductive

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ages are affected worldwide due to infertility (Vander et al., 2018). Among these, 50% of males contribute to it. However, unfortunately, infertility is considered to be a women-centric problem only. Usually, infertility is seen by the wives as a catastrophic role failure, and husbands typically view infertility as an unsettling circumstance rather than a tragic event. Infertility frequently perceived by couples is considered as an issue for women. The clashing views of husbands and wives on infertility frequently resulted in frustration and a lack of communication. These interactions between wives, husbands, and healthcare providers may lead patients to overlook treatment possibilities or adhere to the incorrect course of therapy. (Greil et al., 1988). Frequently, genetic factors contribute to male infertility. Non-genetic causes include hypogonadotropic hypogonadism, testicular maldescence, structural problems with the male genital tract (like sperm duct obstruction and sperm agglutination), genital infections, impotence, previous scrotal or inguinal surgery, varicoceles, chronic illness, medication, chemical exposure, environmental factors, and immunological causes. (Poongothai et al., 2009). Among females are endometriosis, tubal damage, and ovulatory dysfunction (OD) (Grigorescu et al., 2014; Poppe et al., 2002; Vander et al., 2018). The majority of infertility cases are from underdeveloped countries that have poor availability of assisted reproductive techniques (ARTs) (Inhorn & Patrizio, 2015).

Except for ART and spontaneous pregnancy, the thyroid function of males and females also impacts the reproductive systems (Krassas et al., 2010; Vander et al., 2018). Thyroid dysfunction is another primary reason that reduces the chances of pregnancy if conceived; chances of complications increase intensively (Poppe & Velkeniers, 2002).

This review will focus on thyroid function and its impact on male and female infertility and possible effects on pregnancy if thyroid dysfunction occurs during pregnancy (Lazarus, 2011).

### **Hypothyroidism in Female**

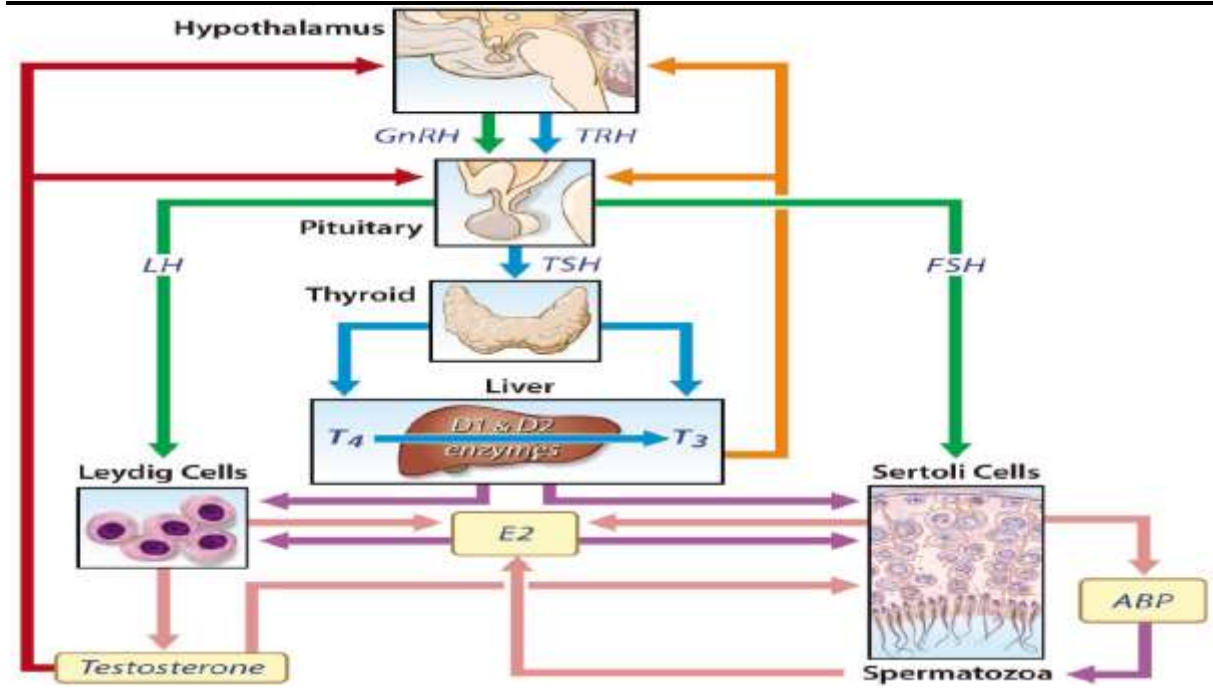
If the thyroid is not functioning correctly, it may change the reproductive cycle by affecting the hormonal system in various ways. It may disturb the luteal phase, increase prolactin levels, or cause sexual hormonal imbalance. Therefore, proper thyroid hormone functioning is necessary for conception and maintaining a healthy pregnancy. Physicians recommend the thyroid profile for women who are not able to conceive naturally within one year of sexual intercourse without using any preventive measures, have multiple miscarriages, or have irregular menstrual cycles (Verma et al., 2012).

If thyroid function is not under control, it may also influence the health of the fetus and mother (Glinoe, 2003). Untreated thyroid dysfunction during pregnancy is harmful to the maternal healthy being and the fetus. The harmful effects of thyroid dysfunction also impair the early childhood development of the growing child's brain, which is unrelated to pregnancy and delivery (Alemu et al., 2016; Sakr & Sakr, 2020).

### **Hypothyroidism in Male**

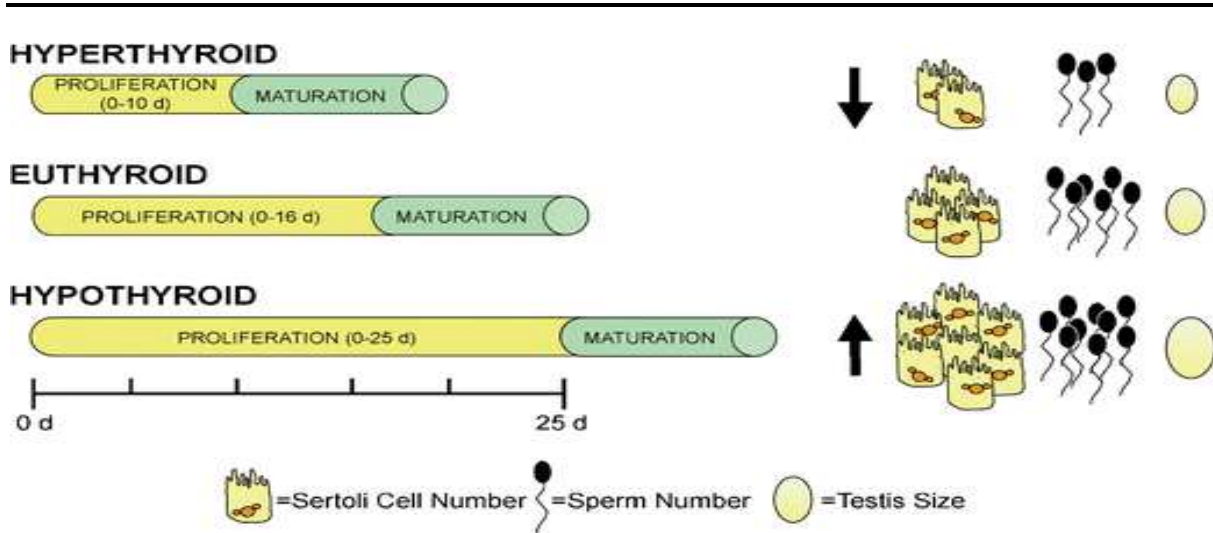
The thyroid gland, which was once thought to have no bearing on spermatogenesis and male fertility, is now understood to impact male reproductive activities substantially. Between 1970 and 2000, much research on the impact of the thyroid gland on fertility was carried out (Singh et al., 2011). Numerous human and animal studies on the impact of thyroid hormone variations on the reproductive system have usually demonstrated that deviations from typical thyroid function result in decreased libido and productiveness (Krassas et al., 2010; Sengupta, 2013). Fortunately, hypothyroidism in men is relatively uncommon, with a 0.1% prevalence rate in the general population (Krassas et al., 2003). The male reproductive system, spermatogenesis, and male fertility have all been linked to the thyroid since the discovery of thyroid receptors on the testicles (Rajender et al., 2011).

**Figure 1 Role of thyroid in testicular development and spermatogenesis**



Further research into the role of thyroid hormones in male reproductive system has begun with the discovery of thyroid hormone receptors on Sertoli cells, the cells that support sperm in the testis. Since Sertoli cells and spermatogenesis are in close proximity, thyroid hormones must have a key regulatory role in sperm formation. Therefore, spermatogenesis and male fertility may be impacted by thyroid function issues (Singh et al., 2011).

**Figure 2 Role of thyroid hormone in sertoli cell development**



Semen quality was negatively impacted by hypothyroidism due to a reduction in the volume of semen and enhanced sperm motility (Krassas et al., 2008). Sperm characteristics, including sperm count, morphology, and motility, are negatively impacted by hypothyroidism, including erectile function. Thyroid hormone assessment is advised in patients with erectile dysfunction and abnormal sperm (Nikoobakht et al., 2012).

### **Physiological Aspects of the Thyroid-Reproductive Function Interplay**

Men and non-pregnant women have the same extrathyroidal hormone metabolism and thyroid hormone secretion. TSH, T3, T4, and serum T4 levels are identical. However, gender differences in the superior thyroid artery's blood flow pattern indicate estrogen influence (Chan et al., 1998).

Hypothyroidism results in a reduction in SHBG (sex hormone-binding globulin) production. As a result, testosterone and estradiol levels are lower in serum, even though their free levels are still within normal range. Hypothyroidism also affects the metabolism of androgens and estrogens. In contrast to hyperthyroidism, there is a decrease in androgen secretion, and the metabolic conversion of testosterone changes from androsterone to androstenedione (Gallagher et al., 1966; Gordon & Southern, 1977; Von, 1840).

### **Clinical Hypothyroidism, Female Reproductive Axis, and Female Infertility**

Reduction in secretions of thyroid hormone leads to hypothyroidism, which may be caused by an autoimmune disorder or may be due to any surgical process of the thyroid gland or treatment carried out by using radioactive iodine (Trokoude et al., 2006). I-131, which is a radioactive iodine, is used to treat thyroid cancer and hyperthyroidism by killing the thyroid tissues while keeping the patient hypothyroid or euthyroid (Mumtaz et al., 2009). Treatment with radioactive iodine necessitates the need for thyroxine for a prolonged period. Chances of hypothyroidism usually develop after the first year of treatment with radioactive iodine (Mohamed et al., 2018). Thyroid hormone in the pituitary thyrotrope exerts negative feedback on serum TSH levels, which in turn regulates the secretion of thyroid hormones T3 (triiodothyronine) and T4 (thyroxine) (Bellastella et al., 2021; Fonseca et al., 2013; Spencer et al., 1990). A minor change in serum TSH leads to a more significant difference in serum TSH concentration (Manji et al., 2006; Pohlenz et al., 1999; Ross, 2001). Blood test results demonstrating a high serum TSH level and low T3 and T4 levels will signify clinical hypothyroidism (Andersen et al., 2002).

According to a survey, about 0.5-0.7% of women at the age of reproduction suffer from hypothyroidism (Bjoro et al., 2000; Jg, 2002). The prevalence rate of infertility in women due to TSH level is reported to be about 0.7-4% with only a few studies (Arojoki et al., 2000; Lincoln et al., 1999)

### **Subclinical Hypothyroidism**

The elevation of serum TSH related to the average free concentration of serum T4 is subclinical hypothyroidism. This term is also helpful for patients who have serum TSH in the upper normal range (Ross, 2001; Trokoude et al., 2006). Multiple studies are available that report the incidence of subclinical hypothyroidism 3-15% depending upon the population studies (Canaris et al., 2000; Vanderpump et al., 1995). Subclinical hypothyroidism is the most common thyroid problem. A rise in TSH level leads to no production of the ovum from the ovaries, which may lead to infertility. Therefore, for a healthy pregnancy, it is crucial to identify and treat subclinical hypothyroidism. Ovulatory dysfunction causes a rise in thyrotrophin release hormone (TRH) associated with a high level of prolactin level (hyperprolactinemia) (Olivar et al., 2003; Raber et al., 2003; Sirohi & Singh, 2018). During the treatment period of an infertile woman, TSH and PRL level is monitored on a routine basis, and a high PRL is diagnosed. Treatment of hypothyroidism is first started before evaluating the other causes (Verma et al., 2012).

### **Thyroid Autoimmunity and Infertility**

Thyroid autoimmunity is the most prevalent autoimmune state that affects up to 4% of women during the age of fertility (Alemu et al., 2016).



It has been explored whether autoimmune disorders and infertility are related. (Downey et al., 1989; Ghazeeri & Kutteh, 2001; Kim et al., 2011). The uniqueness of thyroid autoimmunity (AITD) is in two ways (Gligorovi). Firstly, AITD is the most prevalent autoimmune condition in the female population, affecting 5-10% of women of reproductive age. Second, it is the most frequent cause of thyroid failure (subclinical- and overt hyperthyroidism) (Downey et al., 1989; Whiteford & Gonzalez, 1995).

### **Screening of Thyroid Dysfunction and Therapy Plan**

When a woman is diagnosed with multiple miscarriages or infertility, necessary tests, including serum TSH and serum level of anti-thyroid antibodies, must be checked and monitored (Garber et al., 2012). Levothyroxine therapy should be started if thyroid dysfunction is determined to be caused by subclinical or overt hypothyroidism, especially if menstruation is irregular or if assisted reproductive technologies (ART) are used (Kris et al., 2008). In females who are not pregnant, the normal range of TSH measurement is 0.4 to 4.12 mIU/L. Treatment with levothyroxine is started in childbearing-age women with subclinical hypothyroidism if (TSH $\geq$ 10 mIU/L, 1.6  $\mu$ g/kg/day; TSH $<$ 10 mIU/L, 25-75 $\mu$ g/day) (Hubalewska-Dydejczyk et al., 2021). Pregnancy can also bring about additional changes, such as a rise in estrogen levels from high levels of thyroxin-binding globulin (Brent, 1997).

Suppose a woman has a plan for COH (Controlled ovarian hyperstimulation). In that case, she should begin L-Thyroxine therapy if she has high levels of anti-thyroid antibodies or thyroid stimulating hormone (greater than 2.5 mIU/L). However, in the first 20 weeks of pregnancy, if they are not given L-thyroxin, their thyroxine antibodies, and every four weeks, the TSH level should be tested to see if hypothyroidism develops (Cho, 2015).

### **Social Aspects of Infertility**

Infertility is linked to poor outcomes for both physical and mental health, financial hardship, intense social stigma, a higher chance of domestic abuse, and unstable marriages. Men and women are equally likely to be infertile. However, women are more frequently burdened by infertility in society, especially in cultures where a woman's identity and social standing are strongly correlated with her capacity to procreate (Thoma et al., 2021). Though men were initially neglected in studies on reproduction, that perspective has been investigated in more recent social science research.

Studies on male infertility may throw light on how reproductive technologies exacerbate gender inequality and offer a better place from which to confront it (Belongia et al., 2002).

Thyroid status evaluation is crucial for infertile couples not only because it is prevalent and significant but also because it may be easily treated and often has a preventive effect on infertility (Scoccia et al., 2012).

### **Conclusion**

Millions of people worldwide who are of reproductive age have infertility. The endocrine system is involved in this disorder, and male and female components contribute similarly (20–30%). Thyroid dysfunction is one of the endocrine disorders that is often linked to infertility in women, and there is also evidence that it may have an impact on male fertility and the results of assisted reproductive technology. As ART is usually quick and likely to increase chances of success, thyroid function should, therefore, be closely checked in both male and female partners seeking spontaneous conception as well as in those seeking ART.

## References

- Alemu, A., Terefe, B., Abebe, M., & Biadgo, B. (2016). Thyroid hormone dysfunction during pregnancy: A review. *International journal of reproductive biomedicine*, 14(11), 677.
- Andersen, S., Pedersen, K. M., Bruun, N. H., & Laurberg, P. (2002). Narrow individual variations in serum T4 and T3 in normal subjects: a clue to the understanding of subclinical thyroid disease. *The Journal of Clinical Endocrinology & Metabolism*, 87(3), 1068-1072.
- Arojoki, M, Jokimaa, V, Juuti, A, Koskinen, P, Irjala, K, & Anttila, L. (2000). Hypothyroidism among infertile women in Finland. *Gynecological endocrinology*, 14(2), 127-131.
- Bellastella, G., Maiorino, M. I., Scappaticcio, L., De B., Annamaria, M., Silvia, E., K., & Bellastella, A. (2021). Chronothyroidology: chronobiological aspects in thyroid function and diseases. *Life*, 11(5), 426.
- Belongia, E. A., Naimi, T. S., Gale, C. M., & Besser, R. E. (2002). Antibiotic use and upper respiratory infections: a survey of knowledge, attitudes, and experience in Wisconsin and Minnesota. *Preventive medicine*, 34(3), 346-352.
- Bjoro, T, Holmen, J, Kruger, O, Midthjell, K, Hunstad, K, Schreiner, T, Brochmann, H. (2000). Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). *European journal of endocrinology*, 143(5), 639-647.
- Brent, G. A. (1997). Maternal thyroid function: interpretation of thyroid function tests in pregnancy. *Clinical obstetrics and gynecology*, 40(1), 3-15.
- Canaris, G. J., Manowitz, N. R., Mayor, G., & Ridgway, E C. (2000). The Colorado thyroid disease prevalence study. *Archives of internal medicine*, 160(4), 526-534.
- Chan, S. T, Brook, F., Ahuja, A., Brown, B., & Metreweli, C. (1998). Alteration of thyroid blood flow during the normal menstrual cycle in healthy Chinese women. *Ultrasound in medicine & biology*, 24(1), 15-20.
- Cho, M. K. (2015). Thyroid dysfunction and subfertility. *Clinical and experimental reproductive medicine*, 42(4), 131.
- Downey, J., Yingling, S., McKinney, M., Husami, N., Jewelewicz, R., & Maidman, J. (1989). Mood disorders, psychiatric symptoms, and distress in women presenting for infertility evaluation. *Fertility and sterility*, 52(3), 425-432.
- Fonseca, T. L, Correa, M., Mayrin, C., Maira, P.O., Wittmann, G., Werneck, D. C., Joao P, Drigo, R. A., & Fekete, C. (2013). Coordination of hypothalamic and pituitary T3 production regulates TSH expression. *The Journal of clinical investigation*, 123(4), 1492-1500.
- Gallagher, T. F, Fukushima, D. K, Noguchi, S., Fishman, J., Bradlow, H. L., Cassouto, J., Hellman, L. (1966). Recent studies in steroid hormone metabolism in man. *Recent progress in hormone research*, 22, 283-303.
- Garber, J.R., Cobin, R.H., Gharib, H., Hennessey, J.V., Klein, I., Mechanick, J.I. & Woeber, K.A. (2012). American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract*, 18(6), 988-1028.
- Ghazeeri, G. S., & Kutteh, W. H. (2001). Autoimmune factors in reproductive failure. *Current Opinion in Obstetrics and Gynecology*, 13(3), 287-291.
- Gligorovi, N. (2006). Markets of Thyroid Autoimmunity. *Jugoslav Med Biochem*, 25(4). 373.
- Glinoe, D. (2003). Management of hypo- and hyperthyroidism during pregnancy. *Growth hormone & IGF research*, 13, S45-S54.

- Gordon, G. G, & Southren, A.L. (1977). Thyroid-hormone effects on steroid-hormone metabolism. *Bulletin of the New York Academy of Medicine*, 53(3), 241.
- Greil, A. L., Leitko, T. A., & Porter, K. L. (1988). Infertility: His and hers. *Gender & Society*, 2(2), 172-199.
- Greil, A. L., Slauson, B., Kathleen, & McQuillan, J. (2010). The experience of infertility: a review of recent literature. *Sociology of health & illness*, 32(1), 140-162.
- Grigorescu, V., Zhang, Y., Kissin, D., Sauber, S. E., Sunderam, M., Kirby, R.S., & Jamieson, D. J. (2014). Maternal characteristics and pregnancy outcomes after assisted reproductive technology by infertility diagnosis: ovulatory dysfunction versus tubal obstruction. *Fertility and sterility*, 101(4), 1019-1025.
- Hubalewska, D. A., Trofimiuk, M., Malgorzata, R., Marek, L., Andrzej, B., Tomasz, Z., W., Gietka, C. M. (2021). Thyroid diseases in pregnancy: guidelines of the Polish Society of Endocrinology [Choroby tarczycy w ciąży: zalecenia postępowania Polskiego Towarzystwa Endokrynologicznego]. *Endokrynologia Polska*, 72(5), 425-488.
- Inhorn, M. C, & Patrizio, P. (2015). Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. *Human reproduction update*, 21(4), 411-426.
- Jg, H. (2002). 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*, 87, 489-499.
- Kim, N. Y., Cho, H. J., Kim, H. Y., Yang, K. M., Ahn, H. K., Thornton, S., & Kwak-K., J. (2011). Thyroid autoimmunity and its association with cellular and humoral immunity in women with reproductive failures. *American Journal of Reproductive Immunology*, 65(1), 78-87.
- Krassas, G.E., & Perros, P. (2003). Thyroid disease and male reproductive function. *Journal of endocrinological investigation*, 26, 372-380.
- Krassas, G.E., Poppe, K., & Glinoe, D. (2010). Thyroid function and human reproductive health. *Endocrine reviews*, 31(5), 702-755.
- Krassas, G. E., Papadopoulou, F., Tziomalos, K., Zeginiadou, T., & Pontikides, N. (2008). Hypothyroidism has an adverse effect on human spermatogenesis: a prospective, controlled study. *Thyroid*, 18(12), 1255-1259.
- Lazarus, J. H. (2011). Thyroid function in pregnancy. *British medical bulletin*, 97(1), 137-148.
- Lincoln, S.R., Ke, R.W., & Kutteh, W.H. (1999). Screening for hypothyroidism in infertile women. *The Journal of reproductive medicine*, 44(5), 455-457.
- Manji, N., Boelaert, K., Sheppard, M.C., Holder, R.L., Gough, S.C., & Franklyn, J.A. (2006). Lack of association between serum TSH or free T4 and body mass index in euthyroid subjects. *Clinical endocrinology*, 64(2), 125-128.
- McQuillan, J., Greil, A. L., White, L., & Jacob, M. C. (2003). Frustrated fertility: Infertility and psychological distress among women. *Journal of Marriage and Family*, 65(4), 1007-1018.
- Mohamed, W.M.W., Sayuti, S.C., & Draman, N. (2018). Hypothyroidism and its associated factors after radioactive iodine therapy among patients with hyperthyroidism in the Northeast Coast State of Malaysia. *Journal of Taibah University medical sciences*, 13(5), 432-437.
- Mumtaz, M., Lin, L.S., Hui, K.C., & Khir, A.S.M. (2009). Radioiodine I-131 for the therapy of Graves' disease. *The Malaysian journal of medical sciences: MJMS*, 16(1), 25.

- Nikoobakht, M. R., Aloosh, M., Nikoobakht, N., Mehrcsay, A., Biniiaz, F., & Karjalian, M. A. (2012). The role of hypothyroidism in male infertility and erectile dysfunction. *Urology Journal*, 9(1), 405-409.
- Olivar, A.C., Chaffkin, L.M., Kates, R.J., Allan, T. R., Beller, P., & Graham, N. J. (2003). Is it necessary to obtain serum levels of thyroid stimulating hormone and prolactin in asymptomatic women with infertility? *Connecticut medicine*, 67(7), 393-395.
- Pohlenz, J., Maqueem, A., Cua, K., Weiss, R. E, Van, S. J., & Refetoff, S. (1999). Improved radioimmunoassay for measurement of mouse thyrotropin in serum: strain differences in thyrotropin concentration and thyrotroph sensitivity to thyroid hormone. *Thyroid*, 9(12), 1265-1271.
- Poongothai, J., Gopenath, T.S., & Manonayaki, S. (2009). Genetics of human male infertility. *Singapore Med J*, 50(4), 336-347.
- Poppe, K, & Velkeniers, B. (2002). Thyroid and infertility. *Verhandelingen-Koninklijke Academie voor Geneeskunde van Belgie*, 64(6), 389-399; discussion 400.
- Poppe, K., Glinioer, D., Van S., Andre, T., Herman, D., Paul, S., J, & Velkeniers, B. (2002). Thyroid dysfunction and autoimmunity in infertile women. *Thyroid*, 12(11), 997-1001.
- Poppe, K, & Velkeniers, B. (2004). Female infertility and the thyroid. *Best practice & research Clinical endocrinology & metabolism*, 18(2), 153-165.
- Poppe, K., Velkeniers, B., & Glinioer, D. (2008). The role of thyroid autoimmunity in fertility and pregnancy. *Nature clinical practice Endocrinology & metabolism*, 4(7), 394-405.
- Raber, W., Gessler, A., Nowotny, P., & Vierhapper, H. (2003). Hyperprolactinaemia in hypothyroidism: clinical significance and impact of TSH normalization. *Clinical endocrinology*, 58(2), 185-191.
- Rajender, S., Monica, M. G., Walter, L., & Agarwal, A. (2011). Thyroid, spermatogenesis, and male infertility. *Front Biosci (Elite Ed)*, 3, 843-855.
- Ross, D. S. (2001). Serum thyroid-stimulating hormone measurement for assessment of thyroid function and disease. *Endocrinology and metabolism clinics of North America*, 30(2), 245-264.
- Sakr, M. F, & Sakr, M. F. (2020). *Thyroid Disease During Pregnancy*: Springer.
- Scoccia, B., Demir, H., Kang, Y., Fierro, M. A., & Winston, N. J. (2012). In vitro fertilization pregnancy rates in levothyroxine-treated women with hypothyroidism compared to women without thyroid dysfunction disorders. *Thyroid*, 22(6), 631-636.
- Sengupta, P. (2013). Environmental and occupational exposure of metals and their role in male reproductive functions. *Drug and chemical toxicology*, 36(3), 353-368.
- Singh, R., J Hamada, A., & Agarwal, A. (2011). Thyroid hormones in male reproduction and fertility. *The Open Reproductive Science Journal*, 3(1).
- Sirohi, T., & Singh, H.. (2018). Estimation of serum prolactin levels and determination of prevalence of hyperprolactinemia in newly diagnosed cases of subclinical hypothyroidism. *Journal of family medicine and primary care*, 7(6), 1279.
- Spencer, C.A., LoPresti, J.S., Patel, A., G., R.B, Eigen, A, Shen, D, & Nicoloff, J.T. (1990). Applications of a new chemiluminometric thyrotropin assay to subnormal measurement. *The Journal of Clinical Endocrinology & Metabolism*, 70(2), 453-460.
- Thoma, M., Fledgerjohann, J., C. C., & Adageba, R. K.. (2021). Biological and social aspects of human infertility: a global perspective. In *Oxford research encyclopedia of global public health*.
- Trokoudes, K. M, Skordis, N., & Picolos, M. K. (2006). Infertility and thyroid disorders. *Current Opinion in Obstetrics and Gynecology*, 18(4), 446-451.



- Vander, B. M., & Wyns, C. (2018). Fertility and infertility: Definition and epidemiology. *Clinical biochemistry*, 62, 2-10.
- Vanderpump, M.P.J., Tunbridge, W.M.G., French, J.M.L., Appleton, D, Bates, D, Clark, F, & Tunbridge, F. (1995). The incidence of thyroid disorders in the community: a twenty-year follow-up of the Wickham Survey. *Clinical endocrinology*, 43(1), 55-68.
- Verma, I., Sood, R., Juneja, S., & Kaur, S. (2012). Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. *International journal of applied and basic medical research*, 2(1), 17.
- Von, B.K.A. (1840). Exophthalmos durch Hypertrophie des Zillgewebes in der Augenhöhle. *Wochenschr Helik*, 6, 197-204; 220-228.
- Whiteford, L. M, & Gonzalez, L. (1995). Stigma: the hidden burden of infertility. *Social science & medicine*, 40(1), 27-36.