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Hyperthyroidism and Infertility

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Master's of Science in Nursing-Family Nurse Practitioner

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## PERMISSION

Title           Hyperthyroidism and Infertility

Department   Nursing

Degree        Master of Science

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**Abstract**

This case report intends to focus on the endocrine disorder hyperthyroidism and its effect on fertility. A background of the issues at hand will be provided along with an in depth description of the case in question. The patient in this case report is a 65-year-old female who presented to a primary care clinic with symptoms of hyperthyroidism. Past medical history was unremarkable. A thorough literature review and analysis was performed in order to obtain understanding of the most current research and indications for management of patients who present with hyperthyroid systems. During the view of literature, the focus was directed to the correlation of hyperthyroid conditions and the effects on fertility.

## Background

Hyperthyroidism is a group of endocrine disorders and dysfunction of the thyroid gland that causes increased synthesis of the thyroid hormones (Lee, 2018). The thyroid is a complex gland that works along with the pituitary and hypothalamus glands in both negative and positive feedback mechanisms. Hyperthyroidism can cause a multitude of symptoms, including anxiety, sweating, hyperactivity, heat intolerance and palpitations or feeling that one's heart is racing (Lee, 2018). Graves disease, an autoimmune disorder, is the most common form of hyperthyroidism with approximately 0.5 cases per 1000 population over a twenty-year period (Lee, 2018). Thyroid disorders occur more commonly in women than men and the average age of presentation is between ages 20-40.

Thyroid disorders are also the second most common endocrine disorders affecting women of reproductive age (Medinica, et. al, 2015). The Centers for Disease Control (2016) estimates that around 12.1% of women aged 15-44 encounter problems with fertility. Infertility is defined as the inability to conceive after one year of unprotected sexual intercourse (Mintziori, Kita, Duntas & Goulis, 2015) or after 6 months of unprotected intercourse in women who are older than 35 (Weiss, & Clapauch, 2014). When diagnosing a couple with fertility challenges, it is important to examine all aspects of infertility in order to obtain a correct diagnosis. This paper will focus on hyperthyroidism and its effect on reproductive health and fertility. This is an important topic for a case report and literature analysis, as many Family Nurse Practitioners will be the initial provider for those who are seeking help for infertility. Hyperthyroidism may be easy to overlook in an otherwise young, healthy female. Careful history taking and examination of the patient is key to determining if the patient has any hyperthyroid symptoms. If pregnancy is achieved there can be serious complications during pregnancy if hyperthyroidism is untreated so

correct assessment of these patients is essential. Maternal complications from untreated hyperthyroidism include left ventricular dysfunction and thyroid storm; while complications with fertility may include miscarriage, prematurity, preeclampsia, placental abruption and postpartum hemorrhage (Linardi, Micou, Ilias, Petychaki..., Kokou, 2018).

### **Case Report**

The patient is a 65-year-old female who presented to a primary care clinic with a chief complaint of difficulty sleeping at night and feeling tired during the day. Her past medical history includes benign paroxysmal vertigo and is taking Antivert as needed. She also takes a daily multivitamin supplement. She had no significant past surgical history. Family history includes cardiovascular disease and Alzheimer's Disease in her mother and diabetes in her father.

The patient's report of symptoms included that she goes to bed around 10 p.m. and wakes up a couple of hours later and is unable to fall back asleep. She reported that the problem had been ongoing for about the past six weeks. Each night she identified a good sleep hygiene routine and avoids caffeine. This patient also presented with feelings of her heart racing during the day, a recent 10 pound unintentional weight loss, confusion, irritability and feelings of "hot flashes." She denied any recent changes in bowel and bladder habits. Physical exam revealed a well-dressed, well-nourished young female in no acute distress. Neurological exam is negative; Pupils were round, 3mm, equal and reactive to light. Romberg test was negative. She did have a thyroid nodule on palpation of the neck. Cardiovascular exam revealed regular rate and rhythm, no murmur; pedal pulses palpable without edema to lower extremities. Respirations were even, unlabored with lung sounds clear to auscultation. Bowel sounds were present in four quadrants and abdomen was soft, non-tender without hepatomegaly or splenomegaly.

When considering the initial presenting symptoms of this patient, the differential diagnoses included insomnia, hyperthyroidism, anxiety, atrial fibrillation, and sleep apnea. Sleep apnea was quickly ruled out as she stated she does not snore and has never been told she stops breathing during sleep by her husband. Diagnostic studies for further evaluation included an electrocardiogram (EKG), complete blood count (CBC), basic metabolic panel (BMP) and thyroid hormones (TSH, T3 and T4).

The EKG showed sinus tachycardia, with a rate of 120 beats per minute so atrial fibrillation was ruled out at the visit. Other vital signs were within acceptable limits. The CBC was normal. The BMP was also normal. TSH was 0.13, with reference range 0.3-4. T4 was 2.94 with a reference range 0.7-1.8. T3 was 0.3 with reference range 0.2-0.5. Clinically, with the low TSH and elevated T4 this was a case of untreated hyperthyroidism so she was diagnosed with such.

In management of her symptoms, she was started on propranolol for the tachycardia and “heart racing” symptoms. An ultrasound was ordered for evaluation of the thyroid nodule, which would be completed at a later date. She did tolerate the propranolol well, without any severe hypotensive effects and reported a significant relief in her cardiac symptoms at the follow up appointment. She is referred to endocrinology.

While this patient is currently past the age of fertility, in researching the topic this writer found how closely the thyroid is linked to other hormones within the body, leading to the topic for this paper. Had this patient been of an age where she may have considered pregnancy, it would be very important to discuss fertility and to know what the recommendations are regarding pregnancy and hyperthyroidism. On the other hand, if a patient presents with difficulty achieving pregnancy, hyperthyroidism is one differential that needs to be considered.

### **Literature Review**

In researching the topic of hyperthyroidism and infertility, PubMed, Clinical Key, and CINAHL databases were searched through the University of North Dakota School of Medicine library. Key terms used included “hyperthyroidism,” “infertility,” “thyroid disorders,” “reproductive health.” In addition to articles found via the search text boxes in the above mentioned databases, some articles were found using the references made from other articles related to the topic. The articles were focused on the past 5 years, with the exception of two articles from earlier years that had frequent mention in current research. Prior to examining the relationship between the two, separate discussions regarding the impact on health must be considered.

Hyperthyroidism itself is a widely studied topic. Infertility also has many different mentions in literature; however, the available research and literature on the two topics together are limited and often conflicting (Mintziori, Kita, Duntas & Goulis, 2015) with many of the research topics focused on hypothyroidism and the problems associated with fertility are focused on diagnosing with hypothyroidism. The thyroid gland has a significant role in both male and female fertility. It is estimated that approximately 5.8% of women who have either primary or secondary infertility have a diagnosis of hyperthyroidism (Mintziori, et. al, 2015)(Weiss & Clapauch, 2014). Infertility can be caused by problems with menstruation or with hormonal imbalances, or for unknown reasons, many of these being unrelated to thyroid dysfunction and are not within the scope of this paper. . With the complex feedback system of the thyroid gland, it is important to explore all aspects of reproductive health when reviewing hyperthyroidism.

Although the study from Krassas, Pontikides, Kaltsas, Popadopoulou & Batrinos (1994) is nearly 26 years old, it is still discussed in current research. The study had evaluated female



patients in a specialty thyroid clinic with regards to menstruation as prior to that time, it was thought that most hyperthyroid women experienced hypomenorrhea, oligomenorrhea or amenorrhea. A total of 214 patients with uncontrolled hyperthyroidism were studied, aged between 21-43 years old with controls set for BMI as well as smoking habits. Patients who had long-standing menstruation issues (prior to the onset of hyperthyroid symptoms) were excluded from the study. It was found that 78.5% of these patients had regular menstruation the remainder had irregular cycles and oligomenorrhea. There was no amenorrhea in the group. T4 levels were higher in those with menstrual irregularities. T3 levels did not correlate with either group. Even though menstrual abnormalities are 2.5 more common in those with hyperthyroidism (Mintziori, et. al, 2015), and on average 21.5% of hyperthyroid women experience irregular cycles, (Unuane, Tournaye, Velkeniers, & Poppe, 2011) endometrial biopsies have shown that it is not, in fact, the main cause of infertility in those with hyperthyroidism. Even when the cycles are irregular, women still ovulate and thus have the opportunity to fertilize an egg (Mintziori, et. al, 2015). Hypomenorrhea and polymenorrhea are commonly reported in those with hyperthyroidism. (Dittrich, Beckmann, Oppelt, Hofmann,... Mueller, 2011). Conflicting reports with the menstrual problems occur here with Dittrich, et. al, (2011) reporting that amenorrhea and anovulation are also reported in those with hyperthyroidism. A gap in the literature is whether or not pre existing menstruation problems, prior to hyperthyroidism, were ruled out in these studies.

Structurally, thyroid hormones can affect the endometrium if imbalanced (Mintziori, et. al, 2016). Excess or lack of thyroid can affect the fertilized egg's ability to implant and maintain pregnancy. The endometrial lining is where implantation of the embryo takes place. An unfavorable endometrium will not allow for implantation of the fertilized egg. In consideration

of hyperthyroidism, the thyroid is responsible for regulation of different factors in the implantation process, as well as after implantation (Minziori, et. al, 2016). Excess or lack of thyroid can affect the fertilized egg's ability to implant and maintain pregnancy.

Hormonal imbalances causing infertility associated with hyperthyroidism include increased serum levels of sex hormone binding globulin (SHBG) and estradiol (Weiss & Clapauch, 2014). The estradiol level may be as much as two or three times the normal seen in euthyroid patients (Dittrich, Beckmann, Oppelt, Hoffman,...& Mueller, 2011). Along with those increased levels of estrogen (E2) there may be increased levels of testosterone and androstenedione. Leutenizing hormone (LH) was also found in elevated numbers in women with Grave's disease (Weiss & Clapauch, 2014) and is elevated in both the follicular and luteal phases of the menstrual cycle (Dittrich, et. al, 2011). This alteration in hormones does indirectly influence the menstrual pattern in women (Dittrich, et. al, 2011).

Another consideration to discuss includes oxidative stress. Oxidative stress is an imbalance in the body that occurs when the antioxidant capacity is unable to balance the reactive oxygen species (Kong, Wei, Fedail,... Watanbe, 2015). Oxidative stress has been shown to play an important part in female reproduction (Kong, et. al, 2015) as nitric oxide is one free radical that is recognized in uterine function and development. Kong, et. al, (2015) studied the effect that hyperthyroidism has on uterine function as well as free radicals in a group of rats. In those hyperthyroid rats, there was a reduction in body weight, irritability and anxiety, weakness, and dry brittle hair. With respect to uterine function, the hyperthyroid rats showed no change in uterine weight but did show that thyroid hormones may be the cause for menstrual irregularities by altering the hormone levels (increased estradiol, decreased progesterone) (Kong, et. al, 2015). Tissue sampling also showed an increase in oxidative stress levels in rats with hyperthyroidism.

This does show that hyperthyroidism has a negative effect on regulation of oxidative stress, which then relates to uterine oxidative stress giving another example of the reasons why hyperthyroidism can contribute to female infertility.

A final consideration when researching why hyperthyroidism contributes to infertility is hypothesized to be due to the autoimmune aspect of thyroid disease. Both hyperthyroidism and hypothyroidism have autoimmune causes for the disorders. Thyroid autoimmune processes may account for as many as 20% or higher of women with thyroid disorders (Mintziori, et. al, 2016). Autoimmune hyperthyroidism has been linked with other autoimmune disorders that are also known to affect fertility, including endometriosis, ovarian failure and polycystic ovarian syndrome (Mintziori, et. al, 2016). The autoimmune reaction that occurs in the follicular fluid can damage oocytes and lead to poor oocyte quality and development (Mintziori, et. al, 2016).

Due to the complex mechanism of ovulation and female gonadal structure, infertility is often characterized as a female condition, however, careful consideration of the male and any causative factors that may contribute to infertility needs to be addressed. This may include evaluation for thyroid disorders in the male patient. The thyroid hormone acts on many different areas in the testes, include the Sertoli cells, Leydig cells and spermatozoa (La Vignera, Vita, Condorelli, Mongioli...Calogero, 2017). Hyperthyroidism has been associated with delayed Leydig cell maturation and changes in spermatogenesis as well as increased levels of gonadotropins, SHBG and testosterone, among others (La Vignera, et. al, 2017). Sperm function, including motility and at the mitochondrial level, is reduced when compared with euthyroid patients.

In addition to cellular level changes, men who have hyperthyroidism often have outward concerns regarding sexual performance and desire. Some have increased complaints of erectile

dysfunction, premature ejaculation, decreased sex drive and gynecomastia (La Vignera, et. al, 2017). Gynecomastia is caused by elevated estrogen levels in correlation with low free testosterone (Dittrich, et. al, 2011). Research also suggests a correlation between free T3 and seminal vesicle volume, ejaculate volume, and seminal fructose concentrations; this does imply that the thyroid hormones have a significant part to play on the male glandular function, and should be ruled out when assessing infertility in a couple.

One important aspect to note is that with the treatment of hyperthyroidism using antithyroid drugs, hormone levels normalized. Leutinizing hormone levels returned to normal levels within several weeks of treatment (Dittrich, et. al, 2011). In addition, in men who were treated with antithyroid drugs, the cellular changes (Leydig cell maturation, and spermatogenesis) also returned to baseline (Vignera, et. al, 2017). Another treatment modality for hyperthyroidism, radioactive iodine, may also be used in those planning fertility as it has not been proven to show any significant damage on the gonads (Weiss & Clapauch, 2014). Families should be educated to wait at least 6 months to conceive to ensure that hypothyroidism doesn't develop after the excess thyroid tissue is destroyed (Weiss & Clapauch, 2014).

Unuane & Poppe (2015) state that if surgery is chosen as an initial step for treatment, it may affect fertility as well since the lack of thyroid hormone then may throw off the compensatory mechanism of the thyroid in response to high estrogen. In addition to treating hyperthyroidism with antithyroid drugs, women who are identified as hyperthyroid and have a TSH between 0.3-1.1 mIU/L may be recommended to undergo ovarian hyperstimulation as a fertility treatment. After this occurs, the TSH should be rechecked (Unuane & Poppe, 2015). In those with TSH of less than 0.3 mIU/L, if the Free T3 or T4 are increased it is recommended they should undergo treatment or surgery. If the TSH is less than 0.3 mIU/L and the T3 and T4

are normal, they may not need immediate treatment and can undergo ovarian hyperstimulation with a TSH recheck after the process (Unuane & Poppe, 2015). It is strongly recommended, however, that the patient be in a euthyroid state prior to any ovarian stimulation (Mintziori, et. al, 2016) in order to maintain the most welcoming environment possible for fertilization and implantation.

In review, there are multiple consequences that patients, both male and female, may experience with hyperthyroidism. Pre conception counseling is an important, but often overlooked, consideration when working with those families of childbearing age. A discussion regarding the effects of hyperthyroidism should start ideally before pregnancy or even attempts at pregnancy if the hyperthyroidism is left untreated as untreated hyperthyroidism may precipitate fetal hyperthyroidism (Linardi, et. al, 2018). Fertility a challenge that may present in patients with this disorder, and treatment options must be considered carefully when working with this population. Managing hyperthyroidism in patients who are infertile starts with a careful assessment and diagnostic approach. Close monitoring and education should be provided with these patients when seeking fertility as the antithyroid drugs may cause teratogenicity, hepatotoxicity and agranulocytosis (Linardi, et. al, 2018).

### **Learning Points**

- Hyperthyroidism is classified as an endocrine disorder. It is a treatable disorder that often presents in women of child-bearing age.
- Hyperthyroidism has a negative effect on the fertility of both men and women, causing physical as well as psychological distress.
- Women experience problems with fertility related to menstrual cycle changes, hormonal changes including increased SBGH, estrogen and LH.

- Other hypotheses of infertility with hyperthyroidism include oxidative stress in the uterus and the autoimmune nature of hyperthyroidism.
- Men may also experience fertility issues with hyperthyroidism and is multifactorial in nature.
- Treatment of hyperthyroidism is essential in preventing further complications from infertility, as many patients can successfully achieve pregnancy after they become euthyroid.

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