



THYROID AND PREGNANCY

A high proportion of women with history of miscarriage or infertility may have mild hypothyroidism or positive thyroid antibody status

BACKGROUND

Uncontrolled severe overt thyroid disease can cause infertility, miscarriage, or preterm delivery. Subclinical hypothyroidism, a mild form of hypothyroidism where only thyroid stimulating hormone (TSH) is slightly high, also appears to be associated with higher risks of miscarriage and preterm delivery. The most common cause of hypothyroidism in the United States is autoimmune thyroiditis where the thyroid is attacked by antibodies and destroyed. The marker for autoimmune thyroid disease is the thyroid peroxidase antibody (TPOAb). Several studies also suggested that a high TPOAb level may be associated with infertility or miscarriage.

Currently, the American Thyroid Association recommends checking TSH levels in high-risk women with a history of miscarriage or infertility. Treatment with levothyroxine is recommended for women who have TSH >2.5 mIU/L and is receiving infertility treatment, such as *in-vitro* fertilization. In addition, treatment with levothyroxine can be considered in any woman with a positive TPOAb level and TSH >2.5 mIU/L. However, testing and treatment for subclinical hypothyroidism in pregnancy is still debated because clinical trials have not shown improvement in miscarriage or infertility rates when women with subclinical hypothyroidism or positive TPOAb levels were treated with levothyroxine. This study was done to determine how frequent subclinical hypothyroidism or a positive TPOAb level is seen among high-risk women with a history of miscarriage or infertility.

THE FULL ARTICLE TITLE

Dhillon-Smith RK et al 2020 The prevalence of thyroid dysfunction and autoimmunity in women with history of miscarriage or subfertility. J Clin Endocrinol Metab 105:dga302. PMID: 32593174.

SUMMARY OF THE STUDY

A total of 19,350 non-pregnant women with history of miscarriage or infertility and no history of thyroid disease were recruited from specialty miscarriage or fertility clinics across the United Kingdom from November 2011 to January 2016. Thyroid hormone levels and TPOAb titers were measured. Subclinical hypothyroidism was defined as having high TSH and normal free T₄ levels. Two cutoff levels for TSH was used; >2.5 mIU/L or >4.5 mIU/L.

However, when a cutoff TSH >4.5 mIU/L was used, subclinical hypothyroidism was diagnosed in 2.4% of women. However, a cutoff TSH >2.5 mIU/L was used, subclinical hypothyroidism was diagnosed in 19.9% of women. Subclinical hypothyroidism with TSH >2.5 mIU/L was diagnosed in 16.1% of women with a history of ≥ 3 miscarriages and in 20.1% of women with a history of infertility. Overall, 9.5% of women had positive TPOAb levels. Women with high TSH levels were more likely to have positive TPOAb levels. Women with body mass index (BMI) ≥ 35 kg/m² were 1.7 times more likely to have subclinical hypothyroidism compared to women with normal BMI. Asian women were 1.8 times more likely to have subclinical hypothyroidism compared to white women. Women with a history of infertility were 1.16 times more likely to have subclinical hypothyroidism compared to women with history of one or two miscarriages. Women with BMI ≥ 35 kg/m² were 1.5 times more likely to have positive TPOAb levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that subclinical hypothyroidism and a positive TPOAb is common in women in the United Kingdom with a history of miscarriage or infertility. This suggests a high number of women with history of miscarriage or infertility may benefit from treatment with levothyroxine. However, previous clinical trials have failed



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to show clear improvement in miscarriage or infertility rates when women with subclinical hypothyroidism or positive TPOAb levels were treated with levothyroxine, but all of these studies have flaws. A large, randomized clinical trial would be helpful to determine the need for testing and treatment of subclinical hypothyroid-

ism in high-risk women with history of miscarriage or infertility before they become pregnant. Until this is known, the decision to treat with levothyroxine should be individualized.

— Sun Lee, MD

ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: <https://www.thyroid.org/thyroid-disease-pregnancy/>

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

ABBREVIATIONS & DEFINITIONS

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T₄ level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

Hashimotos thyroiditis or autoimmune thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

TPO antibodies (TPOAb): these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Levothyroxine (LT₄): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.

Miscarriage: this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.

In-vitro fertilization: a procedure when an egg is fertilized outside of the body and then implanted in a woman to achieve a pregnancy

