



## THYROID AND PREGNANCY

### Thyroid hormone therapy and infertility

#### BACKGROUND

Thyroid hormone plays a major role in both achieving pregnancy and carrying a successful pregnancy to term. Women with hypothyroidism have an increased risk of infertility and are more likely to require assisted reproductive technologies (ART), such as in vitro fertilization, to achieve pregnancy. This is also true in women with thyroid autoimmunity (having positive anti thyroid peroxidase (TPO) antibodies) and thyroid hormone levels in the normal range. It is clear that treating overt hypothyroidism (high TSH and low T<sub>4</sub>) improves the success of pregnancies achieved through ART and decreases the miscarriage rate. Whether women with subclinical hypothyroidism (high TSH but normal T<sub>4</sub>) or with only TPO antibodies should also be treated prior to starting ART is less clear. Several initial small studies showed that levothyroxine decreased miscarriage rates and improved live birth rates. Subsequently, a much larger trial showed no benefit of levothyroxine therapy before ART in women with positive TPO antibodies. This study examined all of the studies (meta-analysis) to date to clarify the effect of levothyroxine on birth rates in women with subclinical hypothyroidism and/or positive TPO antibodies using ART to achieve pregnancy.

#### THE FULL ARTICLE TITLE:

Rao M et al. Effect of levothyroxine supplementation on pregnancy outcomes in women with subclinical hypothyroidism and thyroid autoimmunity undergoing in vitro fertilization/intracytoplasmic sperm injection: an updated meta-analysis of randomized controlled trials. *Reprod. Biol. Endocrinol.* 2018. 16:92. PMID: 30249251.

#### SUMMARY OF THE STUDY:

These investigators combined information from 4 clinical trials examining the effect of thyroid hormone treatment of women with subclinical hypothyroidism and/or autoimmune thyroid disease character-

ized by positive TPO antibodies who underwent ART to achieve pregnancy. The 4 studies were published between 2005 and 2017. Two studies included women who had autoimmune thyroid disease based on positive thyroid peroxidase antibodies and 2 included women who had subclinical hypothyroidism defined as a TSH greater than 4-4.5. The causes of infertility and fertility treatment protocols were similar across trials and all studies treated women with thyroid hormone throughout the pregnancy.

These 4 trials individually demonstrated variable effects of thyroid hormone therapy on pregnancy outcomes. When the data were combined and analyzed, the results indicated that levothyroxine therapy in women with subclinical hypothyroidism or autoimmune thyroid disease undergoing ART did not improve most pregnancy outcome measures. Thyroid hormone treatment did not affect pregnancy rates, live births, or preterm births, but did decrease miscarriages.

#### WHAT ARE THE IMPLICATIONS OF THE STUDY?

This study suggests the thyroid hormone therapy given to women with subclinical hypothyroidism and/or autoimmune thyroid disease does not improve the clinical pregnancy rate, live birth rate or preterm birth rate in women achieving pregnancy using ART. However, thyroid hormone supplementation did improve the miscarriage rate relative to women who did not receive therapy. This study suggests that thyroid hormone therapy in some women with subclinical hypothyroidism and/or autoimmune thyroid disease undergoing ART may be beneficial, but that further studies are needed to determine the appropriate timing and dosing of thyroid hormone as well as the type of patient that would benefit the most.

—Whitney Woodmansee MD





## THYROID AND PREGNANCY, continued

### ATA THYROID BROCHURE LINKS

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

Thyroid Hormone Treatment: <https://www.thyroid.org/thyroid-hormone-treatment/>

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

### ABBREVIATIONS & DEFINITIONS

**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). This is characterized by positive TPO antibodies.

**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 with an increased TSH and a decreased T<sub>4</sub> 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.

**TPO antibodies:** 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.

**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.

**Thyroxine (T<sub>4</sub>):** the major hormone produced by the thyroid gland. T<sub>4</sub> gets converted to the active hormone T<sub>3</sub> in various tissues in the body.

**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

**Meta-analysis:** a statistical analysis of several separate but similar experiments or studies in order to test the pooled data for statistical significance

