



## THYROID AND PREGNANCY

### Subclinical hypothyroidism and thyroid autoimmunity are associated with pre-term delivery

#### BACKGROUND

Thyroid hormone is essential to normal brain development in babies. Several studies have shown an increased risk poor pregnancy outcomes when the mother has overt hypothyroidism. These poor outcomes can be decreased or prevented in women with overt hypothyroidism that are treated with thyroid hormone. Poor pregnancy outcomes also are seen in mothers with mild/subclinical hypothyroidism but to a much lesser degree and the effects of treatment with thyroid hormone are less clear. Further, the impact of other thyroid disorders, such as isolated hypothyroxinemia and thyroid autoimmunity with normal thyroid function, on pregnancy outcomes is unclear and controversial.

One particular poor pregnancy outcome is pre-term delivery, meaning the baby is born <37 weeks of pregnancy when the baby is not quite fully developed. Pre-term delivery is increased in mothers with overt hypothyroidism but the impact of mild/subclinical hypothyroidism, isolated hypothyroxinemia and thyroid autoimmunity with normal thyroid function on pre-term delivery has remained unclear.

Given the large variability across study populations and variable patient numbers in previous studies, it is difficult to generalize the available results to provide evidence-based guidelines and recommendations. To address these limitations, the *Consortium on Thyroid and Pregnancy* was developed as a means to study the association of thyroid problems and thyroid autoimmunity in the mother with pre-term birth. The purpose of this study was to investigate whether mild/subclinical hypothyroidism, isolated hypothyroxinemia, and thyroid autoimmunity in the mother are risk factors for pre-term birth.

#### THE FULL ARTICLE TITLE

Korevaar TIM et al for the Consortium on Thyroid and Pregnancy—Study Group on Preterm Birth, 2019

Association of thyroid function test abnormalities and thyroid autoimmunity with preterm birth: a systematic review and meta-analysis. *JAMA* 2019;322:632–641. PMID: 31429897.

#### SUMMARY OF THE STUDY

In this analysis, 19 studies from the United States, Europe, Chile, Australia, Pakistan, and Japan were included, totaling 47,045 study participants. Included participants had data available on serum TSH, FT<sub>4</sub>, thyroid peroxidase antibody (TPOAb), or thyroglobulin antibody concentration, as well as gestational age at birth. Participants who had received treatment for abnormal thyroid-function tests or had preexisting thyroid disease, thyroid-interfering medication use, miscarriage, *in vitro* fertilization, or multiple pregnancies were excluded. The primary outcome of the study was preterm birth, defined as delivery at less than 37 weeks' gestation. Secondary outcomes included gestational age at birth, and very preterm birth (<32 weeks).

Of the study participants, 1234 (3.1%) had subclinical hypothyroidism, 904 (2.2%) had isolated hypothyroxinemia, and 3043 (7.5%) were TPOAb-positive, 226 of whom had serum TSH <2.5 mIU/L. Pre-term birth occurred in 2357 (5.0%) of pregnancies; very pre-term birth occurred in 349 pregnancies (0.7%). As compared with women with normal thyroid function and negative TPOAb, pre-term birth was more common in women with subclinical hypothyroidism (6.1% vs. 5.0), isolated hypothyroxinemia (7.1% vs. 5.0%) and in TPOAb-positive women (6.6% vs. 4.9%). There was also a higher risk of very pre-term birth in women with isolated hypothyroxinemia (1.9% vs. 0.8%) and in TPOAb-positive women (1.7% vs. 0.7%). After adjustment for TPOAb status, subclinical hypothyroidism was no longer associated with pre-term birth. Finally, TPOAb positivity remained a risk factor for pre-term birth even in women with serum TSH <2.5 mIU/L.





## THYROID AND PREGNANCY, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important study that clearly shows that mild/subclinical hypothyroidism, isolated hypothyroxinemia, and TPOAb positivity in pregnant women are associated with a higher risk of pre-term birth. What is unknown is whether thyroid hormone therapy can affect the rate of pre-term birth in any of these groups. The most current American Thyroid Association guidelines for management of thyroid disease during pregnancy state that treatment

with thyroid hormone can be “considered” in TPOAb-positive women with TSH >2.5 mIU/L. This study suggests that thyroid hormone treatment may be beneficial to all TPOAb-positive pregnant women. Finally, the issue of screening pregnant women for thyroid disease is controversial, but this study suggests that if screening is done, then testing for TPOAbs should be included. Further studies are needed to help sort out and resolve these complicated and controversial issues.

— Alan P. Farwell, MD, FACE

### ATA THYROID BROCHURE LINKS

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

**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.

**Overt Hypothyroidism:** clear hypothyroidism an increased TSH and a decreased T<sub>4</sub> level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

**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).

**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:** 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.

**Isolated hypothyroxinemia:** low levels of thyroxine (T<sub>4</sub>) with normal TSH levels, no evidence for pituitary disease and no clinical symptoms for hypothyroidism

**Gestational age:** how many weeks along the pregnancy has been, with normal delivery being at 40 weeks.

