

## COMMENTARY

# TSH and Pregnancy: Finding Your Way Out of the Gray Zone

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*This transcript has been edited for clarity.*

Thyroid dysfunction is quite common during pregnancy, with TPO antibody (TPOAb) positivity occurring in roughly 10% of women of reproductive age. During pregnancy, subclinical hypothyroidism has a prevalence of about 3.5%.

The recent American Thyroid Association (ATA) guidelines,<sup>[1]</sup> published in *Thyroid* in 2017, have very clear treatment recommendations when it comes to the combination of TPOAb positivity and TSH concentrations. For example, for TPOAb-negative women, treatment is recommended if the TSH is above 10 mIU/L.

However, there is also a gray area where women might have a TSH level between 4 mIU/L or the upper limit of your institutional reference range and 10 mIU/L. For TPOAb-negative women who are in this gray area, it can be quite difficult to make a decision about whether to treat them.

The same sort of gray area can also be extracted from the guidelines for TPOAb-positive women, but the TSH range is slightly different. For TPOAb-positive women, treatment is recommended if the TSH is above 4 mIU/L or the institutional reference range. The gray area where treatment is not recommended, but can be considered, is the TSH range between 2.5 and 4 mIU/L or between 2.5 and the upper limit of your institutional reference range.

## Three Tips for Decision-Making

When you have a patient sitting in front of you who is in this gray area, there are a few tricks that you can use when thinking about whether this patient can actually benefit from treatment.

First, take a good look at the patient's history. Certain adverse pregnancy outcomes—mainly miscarriage and preterm birth—have been associated with thyroid dysfunction, particularly TPOAb positivity and high TSH. If a woman who is in the gray area of treatment recommendations already has a medical history of preterm birth or miscarriage, that would definitely be an argument for treating her with levothyroxine.

We also know that thyroid physiology undergoes major changes during pregnancy. Typically, TSH concentrations should decrease during pregnancy because HCG stimulation peaks around the 10th to 12th week of pregnancy. Therefore, TSH levels at the end of the first trimester are of particular relevance if you want to decide whether to treat a woman who is in this gray area.

If the TSH is in the gray area—2.5-4 mIU/L range for TPOAb-positive women or about 4-10 mIU/L for TPOAb-negative women—at the 12th week of pregnancy, when you would expect the TSH to be lower because of HCG stimulation, then that is different from if the woman were in her sixth or 23rd week of pregnancy, when HCG stimulation is less relevant. So here, also, you can have additional arguments for whether you would want to treat your patient. If she doesn't respond well to HCG and TSH isn't suppressed, that's probably a sign of changes in thyroid physiology because of TPOAb positivity, for example.

Another factor that can aid you in clinical decision-making for women in this gray area is the height of the TSH. A recent small, randomized controlled trial<sup>[2]</sup> from Iran showed that the positive effects of levothyroxine on preterm birth do not occur for TSH concentrations below 4 mIU/L. This is actually [the case for both TPOAb-positive<sup>\[3\]</sup>](#) and TPOAb-negative women.

So, if a woman who is TPOAb positive has a TSH of just above the lower limit of the gray zone—2.6, for example—that is very different from if this woman were to have a TSH of 3.9, which is at the upper end of the gray zone. You can use these small differences to think about whether you would want to treat this woman with levothyroxine.

In conclusion, there are three things you can think about when trying to decide whether you want to treat a woman who falls within the gray zone of TSH concentrations according to the recent ATA guidelines. The first is gestational age at presentation, which affects thyroid physiology and HCG stimulation. The second is the actual TSH concentration. Obviously, a higher TSH concentration within that gray area would be another reason to think about treatment. And the third is past medical history. A history of miscarriage or preterm birth could be an additional reason for considering levothyroxine treatment in women within that gray area of the ATA guideline treatment recommendations.

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## References

1. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid*. 2017;27:315-389. [Source](#)
2. Nazarpour S, Ramezani Tehrani F, Simbar M, et al. Effects of levothyroxine on pregnant women with subclinical hypothyroidism, negative for thyroid peroxidase antibodies. *J Clin Endocrinol Metab*. 2018;103:926-935. [Source](#)
3. Dhillon-Smith RK, Middleton LJ, Sunner KK, et al. Levothyroxine in women with thyroid peroxidase antibodies before conception. *N Engl J Med*. 2019 Mar 23. [Epub ahead of print] [Source](#)

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