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Guideline for the assessment of thyroid during pregnancy

Perinatal Thyroid Study Group

Türk Perinatoloji Derneği, İstanbul

Abstract

This guideline, based on the report[1] of Perinatal Thyroid Workshop – 2015 which was prepared in the Perinatal Thyroid Workshop held in Afyonkarahisar, Turkey on November 8–9, 2013 with the participation of the academicians who are the members of the Turkish Perinatal Society and work at universities and training and research hospitals in Turkey, and published in the Issue 2, Volume 23 of the Perinatal Journal on August 2015, aims to provide guidance in clinical practices related with thyroid during pregnancy.

Keywords: Pregnancy, perinatal, thyroid.

***Özet:* Gebelikte tiroid değerlendirme kılavuzu**

Ülkemizin üniversite ile eğitim ve araştırma hastanelerinde görev yapan Türk Perinatoloji Derneği üyesi akademisyenlerin katkısıyla, 8–9 Kasım 2013 tarihlerinde Afyonkarahisar'da düzenlenen Perinatal Tiroid Çalıştayı'nda ortaya çıkan ve Perinatoloji Dergisi'nin Cilt 23, Sayı 2, Ağustos 2015 sayısında yayınlanan rapor[1] esas alınarak hazırlanan bu kılavuz gebelikte tiroid ile ilgili klinik uygulamalarda yol göstermeyi amaçlamaktadır.

Anahtar sözcükler: Gebelik, perinatal, tiroid.

Hypothyroidism During Pregnancy

Since the association of **overt hypothyroidism** with poor gestational outcomes was proven, maternal hypothyroidism should be avoided by initiating treatment as soon as identified during pregnancy.

It is known that subclinical hypothyroidism is more common than overt hypothyroidism.

The association between **subclinical hypothyroidism** and poor gestational outcomes are controversial. While cohort studies showed the association of subclinical hypothyroidism and poor gestational outcomes, randomized controlled studies showed no such association. On the other hand, there is uncertainty in the potential benefits of treatment with oral L-thyroxine for pregnant women with subclinical hypothyroidism.

Since maternal oral L-thyroxine intake cannot treat fetal hypothyroidism in the intrauterine life, it is scientifically not right to say that L-thyroxine treatment of a mother would also treat the possible hypothyroidism in fetus.

Hyperthyroidism During Pregnancy

While **overt hyperthyroidism** has many reasons, it occurs during pregnancy mostly associated with Graves' disease. Hyperthyroidism during pregnancy may cause abortion of mother, hypertension associated with pregnancy, preterm labor, anemia, arrhythmias and coronary failure in more advanced cases and thyroid crisis. Therefore, the treatment is initiated immediately as soon as it is detected during pregnancy, and it is aimed to keep mother in mild hyperthyroidism.

The medication mostly preferred in the treatment is propylthiouracil (PTU) since it passes through placenta at minimal rates (PTU).

Hyperthyroidism during pregnancy is the hyperthyroidism which is seen more common than Graves'

Correspondence: Perinatal Tiroid Çalışma Grubu. Türk Perinatoloji Derneği, İstanbul, Turkey. e-mail: info@perinatal.org.tr

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disease and associated with human chorionic gonadotropin (hCG). Hyperthyroidism associated with hCG courses slighter than Graves' disease. hCG-dependent hyperthyroidism is temporary and does not require treatment.

There is no evidence showing that **subclinical hyperthyroidism** treatment has positive impact on the pregnancy progress, and treatment of subclinical hyperthyroidism is not recommended since treatment may have potential side effects on fetus.

Iodine Insufficiency During Pregnancy

In Turkey, scientific data seem **insufficient** for now to suggest **routine** iodine support for all pregnant women during antenatal care. However, large-scale and society-based studies are required immediately to determine iodine sufficiency prevalence in Turkey.

If the region that pregnant women live is known to have severe iodine insufficiency, iodine supplement should be recommended certainly during antenatal period.

Mild-medium iodine insufficiency during pregnancy was shown to have short- and long-term negative impacts on neurological, behavioral and learning abilities. However, the cause-effect relationship has not been established fully yet.

Should Thyroid Diseases be Screened During Pregnancy?

The benefit of the screening for thyroid dysfunction in the pregnant population has been proved to determine clinical hypothyroidism and to initiate treatment early. This screening should be carried out before conception preferably or in the onset of the pregnancy if possible.

The benefit of screening to determine subclinical hypothyroidism has not been proven; because there is no data available showing the benefits of subsequent thyroxine treatment.

Screening at the onset of pregnancy just requires the measurement of TSH levels. The tests to be carried out for free or total T4 are only required when there is a change in TSH.

Similarly, anti-thyroid antibodies during pregnancy are not recommended to use for routine screening since there is no evidence to make a recommendation in favor of or against screening.

Due to the changes in thyroid physiology during pregnancy, it is very significant to highlight that interpreting thyroid hormone test results during pregnancy is more different.

For that reason, we recommend that each laboratory should calculate percentile values of their own gestational study population for each trimester separately and report the studied results through percentile values.

Considering the current literature, guides and expert opinions generally, it is seen that screening all pregnant women with TSH in the first trimester is not convenient. **Screening with TSH should be carried out for risky cases.**

Pregnant Women Recommended for TSH Screening during Early Pregnancy

- Thyroid dysfunction / surgery underwent (since hypothyroid development rate is 33% after lobectomy)
- Thyroid disease history in the family
- Goiter presence
- Thyroid antibody positivity, especially thyroid peroxidase auto-antibodies (TPOAb increases hypothyroidism risk, and the probability increased 40% in those with TPOAb positivity compared to TPOAb negativity)
- Presence of clinical hypothyroidism findings/symptoms
- Type I diabetes (since hypothyroidism rate increases to 16%)
- Miscarriage and preterm labor
- Presence of vitiligo, adrenal failure, hypoparathyroidism, atrophic gastritis, pernicious anemia, systemic sclerosis, SLE, Sjögren's syndrome associated with autoimmune thyroid dysfunction
- Infertility presence (Although overt and subclinical hypothyroidism rates are as wide as 1–43%)
- Those who underwent head-neck irradiation (since hypothyroidism prevalence is 67% in the 8-year follow-up)
- Morbid obeses whose BMI (body mass index) is >40 (since hypothyroidism was found as 13–19.5%)

- Women over 35 years (The rate of serum TSH value be ≥5 increases together with the age)
- Amiodarone treatment applications (14–18% hyperthyroidism-hypothyroidism)
- Lithium use (6–52 hypothyroidism)
- Exposure to iodinized contrast agents (until 6 weeks before pregnancy, thyroid dysfunction in 20% cases)
- Living in regions with medium level of iodine insufficiency

Lower and upper limit values for serum TSH

- 0.1 – 2.5 mU/L for the first trimester
- 0.2 – 3.0 mU/L for the second trimester
- 0.3 – 3.0 mU/L for the third trimester

Management

As in non-pregnant women, high TSH blood levels make established primary hypothyroidism diagnosis in pregnant women. In the first trimester of pregnancy, there is no sufficient evidence to support a routine screening with only thyroid auto-antibodies, so it is not recommended.

In the current literature, it is not clarified which is the best screening strategy among screening only TSH, only anti-TPO antibody or anti-TPO antibody together with TSH.

TSH >2.5–10.0 mU/L together with normal free T4 level: Subclinical hypothyroidism

TSH >2.5–10.0 mU/L together with low free T4 level: Clinical (overt) hypothyroidism

TSH ≥10.0 mU/L, without considering free T4 level: Clinical (overt) hypothyroidism.

However, it should be careful when interpreting free T4 levels during pregnancy, and ranges specific to trimester determined by each laboratory should be referred, or instead, in second and third trimesters, new reference ranges obtained by multiplying pregestational total T4 reference ranges by 1.5 can be used. Free T4 index can also be used as an alternative reference value to be used during pregnancy. Free T4 index can also be used during pregnancy as a different alternative reference value.

Since the association of overt hypothyroidism with poor gestational outcomes was proven, maternal hypothyroidism should be avoided by initiating treatment as soon as identified during pregnancy.

All pregnant women newly diagnosed with overt hypothyroidism should be treated with thyroid hormone (thyroxine, T4). T4 dose should be adjusted as keeping TSH below 2.5 mIU/L in first trimester and below 3 mIU/L in second and third trimesters (or within TSH ranges specific to trimester). Thyroid function tests should be evaluated within 30–40 days after the onset of treatment and once every 4–6 weeks subsequently.

When using levothyroxine to treat cases with hypothyroidism associated with any reason, it is not required to include routine iodine supplement additionally.

Since there is no study for the gestational outcomes of euthyroid pregnant women with positive TG-antibody, it is not recommended to treat such patients with levothyroxine.

If hypothyroidism diagnosis is established before pregnancy, T4 dose should be arranged as keeping TSH below 2.5 mIU/L in the preconceptional period.

After delivery, the dose administered during pregnancy of most of the hypothyroid women should be decreased to pregestational dose.

As we do not have sufficient evidence about its activities and due to the inconsistencies in free T4 measurement, **it is currently not recommended to treat isolated hypothyroxinemia.**

If there is more demand for thyroid during pregnancy and evidences are available showing that euthyroid women, which have autoimmune thyroid disease at the early periods of gestation, have more risk for subclinical hypothyroidism or overt hypothyroidism in the advanced weeks of gestation, it is required to monitorize TSH once every 4-6 weeks in these women.

Although current literature data are limited, gestational loss is higher in first trimester pregnant women whose thyroid antibody is negative and TSH value is between 2.5 and 5 mIU/L compared to first trimester pregnant women whose TSH value is below 2.5 mIU/L. **However, since the efficiency of treatment cannot be suggested, levothyroxine treatment is controversial.** Studies evaluating treatment efficiency are required for these cases.

Considering the current literature, guides and expert opinions generally, it is seen that screening all pregnant women with TSH in the first trimester is not convenient. **Screening with TSH should be carried out for risky cases.**

Since maternal oral L-thyroxine intake cannot treat fetal hypothyroidism in the intrauterine life, it is scientifically not right to say that L-thyroxine treatment of a mother due to any thyroid dysfunction would also treat the possible hypothyroidism in fetus.

Conflicts of Interest: No conflicts declared.

Reference

1. Api O, Şen C, Yayla M, Kurdoğlu M, Yapar Eyi EG, Sezik M, et al. Perinatal Thyroid Workshop report – 2015. Perinatal Journal 2015;23:73–139.