

The incidence of thyroid dysfunction in pregnant women

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Abstract

Objective: Despite the different data presented in the literature, there is no satisfactory data for the incidence of thyroid dysfunction during pregnancy in Turkey where iodine deficiency is prevalent. In this study, we aimed to present the incidence of thyroid dysfunction during pregnancy.

Methods: A total of 1876 pregnant women, whose thyroid stimulating hormone (TSH) and free T4 values were checked, were included in the study. Weeks of gestations, TSH and free T4 serum levels according to the last menstrual date and ultrasonography were retrospectively screened from the archive of our hospital. TSH reference ranges were accepted as 0.1–2.5 mU/l in the first trimester, 0.2–3.0 mU/l in the second trimester and 0.3–3.0 mU/l in the third trimester. The patients with high TSH value special to the trimester and low free T4 value were considered to have overt hypothyroidism, those with low TSH value and high free T4 value were considered to have overt hyperthyroidism, and the cases with abnormal TSH value but normal free T4 value were considered to have subclinical thyroid dysfunction.

Results: Mean age of the pregnant women included in the study was found as 29.14±5.84 years. While 65.4% (n=1227) of the cases were in their first trimester, 21.1% (n=395) of them were in the second trimester, and 13.5% (n=254) of them were in the third trimester. Hyperthyroidism was found in 5.38% (n=101) of the pregnant women; while 1.22% (n=23) of them had overt hyperthyroidism, 4.16% (n=78) of them had subclinical hyperthyroidism. Of the cases, 15.88% (n=298) had hypothyroidism where 10.18% (n=191) of them had overt hypothyroidism and 5.70% (n=107) of them had subclinical hypothyroidism.

Conclusion: In the pregnant women included in the study, we observed a high rate of hypothyroidism since TSH upper limit was possibly decreased in the first trimester and we were in a risky region for iodine deficiency.

Keywords: Pregnancy, hypothyroidism, hyperthyroidism.

Özet: Gebelerde tiroid fonksiyon bozukluğu sıklığı

Amaç: Literatürde değişik veriler olsa da iyot eksikliği bölgesi olan ülkemizde gebelikte tiroid fonksiyon bozukluğu sıklığına dair tatmin edici veri bulunmamaktadır. Bu çalışmada gebelikte tiroid fonksiyon bozukluğu sıklığını ortaya koymayı amaçladık.

Yöntem: Çalışmaya tiroid stimüle edici hormon (TSH) ve serbest T4 değerleri bakılmış 1876 gebe dahil edildi. Son adet tarihine ve ultrasonografiye göre gebelik haftaları, TSH ve serbest T4 serum düzeyleri hastanemiz kayıt sisteminden retrospektif olarak tarandı. TSH referans aralıkları ilk trimesterde 0.1–2.5 mU/l; ikinci trimesterde 0.2–3.0 mU/l; üçüncü trimesterde 0.3–3.0 mU/l alındı. Trimestere özgü TSH değeri yüksek, serbest T4 değeri düşük hastalar aşikar hipotiroidi, TSH değeri düşük, serbest T4 değeri yüksek olan hastalar aşikar hipertiroidi, TSH değeri anormal olup serbest T4 değeri normal olan olgular subklinik tiroid fonksiyon bozukluğu olarak değerlendirildi.

Bulgular: Çalışmaya dahil edilen gebelerin ortalama yaşları 29.14±5.84 olarak saptandı. Olguların %65.4'ü (n=1227) gebeliklerinin birinci trimesterinde, %21.1'i ikinci trimesterinde (n=395), %13.5'i üçüncü trimesterinde (n=254) idi. Gebelerin %5.38'inde (n=101) hipertiroidi saptandı, %1.22'si (n=23) aşikar hipertiroidi iken %4.16'sı (n=78) subklinik hipertiroidi idi. Yüzde 15.88'inde (n=298) hipotiroidi vardı ve %10.18'inde (n=191) aşikar hipotiroidi, %5.70 (n=107) gebede subklinik hipotiroidi saptandı.

Sonuç: Bu çalışmaya alınan gebelerde, muhtemelen birinci trimesterde TSH üst limitinin aşağı çekilmesi ve iyot eksikliği bakımından riskli bir bölgede bulunmamız nedeniyle yüksek oranda hipotiroidi olgusuna rastlanmıştır.

Anahtar sözcükler: Gebelik, hipotiroidi, hipertiroidi.

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Introduction

Thyroid function tests of the pregnant women have different values than normal women. This has caused to establish new reference ranges unique to pregnancy and ideal trimester. The studies published in mostly western countries and supported by both American Thyroid Association (ATA) and American Endocrine Society (AES) recommend TSH reference range as 0.1–2.5 mIU/L in the first trimester, 0.2–3.0 mIU/L in the second trimester and 0.3–3.0–3.5 mIU/L in the third trimester.^[1–5] The most common tests to evaluate thyroid function are thyroid stimulating hormone (TSH) and free thyroxine (fT4).^[6,7]

Although hypothyroidism is reported as 2–4% and hyperthyroidism as 0.1–0.4% in the general literature, upper limit of the TSH is accepted as 5 mIU/L in the literature.^[8] Also, our country is still a region for iodine deficiency.^[9] Therefore, thyroid dysfunction rate is expected to be higher than western literature. In Turkey, there is no satisfactory data obtained by using this reference range recommended for TSH level.

In our study, we aimed to determine the incidence of thyroid dysfunction through TSH and fT4 levels of the pregnant women in our study group by considering TSH reference range, which have been accepted in recent years, as 0.1–2.5 mIU/L in the first trimester, 0.2–3.0 mIU/L in the second trimester and 0.3–3.0 mIU/L in the third trimester.

Methods

By obtaining the approval of Ethics Board of İstanbul Training and Research Hospital (ITRH), 1876 singleton pregnant women, who admitted to the Pregnancy Clinic of ITRH Gynecology and Obstetrics Department between January 1st, 2010 and January 1st, 2014 and whose TSH and fT4 values were checked, were included into our study. Ages of pregnant women, weeks of gestations according to the ultrasound, and TSH and fT4 levels were retrospectively screened from the archive of our hospital. Anamnesis and clinical evaluation were ignored. TSH and fT4 levels were analyzed with original kits in the Advia Centaur XP immunoassay device (Siemens Healthcare, Malvern, PA, USA) working with chemiluminescence method in the same laboratory. The data of the pregnant women were analyzed by using Microsoft Excel Office 2011 (Microsoft

Corporation, Redmond, WA, USA). Of the pregnant women, mean ages, weeks of gestation, and hypothyroidism and hyperthyroidism rates unique to the trimesters were calculated.

Normal reference range for TSH was accepted as 0.1–2.5 mIU/L in the first trimester, 0.2–3.0 mIU/L in the second trimester and 0.3–3.0 mIU/L in the third trimester. Pregnant women whose TSH levels were over 2.5 mIU/L in the first trimester, over 3 mIU/L in the second and third trimesters were considered to have hypothyroidism. fT4 normal levels were considered as 0.93–1.7 mIU/L. The pregnant women whose TSH levels were above 2.5 mIU/L in the first trimester and over 3 mIU/L in the second and third trimesters but within normal ranges for fT4 were considered to have subclinical hypothyroidism while those with fT4 below 0.93 according to lower limit of laboratory were considered to have overt hypothyroidism.

The pregnant women with TSH levels below 0.1 mIU/L in the first trimester, below 0.2 mIU/L in the second trimester and below 0.3 mIU/L in the third trimester were considered to have hyperthyroidism. Among these pregnant women, those within normal ranges of fT4 were considered to have subclinical hyperthyroidism and those with fT4 levels above 1.7 mIU/L according to the upper limit of laboratory were considered to have overt hyperthyroidism.

Results

Mean age of the pregnant women included in the study was found as 29.14 ± 5.84 (range: 15 to 48) years. Mean week of gestation was 13.95 ± 9.28 and median week of gestation was 10 (range: 5 to 40). While 65.4% ($n=1227$) of the cases were in their first trimester, 21.1% ($n=395$) of them were in the second trimester, and 13.5% ($n=254$) of them were in the third trimester. Mean TSH value was 1.71 ± 2.20 mIU/L and mean fT4 value was 1.05 ± 0.23 mIU/L in all pregnant women. When grouped according to the trimesters, mean TSH value was 1.57 ± 2.25 mIU/L and mean fT4 value was 1.10 ± 0.24 mIU/L in the first trimester, mean TSH value was 1.87 ± 0.68 mIU/L and mean fT4 value was 0.99 ± 1.83 mIU/L in the second trimester, and mean TSH value was 2.15 ± 2.53 mIU/L and mean fT4 value was 0.93 ± 0.13 mIU/L in the third trimester.

Hyperthyroidism was found in 5.38% ($n=101$) of the pregnant women; while 1.22% ($n=23$) of them had overt

hyperthyroidism, 4.16% (n=78) of them had subclinical hyperthyroidism. Hypothyroidism rate was 15.88% (n=298), and overt hypothyroidism was found in 10.18% (n=191) of them and subclinical hypothyroidism in 5.7% (n=107) of them.

The rates for hyperthyroidism, overt hyperthyroidism and subclinical hyperthyroidism of the pregnant women in the first trimester were 7.09%, 1.71% and 5.38%, respectively. The rates for hyperthyroidism, overt hyperthyroidism and subclinical hyperthyroidism in the first trimester were 15.64%, 10.92% and 4.72%, respectively.

During the second trimester, 3.03% of the pregnant women had hyperthyroidism and 16.70% of them had hypothyroidism.

During the third trimester, 0.78% of the pregnant women had hyperthyroidism and 15.74% of them had hypothyroidism. The rates of thyroid dysfunction in all pregnant women and all 3 trimesters are given in the **Table 1**.

Discussion

Thyroid dysfunction is among the most common endocrine problems seen in the pregnant women. In early pregnancy, maternal thyroid functions are affected by the increase in thyroid binding globulin (TBG), stimulation of TSH receptors via human chorionic gonadotropin (hCG) and changes in iodine metabolism.^[6] Serum total T4 and T3 production increases in the first half of pregnancy; draws a curve around week 20 and reaches pregestational period when it reaches a particular stable period. TBG increase causes an increase in total T4 and T3 levels about 1.5 times. Serum fT4 and fT3 levels increase slightly within normal ranges in the beginning; however, as the weeks of gestation progress, they gradually decrease by staying within normal ranges especially in the first and second trimesters. Serum fT4 and fT3 are independent biologically active forms and 0.03% of total T4 and 0.3% of total T3 are in free forms.^[1]

Due to the increase in the production of thyroid hormone, increase of iodine intake about 1.3-1.5 times and transition of iodine from mother to fetus, iodine need during pregnancy increases about 50% and daily intake requirement reaches 250 µg.^[10] Normal thyroid gland can meet the hormone needs increased during pregnancy and keeps thyroid hormone levels within normal ranges. However, in cases with obvious thyroid

Table 1. Percentages (%) of thyroid dysfunction in all pregnant women and all three trimesters.

	All pregnant women	First trimester	Second trimester	Third trimester
Hyperthyroidism	5.38	7.09	3.03	0.78
Overt hyperthyroidism	1.22	1.71	0.50	0
Subclinical hyperthyroidism	4.16	5.38	2.53	0.78
Hypothyroidism	15.88	15.64	16.70	15.74
Overt hypothyroidism	10.18	10.92	8.10	9.84
Subclinical hypothyroidism	5.70	4.72	8.60	5.90

pathology, thyroid hormone production cannot be increased and therefore hypothyroidism may occur in pregnant woman.^[11]

In the first trimester, fetal neurodevelopment is provided by maternal thyroid hormones transferred through placenta.^[12]

It is known that the redundancy or scarcity of maternal thyroid hormone affects fetus and gestational outcomes of mother at each phase of the pregnancy.^[6,13] Maternal hypothyroidism is the most common thyroid dysfunction seen during pregnancy and it is associated with fetal loss, hypertension related with gestation, preterm labor, ablatio placentae and decreased intellectual function in baby.^[11,14] These adverse outcomes are associated with overt hypothyroidism (increased serum TSH and decreased fT4) seen in 0.2% of the pregnancies and subclinical hypothyroidism (increased TSH, normal fT4) seen in 2.3% of the pregnancies.^[11,14] Overt hyperthyroidism is rarer and seen in 0.2% of the cases. It is associated with intrauterine growth restriction, preeclampsia and preterm labor for mother and fetus.^[13] Subclinical hyperthyroidism (decreased TSH, normal fT4) is seen in 1.7% of the cases and it is not associated with poor gestational outcomes.^[15] Although fT4 and fT3 are usually found at a high rate together in hyperthyroidism cases, T3 concentration alone can be found high in a group of hyperthyroidism cases seen rarely which is called T3 toxicosis.

In the first trimester, the case known as gestational thyrotoxicosis or temporary gestational hyperthyroidism develops depending on the hCG secretion with high titration stimulating thyroid TSH receptors. It should be suspected in women who refer for the complaints of nausea and vomiting in the first weeks after temporary hyperthyroidism conception associat-

ed with hyperemesis gravidarum and have thyroid function tests consistent with hyperthyroidism.^[16] In this study, we found hyperthyroidism in 7.1% of the cases in the first trimester, 3.0% of the cases in the second trimester and in 0.8% of the cases in the third trimester. We believe that the reason for the high rate found in first trimester compared to other trimesters and the literature is ruling out the cases with temporary hyperthyroidism associated with gestational thyrotoxicosis and hyperemesis gravidarum and association of autoimmune hyperthyroidism with remission in the second and third trimesters.

If mother has severe iodine deficiency during pregnancy, fetus develops hypothyroxinemia and fetal goiter. In severe iodine deficiency, IQ level decreases 13.5 points compared to normal level. If daily iodine intake decreases below 100 µg during pregnancy, it can be defined as iodine deficiency.^[17] Turkey is a region for iodine deficiency.^[9] In Turkey, the regions with severe and moderate iodine deficiency are more than the regions with slight insufficient and normal iodine concentrations.^[18] In Istanbul, iodine deficiency was reported as 46.2%.^[19] In the USA, moderate iodine deficiency was reported in 7% of the women in fertility period.^[17] The rates in Turkey are higher than the rate reported in the USA.

Although the hypothyroidism incidence is reported as 0.3-2.5% in the literature, it is based on the study of Klein et al.^[8] carried out in 1991 where they considered TSH level above 6 mU/l as hypothyroidism. ATA defined a specific trimester TSH upper limit in 2011, the limit was changed as 2.5 mU/l for the first trimester and it was accepted internationally.^[1]

Temur et al.^[20] from Turkey determined the upper limit of TSH as 5.6 mU/L in their studies including first and second trimesters, and found hypothyroidism incidence as 3.6%. Although their rate was lower than the rate of our study, they found no difference in terms of thyroid dysfunction between pregnant women who had and had not risk factor of thyroid disease, and they emphasized to screen all pregnant women for that reason.

Remarkably, in a study including 4800 pregnant women, subclinical hypothyroidism prevalence was 27.8% when TSH upper limit was accepted as 2.5 mIU/L but the prevalence was 4.0% when this limit was accepted as 4.87 mIU/L.^[21] In our study, we established the upper limit of TSH as 2.5 mIU/L and 15.9% of the pregnant women had hypothyroidism in all

trimesters; 10.2% of them had overt hypothyroidism and 5.7% of them had subclinical hypothyroidism. When we evaluated the pregnant women only in the first trimester, 15.6% of them had hypothyroidism. In the studies published in Turkey, hypothyroidism was reported as 2.8% and 1.6%;^[22,23] we believe that the high rate of hypothyroidism in our study may be associated with changing the upper limit of TSH.

Although there is a consensus that thyroid dysfunction screening should be done to high-risk women who are symptomatic or have history of thyroid disease history, type 2 diabetes or other autoimmune diseases^[24] and who have high risk for thyroid diseases associated subclinical thyroid diseases,^[25] we believe that all pregnant women should be screened as a routine practice in terms of thyroid dysfunction due to the high rate.

Our study was retrospective and therefore had some limitations. We could not access the data of pregnant women who had thyroid dysfunction previously and referred to our hospital. It seems that our higher rate of thyroid dysfunction than the rates reported in the literature is affected by these limitations. It is an expected result to have higher results in countries with iodine deficiency as our country.

Conclusion

In our study region, we found a high rate of thyroid dysfunction incidence. In this study, high rate of hypothyroidism as 15% may result from changing upper limit of TSH to 2.5 mIU/L in the first trimester and to 3 mIU/L in the second and third trimesters. Also, having a study region with iodine deficiency and the pregnant women referred to our hospital due to a previous thyroid disease might increase this rate.

Conflicts of Interest: No conflicts declared.

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