

Evaluation of the Thyroid Functions in Adolescent, Normal and Advanced Age Pregnancies

Adölesan, Normal ve İleri Yaş Gebeliklerde Tiroid Fonksiyonlarının Değerlendirilmesi

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Abstract

We aimed to investigate the thyroid function test (fT4 and TSH) results and the prevalence of hyperthyroidism, euthyroidism, subclinical hypothyroidism, and overt hypothyroidism according to age groups in pregnant women who had applied to our hospital. Six thousand eight hundred and forty-three pregnant women who were in the first trimester and who applied to the hospital for the first time in their current pregnancy were included in the study. Patients were divided into 3 age groups, namely, ≤ 19 years, 20-34 years, and ≥ 35 years. The fT4 and TSH levels were compared between the age groups. The mean serum TSH value of patients was 1.61(0.987, 2.41) mIU/mL. There was no statistically significant difference in the rates of hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hypothyroidism between the three age groups. However, the incidence of hyperthyroidism in pregnant women aged 35 years and older was significantly higher when compared with those aged 35 years and younger. Consistently with the previous studies in our country, the prevalence of hyperthyroidism, subclinical hypothyroidism and overt hypothyroidism was detected as 2.9%, 22.1%, and 0.4%, respectively. Therefore, we recommend regular thyroid testing in pregnancy regardless of age, especially in countries where iodine deficiency is common.

Keywords: Hypothyroidism, Pregnancy, TSH, Thyroid Function

Öz

Bu çalışmada, hastanemize başvuran gebe kadınların tiroid fonksiyon testi (fT4 veTSH) sonuçlarını ve bu sonuçlara göre hipertiroidi, ötiroidi, subklinik hipotiroidi ve aşikar hipotiroidi sıklığını yaş gruplarına göre değerlendirdik. Mevcut gebeliğinde ilk defa hastaneye başvuran birinci trimesterde olan 6843 gebe çalışmaya dahil edildi. Hastalar 19 yaş altı, 20-34 yaş arası ve 35 yaş üzeri şeklinde 3 gruba ayrıldı. fT4 ve TSH değerleri gruplar arasında karşılaştırıldı. Gebelerin ortalama TSH değerleri 1.61 (0.987, 2.41) mIU/mL idi. Çalışma grupları arasında hipertiroidi, ötiroidi, subklinik hipotiroidi ve aşikar hipotiroidi açısından istatistiksel olarak anlamlı fark izlenmedi. Fakat, 35 yaş üzerindeki gebelerde hipertiroidi sıklığı 35 yaş altındaki gebelere göre daha fazla izlendi. Ülkemizdeki diğer çalışmalara benzer şekilde sırası ile; hipertiroidi, subklinik hipotiroidi ve aşikar hipotiroidi sıklığı %2.9, %22.1 ve %0.4 olarak saptanmıştır. Bu nedenle, özellikle ülkemiz gibi iyot eksikliği sık olan bölgelerde yaş ayrımı gözetmeksizin gebelerde tiroid fonksiyonlarının çalışılmasını öneriyoruz.

Anahtar Kelimeler: Gebelik, Hipotiroidi, TSH, Tiroid Fonksiyonu

Introduction

Thyroid hormone mechanism is affected by the physiological changes of the pregnancy. During pregnancy, the thyroid volume enlarges by approximately 10% to 30%, the thyroxine (T4) and triiodothyronine (T3) production increases up to 50% and the iodine requirement increases due to urinary excretion of iodine (1). Adequate thyroid hormone levels are critical for maintaining the pregnancy and the normal fetal development. During the first half of gestation, the fetus depends entirely

on the maternal thyroid hormones since the baby's own thyroid gland does not function (2).

The reference intervals for thyroid function tests during pregnancy are different from the non-pregnant adult reference ranges. According to recent American Thyroid Association (ATA) guidelines, the reference range for TSH should be lower than 2.5 mIU/L during the first trimester and lower than 3.0 mIU/L during the second and third trimesters. The recommended lower physiological cutoff is 0.1 mIU/L in the first trimester, 0.2 mIU/L in the second trimester and 0.3 mIU/L in the third trimester (3). Overt hypothyroidism is diagnosed by serum TSH above 2.5 mIU/L and decreased fT4, or by serum TSH level greater than 10mIU/L with fT4 within the normal range. Subclinical hypothyroidism is defined as serum TSH between 2.5-10 mIU/L in the presence of normal fT4 (4). Hyperthyroidism is diagnosed when a serum TSH level is lower than 0.1 mIU/L (5).

The prevalence of subclinical hypothyroidism in pregnancy ranges from 1.5% to 42.9%, and affects up to 15% of pregnancies in the US and 17% in the Europe (6). Overt hypothyroidism complicates 1-3 per 1000 pregnancies (7). Subclinical or overt

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hypothyroidism has been associated with adverse effects such as preeclampsia, placental abruption, postpartum hemorrhage, cardiac dysfunction, low birth weight and intrauterine fetal death (7). On the other hand, hyperthyroidism has been associated with preeclampsia, heart failure, preterm delivery, intrauterine growth retardation, thyrotoxicosis and hyperemesis gravidarum (7, 8).

According to the World Health Organization (WHO), adolescent pregnancy period is between 10 and 19 years of age (9); and pregnancies over the age of 35 are described as advanced maternal age (10). Adolescent period and advanced maternal age may have a negative impact on pregnancy when compared to any other age group (9, 10). In the present study, we examined the thyroid functions of adolescent age, normal age and advanced maternal age pregnancies that were followed up in our hospital.

Material and Method

The study group was composed of 6843 pregnant women, who had applied to our Gynecology and Obstetrics Department of Mugla Sıtkı Kocman University Education and Research Hospital between January 2012 and November 2019 and whose pregnancies were confirmed by observing the fetal heartbeat ultrasound in first trimester and by carrying out the routine blood tests. Data were extracted retrospectively from the electronic data processing system of our Hospital (Karmed Data Processing Systems). Age, TSH and fT4 levels at the time of admission were recorded. TSH and fT4 hormone levels were determined by electrochemiluminescence immunoassay (ECLIA) methods on a COBAS 8000 (e801) immunoassay analyzer (Roche Diagnostics GmbH; Mannheim, Germany).

Pregnant women with singleton gestations and those with no history of thyropathy, autoimmune disease, goiters and recent or previously taken medication that may affect the thyroid hormone levels served as the study group. Women with twin pregnancies, those with thyroid (interfering) medication before or during pregnancy, and with preexisting thyroid disease were excluded from the study. Participants were divided into three groups based on their age: 19 and less, 20-34, and ≥ 35 years. Serum levels of fT4 and TSH were compared among the groups. In accordance with the ATA and Turkish Endocrinology and Metabolism Association guidelines; women with a reference range for TSH between 0.1 and 2.5 mIU/L were accepted as euthyroid, women with TSH level in the range between 2.5 and 10 mIU/L and fT4 level within the normal range (0.61-1.2 mIU/L) were considered as subclinical hypothyroid, and those with a level of TSH greater than 10 mIU/L, irrespective of the fT4 level, were diagnosed to have overt hypothyroidism.

Appropriate treatment was initiated by the Endocrinologist for pregnant women with abnormal thyroid function.

Ethical approval was obtained (Date:13/02/2020, Decision No:03/111) and the study was conducted in accordance with the Helsinki Declaration.

Data were analyzed using the IBM SPSS V22. Differences among the age groups for fT4 and TSH were analyzed by one-way analysis of variance (ANOVA) using Tukey correction. Chi-square test was used to analyze the status of TSH levels under 2.5 and over 2.5 according to age groups. Results of the analysis were presented as the mean values and standard deviation for quantitative data, and as frequency (percentage) for categorical data. All p values were 2-sided, and values less than 0.05 were considered statistically significant.

Results

In total, 6843 pregnant women were recruited who fulfilled the inclusion criteria: 346 (5.05%) with adolescent age, 5294 (77.36%) with normal age, and 1203 (17.58%) with advanced maternal age pregnancies. The mean age of the pregnant women in this study was 28.7 ± 5.9 years (min:15, max:47) and the mean TSH level was 1.61 (0.987, 2.41) mIU/L in the whole group. Compared to each other, the mean TSH was 1.74 (1.15, 2.48) mIU/L for adolescent age pregnancy group; 1.61 (0.995, 2.42) mIU/L for normal age pregnancy group; and 1.57 (0.906, 2.36) mIU/L for advanced maternal age pregnancy group ($p=0.877$) (Table 1).

According to baseline levels of TSH; subclinical hypothyroidism was diagnosed in 23.7% ($n=82$) of adolescent age pregnancies, in 22.3% ($n=1178$) of normal age pregnancies, and in %20.8 ($n=250$) of advanced maternal age pregnancies. Overt hypothyroidism was observed in 0.3% ($n=1$) of adolescent age pregnancy group, in 0.4% ($n=20$) of normal age pregnancy group, and in 0.6% ($n=7$) of advanced maternal age pregnancy group. Hyperthyroidism in adolescent age, normal age and advanced maternal age groups was found in 1.2% ($n=4$), in 2.6% ($n=136$), and in 5% ($n=60$), respectively. And finally, the frequency of euthyroidism was 74.9% ($n=259$) in adolescent age women, 74.8% ($n=3960$) in normal age women, and 73.6% ($n=886$) in advanced maternal age women (Table 2, Figure 1).

The rates of hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hypothyroidism were similar in each group ($p>0.05$). However, the incidence of hyperthyroidism in pregnant women aged 35 years and older was nearly twice as frequent as that in those aged 35 years and younger ($p<0.001$) (Table 3).

Table 1. Comparison of TSH and FT4 values according to age groups

Age Groups	Subjects (n)	Age (year)	TSH (mIU/L)	FT4 (mIU/L)
≤19	346	18.3±1.2	1.745 (1.15, 2.48)*	14.36±2.67
20-34	5294	27.3±3.9	1.61 (0.995, 2.42)	14.52±3.48
≥35	1203	37.8±2.7	1.57 (0.906, 2.36)*	14.46±3.71
Entire	6843	28.7±5.9	1.61 (0.987, 2.41)	14.51±3.49
P value	-	-	0.006	0.737

Data are presented as mean±SD for normally distributed variables and as median and quartiles (25th–75th percentiles) for non-normally distributed variables.

TSH: thyroid stimulating hormone, FT4: Free thyroxine

*p<0.05, indicating significant difference between groups with Kruskal Wallis test

Table 2. Comparison of hyperthyroidism, euthyroidism, subclinic hypothyroidism and overt hypothyroidism prevalence according to age groups

Age Groups (year)	Hyperthyroidism ^a n (%)	Euthyroidism ^β n (%)	Subclinical hypothyroidism [‡] n (%)	Overt hypothyroidism ^μ n (%)
≤19 (n:346)	4 (1.2%)	259 (74.9%)	82 (23.7%)	1 (0.3%)
20-34 (n:5294)	136 (2.6%)	3960 (74.8%)	1178 (22.3%)	20 (0.4%)
≥35 (n:1203)	60 (5%)	886 (73.6%)	250 (20.8%)	7 (0.6%)
Entire (n:6843)	200 (2.9%)	5105 (74.6%)	1510 (22.1%)	28 (0.4%)
P value	<0.001*	>0.05	>0.05	>0.05

Data are presented as percentage.

*p value is indicating significant difference between groups with ChiSquare test

^a: TSH <0.1mIU/L

^β: TSH is in the range of 0.1-2.5 mIU/L

[‡]: TSH is in the range of 2.5-10 mIU/L and fT4 values are within normal limits

^μTSH >10 mIU/L or fT4 values below the reference values

Table 3. Comparison of hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hypothyroidism prevalence of age groups <35 and ≥35

Age Groups (year)	Hyperthyroidism ^a	Euthyroidism ^β	Subclinical hypothyroidism [‡]	Overt hypothyroidism ^μ	p*
<35 (n:5640)	140 (2.5%)	4219 (74.8%)	1260 (22.3%)	21 (0.4%)	<0.001
≥35 (n:1203)	60 (5%)	886 (73.6%)	250 (20.8%)	7 (0.6%)	
Total (n:6843)	200 (2.9%)	5105 (74.6%)	1510 (22.1%)	28 (0.4%)	

^a: TSH <0.1 (mIU/L)

^β: TSH (0.1-2.5 (mIU/L))

[‡]: TSH is in the range of 2.5-10 (mIU/L) and fT4 values are within normal limits according to our hospital reference values (0.61-1.2 ng/dL)

^μTSH >10 (mIU/L) or fT4 values below the hospital reference values <0.61

*ChiSquare test

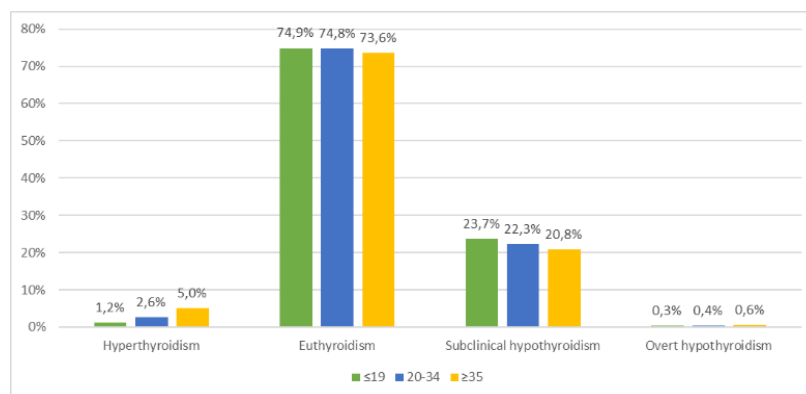


Figure 1. Thyroid profiles and their distribution according to age groups.

Discussion

Thyroid disorders are one of the most frequent endocrine disorders of pregnancy (11). Unfortunately, the normal physiological changes of pregnancy usually mask some of the obvious signs and symptoms of these disorders.

Untreated thyroid disorders have been associated with adverse maternal and fetal outcomes. Taylor PN et al. reported an increased risk of miscarriage, preterm delivery, growth restriction, preeclampsia, and gestational diabetes mellitus in pregnant women with hypothyroidism (2). In another study, children born to mothers with untreated hypothyroidism during pregnancy were shown to have delayed mental and motor functions (12). In a retrospective study conducted over a period of 28 years, it was concluded that hyperthyroid women with uncontrolled disease are at higher risk for preeclampsia, intrauterine growth restriction, spontaneous preterm labor, preterm birth, gestational diabetes mellitus, cesarean delivery, and still birth; and their newborns have lower birth weight than those of euthyroid mothers (13).

Using the ATA cutoffs for TSH (<2.5 mIU/L for the first, and <3.0 mIU/L for the second and third trimesters), Dhanwal KD et al. found 44.3%, 32.0%, and 34% of women from different regions of India to have hypothyroidism in the first, second, and third trimester, respectively (14). The overall prevalence of hypothyroidism in North India was reported to be 6.3% (overt 2.9% and subclinical 3.4%), and a significantly higher incidence of gestational hypertension was found in the overt hypothyroid group (15). The hypothyroidism prevalence in our overall study population was 22.5%, of which 22.1% was subclinical and 0.4% was overt hypothyroidism.

According to a study by Yassaee F et al. in Iran, subclinical and overt hypothyroidism was present in 4.65% among 3158 women. Patients were divided into 4 age groups (<20; 20-25; 25-30; and >30 years), and the number of pregnant women with hypothyroidism was more common in the group of 25-30 years of age. However, the rate of subclinical and overt hypothyroidism among the age groups was not evaluated (16). There was no difference in subclinical and overt hypothyroidism rates between the adolescent age, normal age and advanced maternal age pregnancy groups in our study.

A study in our country by Gunkaya OS et al. stated a prevalence of 8.7%, 8.6%, 3.6%, and 3.6% for hypothyroidism, subclinical hypothyroidism, hyperthyroidism, and subclinical hyperthyroidism, respectively (17). Another study in Turkey from Aegean region found a mean TSH level of 1.68 ± 1.69 mIU/L; and euthyroidism, hyperthyroidism and hypothyroidism were reported in 81.14%, 2.47% and 16.38% of pregnant women (18). Ödöl E. et al. stated a prevalence of 4% for subclinical hypothyroidism in our country from Black Sea region, respectively

(19). Karcaaltincaba D. et al. stated a prevalence of 22.3% and 1.6% for subclinical hypothyroidism and overt hypothyroidism in middle Anatolia region, respectively (20). The mean TSH level and the rate of thyroid disorders in the present study were consistent with recently published data from our country. This might be because we live in a region where iodine deficiency is prevalent.

Thung SF et al. reported that approximately 8 million dollars are saved for every 100.000 pregnant women who were screened for hypothyroidism, and that the hypothyroidism prevalence is reduced to 0.25% by the screening of TSH levels (17). Due to its design, whether could not determine the cost-effectiveness of screening for hypothyroidism or the incidence rates of associated adverse maternal and fetal outcomes, which was a limitation of our study.

Normal lower limit of TSH in pregnancy has been a subject of debate. Ajmani SN et al. reported a hyperthyroidism prevalence of 1.25%, using the ATA criteria (21). Guan HX et al. reported 1.1% prevalence in their study, in which the hyperthyroidism was diagnosed when TSH is less than 0.3 mIU/L (22). Rajput et al. reported 3.7% of pregnant women to have hyperthyroidism. In this study, women with TSH value <0.1 mIU/L were classified as having hyperthyroidism (23). A study on 1311 pregnant women living in Belgium by Moreno-Reyes R et al. reported that the mean TSH level was 1.3 (0.8-1.9) mIU/L, and the frequencies of hyperthyroidism in the first and third trimesters were 3.3% and 1.9%, respectively (24). The frequency of low serum TSH in our study was similar in the first trimester (2.9%). Third trimester values of TSH were not assessed. Unlike many other studies, we observed no significant differences in terms of thyroid disorders between the adolescent age, normal age and advanced maternal age pregnancy groups. Although statistically non-significant, the frequency of hyperthyroidism tended to be higher in mothers of advanced age when compared to mothers with <35 years of age.

We didn't evaluate BMI, gravidas, parities and pregnancy outcomes of the patients. This is the major limitation of the study.

In conclusion; because of the high prevalence, thyroid dysfunction will always keep its importance in a pregnant woman. In a country like ours, where iodine deficiency is common, the first trimester screening is essential. This study was designed to estimate the prevalence of thyroid disorders in first-time mothers of different ages and could not find a statistically significant difference between the three age groups. Therefore, we recommend routine screening of thyroid dysfunction regardless of age, especially during the first trimester. Further studies in populations of different ethnic backgrounds should be carried out to clarify the relationship between the degree of thyroid dysfunction and the associated adverse maternal/fetal outcomes.

Ethics Committee Approval: Clinical Research Ethical Board of Muğla Sıtkı Koçman University was obtained with the letter dated 13.02.2020 and numbered 03/111.

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