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Hypothyroidism prevalence in pregnant women according to age groups

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Abstract

Objective: Investigation of the thyroid function test (fT3, fT4 and TSH) results and the prevalence of overt/subclinical hypothyroidism according to age groups in patients who had applied to our hospital and diagnosed with pregnancy.

Material and Methods: Two thousand nine hundred and thirty-six women diagnosed with pregnancy for the first time upon seeing the fetal heartbeats with ultrasonography between January 2015 and December 2018, were included in our study. Patients were divided into 5 age groups, namely, the age groups of ≤18 years of age, 19-25 years, 26-35 years, 36-45 years and >45 years of age. The fT3, fT4 and TSH levels were statistically compared between all the patients and age groups.

Results: Two thousand nine hundred and thirty-six pregnant women were included in the study. The mean fT3 value was found as 3.180±0.519 (pg/mL), fT4 value as 1.051±0.258 (ng/dl) and TSH value was found as 2.000±1.595 (mIU/mL) in all the population. The mean fT3, fT4 and TSH values were not statically different among the age groups (p=0.06, p=0.08 and p=0.829, respectively). No statistically significant differences were found among all the age groups as regards hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hypothyroidism (p=0.200).

Conclusion: Consistently with the previous studies in our country, the prevalence of subclinical hypothyroidism was found as high as 22.7% in our study. We think that scanning for hypothyroidism must be performed in the pregnancy period without discriminating between risk groups in our country, which is located in the iodine deficiency region. However, considering the different age groups, we believe that TSH levels must be measured with the same apprehensiveness for each age group since no statistically significant differences are found between age groups.

Keywords: Pregnancy, Subclinical hypothyroidism, TSH

Introduction

Thyroid hormone is an essential hormone for normal pregnancy physiology. Moreover, it is a critical factor for fetal development. The reason for the increase in thyroxine binding globulin (TGB) and β-HCG levels is the decrease in fT3 (free triiodothyronine), fT4 (free thyroxine) and TSH (Thyroid Stimulating Hormone) levels (1). Due to these physiological changes in thyroid hormone levels observed during the gestation period, it becomes imperative to determine reference intervals for this period. The American Thyroid Association (ATA) has demonstrated thyroid hormone values specified for pregnancy in its published guidelines (2). TSH value must be 2.5 mIU/L or lower during the first trimester of pregnancy, and 3.0 mIU/L or lower during the second and third trimesters. However, the physiologic lower limits, have been determined as 0.1 mIU/L for the first trimester, 0.2 mIU/L for the second trimester, and 0.3 mIU/L for the third trimester.

The frequency of hypothyroidism during pregnancy is 0.3 to 0.5% for overt hypothyroidism, and 2 to 3% for subclinical hypothyroidism (3). Functional disorders of the thyroid especially within the first half of the pregnancy have been associated with increased abortus risk, retardation of intrauterine development, hypertensive disorders, preterm labor and also lower IQ in the newborn (4).

Overt hyperthyroidism is defined as the low fT4 levels together with low levels of TSH. However, subclinical hyperthyroidism is the condition of normal fT4 levels together with low levels of TSH. Hyperthyroidism during pregnancy is a much rare condition as compared to hypothyroidism with a prevalence of about 0.2% (5). An untreated hyperthyroidism during pregnancy has been associated with perinatal complications such as

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preeclampsia, preterm labor, fetal loss and hyperemesis gravidarum (6, 7).

Diagnosis and treatment of functional thyroid disorders in pregnancy in time will allow the prevention of potential maternal and fetal complications. In recent years, the number of adolescent pregnancies has increased with the increasing refugee population in our country. In addition, pregnancies with advanced maternal ages have increased with the frequent use of assisted reproductive techniques. Therefore, we thought that it would be appropriate to evaluate thyroid function tests according to different age groups. In this study, we aimed at evaluating the TSH, fT4 and fT3 levels determined during the first trimester mainly based on different age groups, and to investigate the prevalence of thyroid function disorders during pregnancy.

Material and Methods

This study was planned as a retrospective study in Ankara, University of Health Sciences, Gülhane Education and Research Hospital, Gynecology and Obstetrics Clinic. Approval of the Ethics Committee was obtained for the study (Date:18/12/2018, Decision No:18/327). The study was conducted in accordance with the Helsinki Declaration.

Two thousand nine hundred and thirty-six women who had applied to our hospital between January 2015 and December 2018, diagnosed with pregnancy for the first time upon seeing the fetal heartbeats with ultrasonography and routine pregnancy tests were carried out in the Gynecology and Obstetrics Clinic of our Hospital were included in our study. Patients' data were accessed through the data processing system of our Hospital (Fonet Data Processing Systems). Ages at admission and fT3, fT4 and TSH levels of patients were recorded.

fT3, fT4 and TSH hormone tests were run in the Biochemistry Laboratory of our Hospital using the 10-cc blood samples harvested from the antecubital vein at admission. In these tests, TSH hormone levels were determined using the two-side immune-enzymatic assay (sandwich) method, fT4 hormone was determined using the two-step enzyme immunoassay method, and fT3 hormone was determined using the competitive binding immune-enzymatic assay method with Beckman Coulter DXI-600 immunoassay analyzer (Beckman Coulter, Inc., CA, USA).

According to ATA recommendations, the patients with singleton pregnancy, no history of thyroid pathology or autoimmune disease, no goiters and no use of medicines affecting the thyroid hormone levels were included the study. The exclusion criteria determined as twin pregnancies, women who used thyroid interfering medication before pregnancy or during pregnancy, women who had pre-existing thyroid disease.

With the purpose of comparing the thyroid function tests of patients included in the study between the age groups, patients were divided into 5 groups as <18 years of age, 18-25 years of age, 26-35 years of age, 36-45 years of age and >45 years of age. Levels of fT3, fT4 and TSH were compared among the entire group of patients and among the age groups. According to the World Health Organization (WHO), the adolescent pregnancy period is between 10-18 years old (8); pregnancies at ages older than 35 years are described advanced maternal age (9) and pregnancies at ages older than 45 years are described very advanced maternal age groups (10).

Furthermore, all the above-mentioned age groups were compared with each other as regards hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hyperthyroidism. TSH range between 0.1 and 2.5 mIU/L was accepted as euthyroidism based on the American Thyroid Association (ATA) guidelines and Turkish Endocrinology and Metabolism Association Guidelines. Pregnant women with TSH levels in the range between 2.5 and 10 mIU/L and fT4 levels in the range of 0.61-1.2 mIU/L, which is the reference range used in our Hospital, were accepted as subclinical hypothyroidism. Patients with TSH levels >10 mIU/L or fT4 levels >1.2 mIU/L were accepted as overt hypothyroidism.

Data were analyzed using the IBM SPSS V23. The one-way variant analysis was used to compare the mean T3, T4 and TSH values based on age groups. 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 categoric data. The level of significance was accepted as $p<0.05$.

Results

Two thousand nine hundred and thirty-six pregnant women were included in the study. The mean age of the pregnant women was 29.09±5.97 (min:13, max:52). The mean fT3 value was 3.180±0.519 (pg/mL), fT4 value was 1.051±0.258 (ng/dl) and TSH value was 2.000±1.595 (mIU/mL) for the entire group. Also, the mean values of fT3, fT4 and TSH were determined for all the age groups. (Table 1, Figure 1)

The mean fT3 value did not differ among the age groups ($p=0.06$). The mean fT3 value in the age group of 45 years of age or older was found lower than the values in age groups of 18 years or younger and the age group between 19 and 25 years of age ($p<0.05$). The mean fT4 values also did not differ among the age groups ($p=0.08$). The mean TSH values did not differ based on age groups ($p=0.829$) (Table 1).

Considering patients diagnosed with subclinical hypothyroidism; when fT4 is within the normal range (0.61-1.2 mIU/L), the rate of the pregnant women with TSH value between 2.5-10.0 mIU/L for the different age groups were; 17.5% for 18 years old or younger (n= 57), 22.4% for those in the age range of 19 and 25 years (n= 829), 22.6% for those in the age range of 26 and 35 years (n= 1596), 24% for those in the age range of 36-44 years (n= 420) and 23.5% for those 45 years of age or older (n= 34); respectively. (Table 2, Figure 2)

Considering patients diagnosed with overt hypothyroidism the rate of the pregnant women with TSH values were >10 (mIU/L) for the different age groups were; 1.75% for 18 years old or younger (n= 57), 2.5% of those in the age range of 19 and 25 years (n= 829), 1.82% of those in the

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age range of 26 and 35 years (n= 1596), 2.1% of those in the age range of 36-44 years (n= 420). (Table 2, Figure 2)

The rate of the pregnant women who has normal TSH values (between 0.1-2.5 mIU/L) called as euthyroidism, in different groups were; 78.9% for 18 years old or younger ages (n= 57), 72.5% for the age range of 19 and 25 years (n= 829), 72.1% for the age range of 26 and 35 years (n= 1596), 71.9% for the age range of 36-44 years (n= 420), 73.5% for 45 years of age or older (n= 34). (Table 2)

Upon evaluation based on TSH levels, it was seen that TSH values were <0.1 mIU/L in 1.75% in the pregnant women 18 years old or younger (n= 57), in 2.5% of those in the age range of 19 and 25 years (n= 829), in 1.82% of those in the age range of 26 and 35 years (n=1596), 2.1% of those in the age range of 36-44 years (n= 420) (hyperthyroidism). (Table 2, Figure 2)

No statistically significant differences were found in all the age groups as regards hyperthyroidism, euthyroidism, subclinical hypothyroidism and overt hypothyroidism. (p=0.200).

Table 1. Comparison of fT3, fT4 and TSH values according to age groups

Age Groups (year)	Age (average ±SD)	T3 (pg/ml)	T4 (ng/dl)	TSH (mIU/l)
≤18 (n=57)	17,3±1,1	3,28±0,529[b]	1,12±0,232[ab]	1,92±1,164
19-25 (n=829)	23,02±1,2	3,29±0,531[b]	1,06±0,252[ab]	2,05±1,438
26-35 (n=1596)	29,85±2,8	3,16±0,495[ab]	1,04±0,262[a]	1,98±1,765
36-44 (n=420)	38,35±2,11	3,06±0,547[ab]	1,07±0,263[ab]	1,97±1,270
≥45 (n=34)	47,7±2,1	2,92±0,384[a]	1,16±0,157[b]	1,84±0,930
Total (n=2936)	29,09±5.97	3,18±0,519	1,05±0,258	2,00±1,595
p*	.	0,06	0,08	0,829

*One Way ANOVA, a-b: There is no difference between age groups with the same letter

Table 2. Comparison of TSH values according to age groups

Age Groups (year)	Hyperthyroidism [α]	Euthyroidism[β]	Subclinical hypothyroidism[¥]	Overt hypothyroidism [µ]	p*
≤18 (n=57)	1 (1,75 %)	45 (78,9%)	10 (17,5%)	1 (1,75%)	
19-25 (n=829)	21 (2,5%)	601 (72,5%)	186 (22,4 %)	21 (2,5%)	
26-35 (n=1596)	29 (1,82%)	1151 (72,1%)	361 (22,6%)	55 (3,4%)	0,200
36-44 (n=420)	9 (2,1%)	302 (71,9%)	101 (24%)	8 (1,9%)	
≥45 (n=34)	-	25 (73,5%)	8 (23,5%)	1 (2,9%)	
Total (n=2936)	60 (2%)	2124 (72,3%)	666 (22,7%)	86 (2,9%)	

[α]: 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), [µ] TSH> 10 (mIU / L) or fT4 values below the hospital reference values <0.61, *Chi Square test

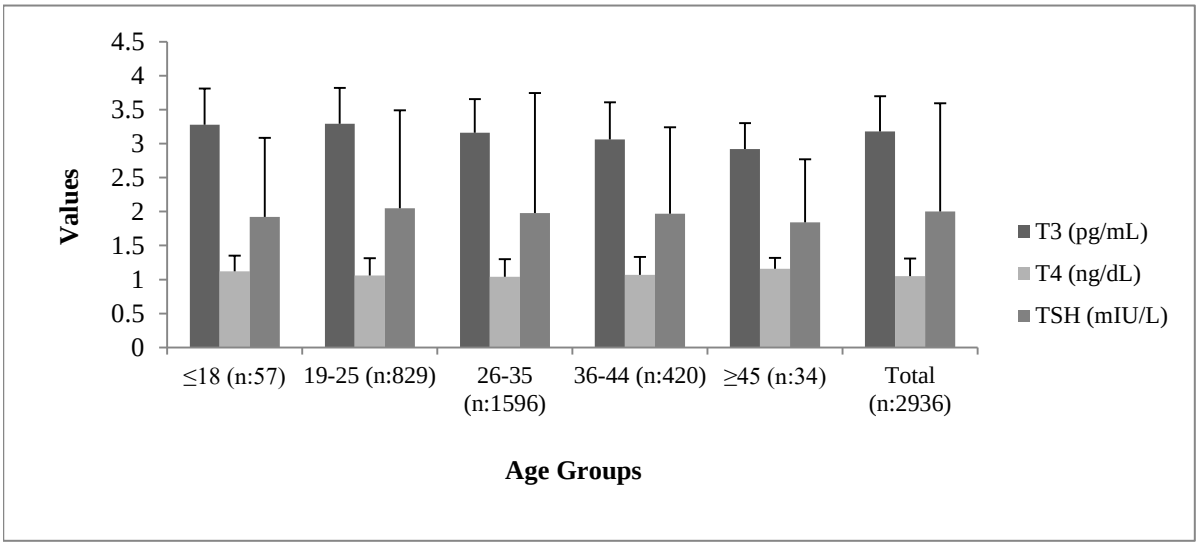

Figure 1. fT3, fT4 and TSH values according to age groups

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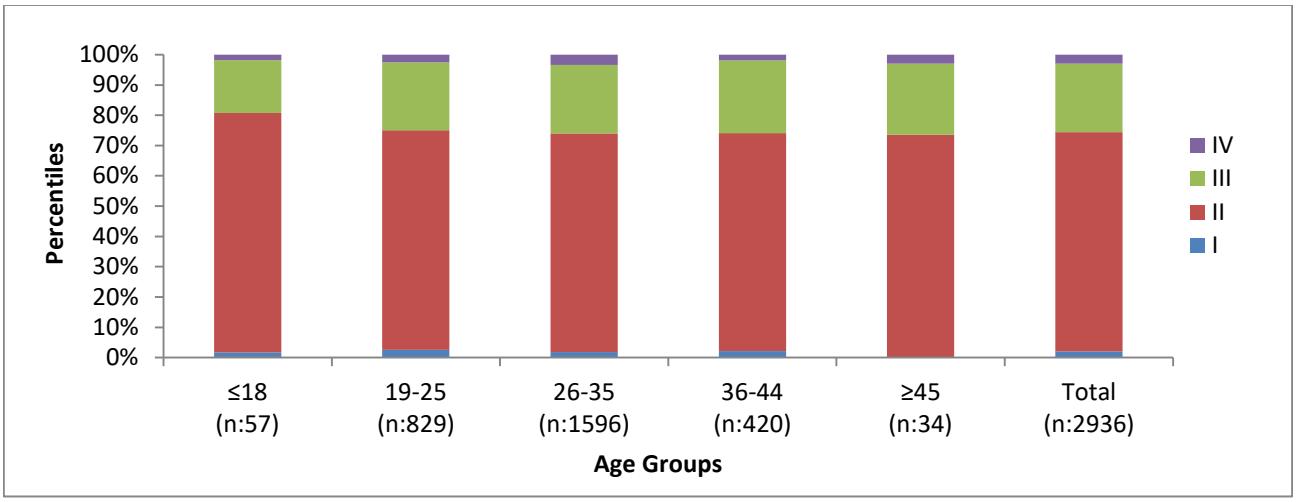

Figure2. Distribution of clinical conditions due to Thyroid values by age groups.
I: Hyperthyroidism, II:Euthyroidism, III:Subclinical hypothyroidism, IV:Overt hypothyroidism

Discussion

In our study, the prevalence of subclinical hypothyroidism in patients admitted to our hospital, which is a tertiary center and diagnosed with pregnancy, was found as high as 22.7%. However, no statistically significant differences were found among the age groups. Thyroid pathologies are the second most common endocrine disease in women of reproductive age, following gestational diabetes mellitus. (5). Fetal and placental development in pregnancy (especially in early pregnancies) are related to maternal thyroid hormones (11). The fetal thyroid gland synthesizes thyroid hormone only after the second half of pregnancy, and therefore, maternal thyroid hormone levels play a critical role in the early periods (12). Even if the signs of thyroid diseases are overt, physiologic changes of pregnancy can mask such signs.

In the current literature, untreated thyroid disorders have been associated with increased maternal and fetal complications from the preconception period till the postpartum period (13). However, Ong et al. did not find any association between functional thyroid disorders and increased complications of pregnancy in the first trimester (14). In addition to overt thyroid disorders, neurodevelopmental outcomes were also investigated in infants born from pregnant women following the administration of subclinical hypothyroidism treatment. In the study of Casey et al, there was no IQ difference between the babies of the pregnant women who were diagnosed and treated with subclinical hypothyroidism and followed up without treatment (15). However, treatment is recommended for subclinical hypothyroidism (5). Since neurocognitive improvement following the treatment of subclinical hypothyroidism has not been clinically proven and also subclinical hypothyroidism incidence is about 2%, American College of Obstetricians and Gynecologists (ACOG) does not recommend routine thyroid scanning during pregnancy (16). However, routine scanning appears more rational based on subclinical hypothyroidism prevalence found as 22.7% and overt hypothyroidism prevalence as 2.9% and considering the conditions of our country, which is a region of iodine deficiency.

The pregnant women are diagnosed as overt hypothyroidism if the TSH values specific for the trimester are increased (TSH >2.5 mIU/ml for the first trimester) and fT4 levels are decreased. In cases where TSH level is >10 mIU/ml, overt hypothyroidism diagnosis is made without regarding the T4 levels. In the patients included in our study, the prevalence of overt hypothyroidism was found as 2.9%. In the study of Güzel et al., overt hypothyroidism prevalence was found as 10.18% (18). However, the number of patients in this study was meager compared to our study. Iodine deficiency is a common condition in our country. Compared to developed countries, we think that the reason for the higher frequency of hypothyroidism in our country is iodine deficiency (19).

In subclinical hypothyroidism cases TSH levels are in the range of 2.5-10 mIU/ml, and fT4 levels are normal. In the patients included in our study, subclinical hypothyroidism prevalence was found at 22.7%. In our country, this rate was found as 15.6% in the study of Güzel et al., and 16.38% in the study of Seven et al. (17, 18). The prevalence of subclinical hypothyroidism in the USA has been reported as 2-2.3% (20). Hypothyroidism prevalence as high as 21.5% had been shown in India previously (6). In the study of Li and colleagues in China, subclinical hypothyroidism prevalence was found as 27.8% (21). Although it has been suggested that the proportional differences in our country are related to the iodine intake varying according to the areas that studies are carried out in, it is also seen that subclinical hypothyroidism prevalence is high consistently with other Asian countries. Together with this, such variable proportions and prevalence found very high depending on the cutoff value for TSH as 2.5 mIU/ml indicates that population-specific values should be determined (22, 23).

In hyperthyroidism cases, TSH levels are <0.1 mIU/ml. In the patients included in our study, hyperthyroidism prevalence was found at 2%. This rate was found as 5.38% in the study of Güzel et al., and 2.47% in the study of Seven et al. in our country (17, 18). We think that the differences in these studies conducted in the same country are caused by regional differences (19).

In a study investigating the relationship between age and thyroid functions, it was found that serum TSH levels increased with the increasing age; however, there are no changes in fT4 levels, and there were no age-dependent increases in thyroid diseases (24). However, in another study investigating the changes in TSH with age, it was shown similarly with the above that TSH levels increased with age; however, taking the TSH >2.5 level as the basis in the advanced age group can lead to erroneous hypothyroidism diagnoses (25).

However, this age-dependent change is especially marked in 50 years of age and afterward, and this corresponds to the end of the reproductive period. In our study, when we compared the different age groups of pregnant women with each other, no statistically significant differences were seen in mean TSH values (p=0.829). No statistically significant differences were found in the comparison of various age groups as regards subclinical hypothyroidism and overt hypothyroidism (p=0.200).

The most important limitation of our study is that it reflects the thyroid function test results in pregnant women coming from a particular area. More comprehensive results can be obtained through analyses carried out on data from different areas.

Conclusion

Subclinical hypothyroidism prevalence was high as 22.7% in our study like in previous studies carried out in our country. We think that hypothyroidism scanning must be performed in the pregnancy period without discriminating between risk groups in our country, which is located in the iodine deficiency region. However, considering the different age groups, no statistically significant differences are found between age groups. We believe that TSH levels must be measured with the same apprehensiveness for each age group.

Conflict of interest statement: The authors declare that there is no actual or potential conflict of interest.

Author's contributions: BÇ*, BÇ, ÖŞK, CŞ, REP, KEK; Design of research, data collection and Patient examinations, **BÇ*;** preparation of article and revisions

Ethical issues: Author declare, originality and ethical approval of research. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

References

1. Tekin YB, Güven ESG. Gebelikte tiroid hastalıkları ve neonatal sonuçları. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi. 2014;11(4).
2. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011;21(10):1081-125.
3. Altomare M, La Vignera S, Asero P, Recupero D, Condorelli R, Scollo P, et al. High prevalence of thyroid dysfunction in pregnant women. Journal of endocrinological investigation. 2013;36(6):407-11.
4. Vanderpump M, Tunbrldge W, French J, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: a twenty - year follow - up of the Whickham Survey. Clinical endocrinology. 1995;43(1):55-68.
5. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, 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(3):315-89.
6. Rajput R, Goel V, Nanda S, Rajput M, Seth S. Prevalence of thyroid dysfunction among women during the first trimester of pregnancy at a tertiary care hospital in Haryana. Indian journal of endocrinology and metabolism. 2015;19(3):416.
7. Güler AE, Yıldız B, Çakmak B, Güler ZÇD, Kıncı MF. Are Thyroid Functions Effective in Pregnant Women with Hyperemesis Gravidarum? 2019.
8. Keskin U, Kıncı MF. Adolesan Dönemi ve Gebelikler. Turkiye Klinikleri Family Medicine-Special Topics. 2018;9(5):33-8.
9. De Cicco S, Zhang L, Simpson P, Hibbard JU, Kriegel AJ, Palatnik A. 233: The association between fetal growth restriction and advanced maternal age. American Journal of Obstetrics & Gynecology. 2019;220(1):S168-S9.
10. Hoover E, Yankowitz J, Louis J. Very advanced maternal age and perinatal outcomes. American journal of obstetrics and gynecology. 2019;220(1).
11. Krassas G, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocrine reviews. 2010;31(5):702-55.
12. Cooper DS, Biondi B. Subclinical thyroid disease. The Lancet. 2012;379(9821):1142-54.
13. Li Y, Shan Z, Teng W, Yu X, Li Y, Fan C, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25–30 months. Clinical endocrinology. 2010;72(6):825-9.
14. Ong GS, Hadlow NC, Brown SJ, Lim EM, Walsh JP. Does the thyroid-stimulating hormone measured concurrently with first trimester biochemical screening tests predict adverse pregnancy outcomes occurring after 20 weeks gestation? The Journal of Clinical Endocrinology & Metabolism. 2014;99(12):E2668-E72.
15. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics & Gynecology. 2005;105(2):239-45.
16. Obstetricians ACo, Gynecologists. Practice Bulletin No. 148: Thyroid disease in pregnancy. Obstetrics and gynecology. 2015;125(4):996.
17. Seven A, Kucur SK, Polat M, Yüksel B, Işıklar Ö, Keskin N. Gebelerde Birinci Trimester Tiroid Fonksiyon Testi Sonuçlarının Değerlendirilmesi. Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi. 2016;3(2):5-8.

18. Güzel D, Aydın DS, Çilesiz Göksedef BP, Boran AB. The incidence of thyroid dysfunction in pregnant women. PERINATAL. 2015;23(2):96-100.

19. Cetinkaya K, Ingec M, Cetinkaya S, Kaplan I. (2012). Iodine deficiency in pregnancy and in women of reproductive age in Erzurum, Turkey. Turkish Journal of Medical Sciences, 42(4), 675-680.

20. Allan W, Haddow J, Palomaki G, Williams J, Mitchell M, Hermos R, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. Journal of medical screening. 2000;7(3):127-30.

21. Teng X, Shan Z, Chen Y, Lai Y, Yu J, Shan L, et al. More than adequate iodine intake may increase subclinical hypothyroidism and autoimmune thyroiditis: a cross-sectional study based on two Chinese communities with different iodine intake levels. European journal of endocrinology. 2011;164(6):943-50.

22. Maraka S, Ospina NMS, O'Keeffe DT, Espinosa De Ycaza AE, Gionfriddo MR, Erwin PJ, et al. Subclinical hypothyroidism in pregnancy: a systematic review and meta-analysis. Thyroid. 2016;26(4):580-90.

23. Völzke H, Alte D, Kohlmann T, Lüdemann J, Nauck M, John U, et al. Reference intervals of serum thyroid function tests in a previously iodine-deficient area. Thyroid. 2005;15(3):279-85.

24. Bremner AP, Feddema P, Leedman PJ, Brown SJ, Beilby JP, Lim EM, et al. Age-related changes in thyroid function: a longitudinal study of a community-based cohort. The Journal of Clinical Endocrinology. 2012;97(5):1554-62.

25. Surks MI, Hollowell JG. Age-Specific Distribution of Serum Thyrotropin and Antithyroid Antibodies in the U.S. Population: Implications for the Prevalence of Subclinical Hypothyroidism. The Journal of Clinical Endocrinology & Metabolism. 2007;92(12):4575-82. doi: 10.1210/jc.2007-1499.