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Gestational outcomes of thyroid function in the first trimester

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Abstract

Objective: In this study, we aimed to determine the frequency of potential poor perinatal outcomes in pregnant women with thyroid dysfunction in the first trimester.

Methods: A total of 1000 pregnant women whose weeks of gestation varied between 4 and 43 and who admitted to the obstetrics clinic of our hospital between 2012 and 2015 were included in our study. The pregnant women whose thyroid functions were checked in the first trimester were evaluated in terms of abortion, early preterm, late preterm, total preterm, premature rupture of membranes, intrauterine growth retardation, oligohydramnios, preeclampsia, gestational hypertension, gestational diabetes, late term pregnancy, postterm pregnancy, delivery type, 1-minute and 5-minute Apgar scores, birth weight, newborn intense care needs, and they were associated with the data of thyroid function tests in the first trimester (serum TSH, free T4, and free T3 levels).

Results: In our study, hypothyroidism incidence was 8.7%, sub-clinical hypothyroidism incidence was 8.6%, hyperthyroidism incidence was 3.6% and sub-clinical hyperthyroidism incidence was 3.6% in the patients. The patients who were and were not found to have thyroid function pathology were assessed in terms of abortion, early preterm, late preterm, total preterm, intrauterine growth retardation, oligohydramnios, preeclampsia, gestational hypertension, gestational diabetes mellitus, late term pregnancy, postterm pregnancy, delivery type, 1-minute and 5-minute Apgar scores, cesarean indications and incidence, birth weight and newborn intense care needs, and no statistically significant difference was found in the patients who underwent treatment. Early rupture of membranes was observed more frequently in the group with hypothyroidism.

Conclusion: Although there is no certain consensus for performing routine thyroid function test in the first trimester in endocrine study groups examining first trimester thyroid functions of pregnant women, TSH screening is considered important, especially in risky pregnant women, in countries where endemic iodine deficiency such as Turkey due to the potential harms of thyroid function pathology on fetus.

Keywords: First trimester, pregnancy, thyroid dysfunction.

Özet: İlk trimesterde tiroid fonksiyonunun gebelik sonuçları

Amaç: Bu çalışma ilk trimesterde tiroid disfonksiyonu olan gebelerde oluşabilecek kötü perinatal sonuçların sıklığının belirlenmesi amacıyla yapıldı.

Yöntem: Çalışmaya, hastanemiz gebe polikliniğine 2012–2015 tarihleri arasında başvuran, gebelik haftası 4 ile 43 hafta arasında değişen 1000 gebe alındı. İlk trimesterde tiroid fonksiyonlarına bakılan gebeler; abortus, erken preterm, geç preterm, toplam preterm, erken membran rüptürü, intrauterin gelişme geriliği, oligohidroamniyoz, preeklampsi, gestasyonel hipertansiyon, gestasyonel diyabet, geç term gebelik, postterm gebelik, doğum şekli, 1. dk ve 5. dk Apgar skorları, doğum tartısı, yenidoğan yoğun bakım gereksinimleri açısından değerlendirilerek ilk trimester tiroid fonksiyon testleri verileri (serum TSH, serbest T4, serbest T3 düzeyleri) ile ilişkilendirildi.

Bulgular: Çalışmamızda hastalarda hipotiroidi sıklığı %8,7, subklinik hipotiroidi sıklığı %8.6, hipertiroidi sıklığı %3.6 ve subklinik hipertiroidi sıklığı %3.6 olarak saptandı. Tiroid fonksiyon patolojisi tespit edilen ve edilmeyen hastalar abortus, erken preterm, geç preterm, toplam preterm, intrauterin gelişme geriliği, oligohidroamniyoz, preeklampsi, gestasyonel hipertansiyon, gestasyonel diyabet, geç term gebelik, postterm gebelik, doğum şekli, 1. dk ve 5. dk Apgar skorları, sezaryen endikasyonları ile sıklığı, doğum tartısı, yenidoğan yoğun bakım gereksinimi açısından incelendiğinde, tedavi alan hastalar açısından istatistiksel olarak anlamlı bir fark bulunmadı. Hipotiroidi saptanan gebe grubunda erken membran rüptürü daha sık olarak gözlendi.

Sonuç: Gebelerde ilk trimester tiroid fonksiyonlarını irdeleyen endokrin çalışma gruplarında ilk trimesterde rutin tiroid fonksiyon testi yapılması açısından kesin bir fikir birliği olmamakla birlikte, tiroid fonksiyon patolojisinin fetüse olası potansiyel zararları nedeniyle, Türkiye gibi endemik iyot eksikliğinin bulunduğu ülkelerde, başta riskli gebeler olmak üzere, TSH taramasının önemli olduğu düşünülmektedir.

Anahtar sözcükler: İlk trimester, gebelik, tiroid fonksiyon bozukluğu.

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Introduction

Thyroid disorders are the endocrine pathologies seen mostly during reproductive ages. Depending on the physiological changes developing during pregnancy, thyroid hormone levels also change. In parallel with this, thyroid gland dysfunctions can be seen widely during pregnancy and the changes may cause problems for newborn and mother. With proper treatment and management, pregnancy period can be completed normally.

Sufficient levels of thyroid hormones are also needed for the development of health fetus during pregnancy as in fertility.[1,2] Maternal thyroid disorders seen during pregnancy have been associated with fetal loss, preeclampsia, preterm labor, ablatio placentae, and losses in the fetal intellectual functions.[3,4] Fetus is not capable of producing its own thyroid hormones until 10–12 weeks of gestation; until these weeks, it meets this need through maternal thyroxine (T4); T4 passes through the placenta and it is used by fetus. In case of maternal hypothyroidism, thyroid hormones required by fetus cannot be met by mother sufficiently. The development of fetal neuropsychomotor can be affected negatively during the early gestational periods in particular. It has been observed that Intelligence Quotient (IQ) scores of such fetuses are lower.[4,5] In our study, we have assessed the data of fetus and pregnant women who had risk factors in terms of thyroid disorders during pregnancy and found to have pathologies in the first trimester thyroid function tests.

Methods

In our retrospective study, we evaluated the hospital data of pregnant women who underwent thyroid function tests during the admission in the first trimester (6–14 weeks of gestation) at Gynecology and Obstetrics Clinic of Kanuni Sultan Süleyman Training and Research Hospital between 2013 and 2016 and whose gestational follow-ups and deliveries were carried out in our clinic. We obtained the approval no. 2015/33 from the local ethic committee of our hospital. A total of 1000 pregnant women, of whose 755 had normal results for thyroid function tests and 245 had pathology according to the thyroid function tests, were included in the study.

We distributed the pregnant women, who were included in the study, into the groups according to the following criteria; thyroid stimulant hormone (TSH) reference range was considered 0.1–2.5 mU/L and free T4 (FT4) reference range was considered 0.93–1.71 ng/dL. Hyperthyroidism – Group 1: Those with TSH value below 0.1 mU/L and FT4 value above 1.71 ng/dL; Hypothyroidism – Group 2: Those with TSH value above 10 mU/L without considering the FT4 data and those with TSH value between 2.5 and 10 mU/L and FT4 value below 0.93 ng/dL; Sub-clinical hyperthyroidism – Group 3: Those with TSH value below 0.1 mU/L and normal values for FT4 and free T3 (FT3); Sub-clinical hypothyroidism – Group 4: Those with TSH value between 2.5 and 10 mU/L and normal level of FT4 values.

We compared the patients who underwent thyroid function in the first trimester in terms of the variables such as the demographic characteristics (age, gravida, parity, abortion, curettage), obstetric outcomes [abortion, early preterm labor, late preterm labor, premature preterm rupture of membranes, premature rupture of membranes (PROM), preeclampsia, intrauterine growth retardation (IUGR), oligohydramnios, gestational diabetes mellitus (GDM), gestational hypertension (GHT), late term labor, postterm labor, term labor and cesarean indications], birth weight, 1-minute and 5-minute Apgar scores, newborn intense care need and whether the pregnant women underwent treatment for thyroid dysfunctions or not.

The exclusion criteria of our study were as below: (1) Multiple pregnancy, the decision for curettage due to fetus with anomaly or associated reason, (2) presence of additional systemic diseases in pregnant woman [rheumatismal diseases: Systemic lupus erythematosus (SLE), Behcet's disease, rheumatoid arthritis; endocrine disorders: Type 1 and 2 diabetes; autoimmune disorders], (3) placental insertion anomaly, and (4) missing hospital records of pregnant woman or not performing the follow-ups in our clinic.

For the statistical analyses of the results in our study, we used IBM Statistical Package for the Social Sciences-22 (IBM SPSS-22) software (SPSS Inc., Chicago, IL, USA). We checked the conformability of parameters to the normal distribution by Shapiro-Wilk test. When analyzing the study data for comparing the descriptive statistical methods (mean, standard deviation, and frequency) as well as quantitative data, we used Kruskal-Wallis test to compare the parameters

showing normal distribution between more than two groups, and Mann-Whitney U test to determine the group creating the difference. For the qualitative data comparison, we used chi-square test. We considered the value p<0.05 statistically significant.

Results

A total of 1000 pregnant women with ages between 16 and 49 years, who underwent first trimester thyroid function test at the Gynecology and Obstetrics Clinic of Kanuni Sultan Süleyman Training and Research Hospital between 2013 and 2016 and whose medical records could be reached completely, were included in the study.

The mean age of the cases was 29.75±5.63 years. Of the cases, 755 (75.5%) were diagnosed euthyroid, 36 (3.6%) were diagnosed hyperthyroid, 87 (8.7%) were diagnosed hypothyroid, 36 (3.6%) were diagnosed sub-clinical hyperthyroid and 86 (8.6%) were sub-clinical hypothyroid, and the cases were evaluated in these five groups. Since we are a reference clinic, it should be noted that these data do not reflect Turkish incidences. No statistically significant difference was found among the groups in terms of mean ages and the numbers of gravida, parity and abortus (p>0.05) (**Table 1**).

There was a statistically significant difference among the groups in terms of the weeks for performing thyroid function tests (TFT). As a result of the pairwise comparisons to determine the group creating the difference, TFT weeks of hyperthyroid group was significantly higher than the weeks of euthyroid (p=0.028) and hypothyroid (p=0.007) groups. Similarly, TFT weeks of sub-clinical hyperthyroid group was significantly higher than the weeks of euthyroid (p=0.038) and hypothyroid (p=0.011) groups. There was no significant difference among other groups in terms of the weeks for performing TFT (**Table 1**).

There was no statistically significant difference among the groups in terms of birth weights, 1-minute and 5-minute Apgar scores, abortion incidence and fetal sex distributions (p>0.05). There was also no statistically significant difference among the groups in terms of early preterm, late preterm, total preterm and late term incidences and newborn intense care need rates (p>0.05) (**Table 2**).

There was a statistically significant difference among the groups in terms of the PROM incidence (p=0.012). As a result of the pairwise comparisons to determine the group creating the difference, PROM incidence was found significantly higher in hypothyroid group (2.3%) than the euthyroid group (0.1%) (p=0.030). There was no significant difference among other groups in terms of PROM incidence (p>0.05) (**Table 3**). There was also no statistically significant difference among the groups in terms of the incidences of IUGR, oligohydramnios, preeclampsia, postterm pregnancy, GDM and GHT (p>0.05) (**Table 3**). Similarly, there was also no statistically significant difference among the groups in terms of delivery types (**Table 2**) and cesarean indications (**Table 4**) (p>0.05).

Discussion

In the literature, hyperthyroidism and hypothyroidism are associated with abortion frequency.[6] Similarly, Rao et al.[7] found in their studies the abortion frequency 4.29% in the first trimester in pregnant women with hypothyroid. However, Vaidya et al.[8] did not find the incidence of thyroid disorders higher in the pregnancies

Table 1. General characteristics of the cases by groups.

	Euthyroid	Hyperthyroidism Group 1	Hypothyroidism Group 2	Sub-clinical hyperthyroidism Group 3	Sub-clinical hypothyroidism Group 4	p
Age (year)	29.65±5.61	30.00±5.12	30.30±5.73	31.06±5.80	29.44±5.84	0.508*
Number of gravida (n)	2.6±1.46 (2)	2.64±1.29 (2.5)	2.7±1.42 (3)	2.75±1.16 (3)	2.41±1.31 (2)	0.404†
Number of parity (n)	1.19±1.06 (1)	1.22±0.93 (1)	1.23±1.05 (1)	1.31±0.89 (1)	1.07±1.02 (1)	0.614†
Number of abortion (n)	0.37±0.78 (0)	0.36±0.8 (0)	0.43±0.83 (0)	0.42±0.77 (0)	0.28±0.61 (0)	0.902†
Number of curettage (n)	0.03±0.21 (0)	0.06±0.23 (0)	0.05±0.21 (0)	0.03±0.17 (0)	0.06±0.32 (0)	0.750†
Week for TFT	9.41±2.71 (9)	10.28±2.17 (10)	9.01±2.73 (8)	10.25±2.35 (10)	9.57±2.95 (9)	0.023†,‡
Week of gestation	38.29±3.94 (39)	38.14±2.84 (39)	38.24±4.2 (39)	38.72±1.32 (39)	38.47±4.19 (39)	0.510†

*One-way ANOVA test; †Kruskal-Wallis test; ‡p<0.05. The results are presented in mean ± standard deviation (median) format. **TFT:** thyroid function tests.

Table 2. General characteristics of the newborns by groups.

	Euthyroid	Hyperthyroidism Group 1	Hypothyroidism Group 2	Sub-clinical hyperthyroidism Group 3	Sub-clinical hypothyroidism Group 4	p
Total birth weight (g) (n=983)	3217.02±567.90 (3260)	3034.86±684.29 (3160)	3194.35±730.58 (3340)	3233.47±450.09 (3242.5)	3242.59±671.69 (3300)	0.475*
1-minute Apgar score (n=983)	8.41±1.18 (9)	7.56±2.06 (8)	8.44±1.22 (9)	8.64±0.59 (9)	8.33±1.46 (9)	0.074*
5-minute Apgar score (n=983)	9.56±0.89 (10)	9.03±1.4 (9.5)	9.45±1.31 (10)	9.69±0.52 (10)	9.46±1.31 (10)	0.124*
Abortion	14 (1.9%)	0 (0%)	2 (2.3%)	0 (0%)	1 (1.2%)	0.793†
Sex (n=983)						
Male	373 (50.3%)	17 (47.2%)	47 (55.3%)	13 (36.1%)	54 (63.5%)	0.052†
Female	368 (49.7%)	19 (52.8%)	38 (44.7%)	23 (63.9%)	31 (36.5%)	
Early preterm	23 (3%)	2 (5.6%)	2 (2.3%)	0 (0%)	4 (4.7%)	0.599†
Late preterm	78 (10.3%)	7 (19.4%)	8 (9.2%)	3 (8.3%)	5 (5.8%)	0.244†
Total preterm	100 (13.2%)	9 (25%)	10 (11.5%)	3 (8.3%)	9 (10.5%)	0.204†
Late term	64 (8.5%)	7 (19.4%)	6 (6.9%)	2 (5.6%)	4 (4.7%)	0.092†
Intense care need	58 (7.7%)	4 (11.1%)	6 (6.9%)	1 (2.8%)	10 (11.6%)	0.460†

*Kruskal-Wallis test; †chi-square test. The results are presented in mean ± standard deviation (median) format.

of cases with previous history of abortion. We also did not find any statistically significant difference between euthyroid cases and those found to have thyroid pathology in terms of abortion frequency, and found the abortion frequency 1.7%. Although thyroid disorders are considered a reason for abortion, overt hyperthyroidism and hypothyroidism rather coexist with infertility;[9] therefore, since it is more difficult for such patients to get pregnant, further and wider studies are needed to suggest that abortion may increase in thyroid patients.

Stagnaro-Green et al.[10] carried out their study on 124 pregnant women and found that the cases out of 28 pregnant women whose serum TSH levels before 15 weeks of gestation were above 97.5th percentile had preterm labor before 32 weeks of gestation. On the other hand, Ashoor et al.[11] found no statistically significant difference between the pregnant women who had thyroid dysfunction between 11 and 13 weeks of gestation and those who had no thyroid dysfunction during the same weeks in terms of early preterm labor. Similarly, we did not find any statistically significant

Table 3. Other characteristics of the cases by groups.

	Euthyroid	Hyperthyroidism Group 1	Hypothyroidism Group 2	Sub-clinical hyperthyroidism Group 3	Sub-clinical hypothyroidism Group 4	p
Delivery type (n=983)						
NSD	431 (58.2%)	21 (58.3%)	57 (67.1%)	17 (47.2%)	44 (51.8%)	0.203
C/S	310 (41.8%)	15 (41.7%)	28 (32.9%)	19 (52.8%)	41 (48.2%)	
C/S indication (n=413)	309 (41.7%)	15 (41.7%)	28 (32.9%)	19 (52.8%)	41 (48.2%)	0.202
PROM	1 (0.1%)	0 (0%)	2 (2.3%)	0 (0%)	0 (0%)	0.012†
IUGR	36 (4.8%)	2 (5.6%)	6 (6.9%)	1 (2.8%)	7 (8.1%)	0.602
Oligohydramnios	33 (4.4%)	2 (5.6%)	3 (3.4%)	1 (2.8%)	3 (3.5%)	0.960
PE	38 (5%)	1 (2.8%)	6 (6.9%)	0 (0%)	6 (7%)	0.470
Postterm pregnancy	3 (0.4%)	0 (0%)	0 (0%)	0 (0%)	2 (2.3%)	0.151
GDM	45 (6%)	3 (8.3%)	7 (8%)	3 (8.3%)	2 (2.3%)	0.493
GHT	6 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.743

*Chi-square test; †p<0.05. The results are presented in n (%) format. **C/S:** cesarean section; **PROM:** premature rupture of membranes; **GDM:** gestational diabetes; **GHT:** gestational hypertension; **IUGR:** intrauterine growth retardation; **NSD:** normal spontaneous delivery; **PE:** preeclampsia.

Table 4. Cesarean indications by groups (n=412).

	Euthyroid	Hyperthyroidism Group 1	Hyperthyroidism Group 2	Sub-clinical hyperthyroidism Group 3	Sub-clinical hypothyroidism Group 4	p*
Previous C/S	206 (66.7%)	8 (53.3%)	16 (57.1%)	15 (78.9%)	24 (58.5%)	0.247
Fetal distress	17 (5.5%)	3 (20%)	3 (10.7%)	3 (15.8%)	3 (7.3%)	
PE	17 (5.5%)	0 (0%)	3 (10.7%)	0 (0%)	4 (9.8%)	
Breech presentation	21 (6.8%)	0 (0%)	1 (3.6%)	0 (0%)	1 (2.4%)	
Non-progressive	17 (5.5%)	0 (0%)	1 (3.6%)	0 (0%)	3 (7.3%)	
Other	31 (10%)	4 (26.7%)	4 (14.3%)	1 (5.3%)	6 (14.6%)	

*Chi-square test. The results are presented in n (%) format. **C/S:** cesarean section; **PE:** preeclampsia.

risk in our study between hypothyroidism and sub-clinical hypothyroidism cases in terms of preterm labor frequency.

However, Ashoor et al.[12] calculated the rate of late preeclampsia 13% in those whose gestational serum TSH levels were above 97.5th percentile between 11 and 13 weeks of gestation, and found this rate statistically significant. In our study, we calculated total preeclampsia rate 6.9% and found that thyroid function data had no statistically significant impact on preeclampsia. Excluding pregnant women who had chronic hypertension and additional diseases and morbidities, which are accepted as risk factors in terms of preeclampsia development, from our patient groups was the reason for low preeclampsia rates in our study compared to the study of Ashoor et al.

In their study, Allan et al.[13] could not obtain statistically significant findings in data such as GHT, ablatio placentae, 5-minute low Apgar score and delivery by cesarean section in pregnant women whose TSH values were 10 mU/L and above. While we obtained results consistent with the literature, we also found no statistically significant results in terms of GHT, ablatio placentae, 5-minute Apgar scores and increased cesarean section rates. In terms of sub-clinical hyperthyroidism and gestational outcomes, Casey et al.[14] could not obtain statistically significant results, as in our study, for the rates of GHT, preeclampsia, GDM, ablatio placentae and delivery by cesarean section. Regarding to the sub-clinical hyperthyroidism data, "Guideline for the assessment of thyroid during pregnancy" published by Turkish Perinatology Society in 2015 does not recommend sub-clinical hyperthyroidism treatment during pregnancy since there is no evidence that sub-clinical hyperthyroidism treatment would have a positive impact on the gestational progress and the treatment may have adverse effects on fetus.[15]

Nazarpour et al.[16] indicated in their study that overt hyperthyroidism and hypothyroidism have negative impacts on gestational outcomes, and overt hyperthyroidism is associated with preterm labor, intrauterine growth retardation, low birth weight, preeclampsia and fetal thyroid dysfunction. On the other hand, we found in our study that the incidence and frequencies of preterm labor, intrauterine growth retardation, low birth weight and preeclampsia were not statistically significant in pregnant women with overt hyperthyroidism.

While Chen et al.[17] found in their study that hyperthyroidism was risky in pregnant women in terms of the development of IUGR and premature rupture of membranes, we calculated IUGR rate 5.2% in our study and found that it was not statistically significant. On the other hand, we calculated premature rupture of membranes 2.3% and 0.1% in hypothyroid and euthyroid pregnant women, respectively, and found that they were not statistically significant. However, we considered that the low number of cases in PROM patients and most of these patients having delivery in the first 12–18 hours were the limitations of our study. In addition, we found no significant difference among hyperthyroidism, sub-clinical hyperthyroidism and sub-clinical hypothyroidism in terms of PROM incidence.

Another important problem in our country is that the physicians from different fields facing with thyroid pathology in pregnant women have insufficient knowledge on the normal and pathological thyroid values during pregnancy.[15,18] This may lead to problems about diagnosis and treatment arrangements during pregnancy. Although the salts for daily nutritional consumption are reinforced with iodine in particular, we see that pregnant women and the general population in Turkey have insufficient iodine intake.[19] Therefore, in order not

to encounter adverse gestational outcomes, it can be a proper practice to screen pregnant women in this respect in our country where endemic iodine insufficiency is a fact.[4,5,19]

Conclusion

In terms of the parameters, by which we assessed gestational outcomes, we could not find statistically significant parameters to impact pregnancy negatively. In our study, we found hypothyroidism 8.7%, sub-clinical hypothyroidism 8.6%, hyperthyroidism 3.6% and sub-clinical hyperthyroidism 3.6% in the pregnant population that we reviewed. Compared to the euthyroid pregnant women, we found no additional risk factor in these pregnancies found to have thyroid dysfunction in terms of abortion rates, preterm labor risk, intrauterine growth retardation frequency, oligohydramnios potential, preeclampsia risk, gestational hypertension and/or gestational diabetes possibilities, postterm pregnancy condition, delivery type and cesarean possibility, Apgar scores, birth weight and newborn intense care needs. While PROM data were significant only, we considered that the number of cases in our study were limited. On the other hand, since screening all pregnant women in terms of thyroid pathologies would have adverse effects on fetal neuropsychomotor development at an early period even though not in terms of gestational outcomes and such fetuses might have lower IQ scores,[4,5,19] TSH screening can be recommended particularly for risky pregnancies in countries with endemic iodine insufficiency like Turkey. To make assertive recommendations, well-designed, prospective, randomized controlled studies to be conducted according to Turkish conditions are needed.

Conflicts of Interest: No conflicts declared.

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