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Effects of maternal first trimester thyroid stimulant hormone levels on birth weights of fetuses born at term

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Abstract

Objective: We aimed to investigation the relationship between first trimester maternal thyroid stimulant hormone (TSH) levels and fetal birth weight in pregnants with TSH results within normal ranges.

Methods: A total of 193 patients meeting study criteria were separated into two groups according to their TSH levels found at first trimester as those between 0.4 and 2.5 mU/L, and those between 2.5 and 4.2 mU/L. There were 162 patients in the first group (Group 1) with TSH level between 0.4 and 2.5 mU/L, and 31 patients in the second group (Group 2) with TSH level between 2.5 and 4.2 mU/L. Birth weights were also categorized under three groups which were <2500 g, 2500–3500 g and >3500 g. These three fetal weight groups and two TSH groups established according to their first trimester measurements were compared.

Results: When both groups were compared in terms of demographic data and fetal weight, there was no significant difference between two groups in terms of the parameters analyzed. In both TSH groups, distribution percentages of the patients were found statistically similar according to fetal birth weights.

Conclusion: We found that normal TSH levels have no effect on fetal birth weight and that a further examination may not be required in terms of thyroid functions when TSH level is found within normal ranges at first trimester in terms of affecting fetal weight.

Keywords: Thyroid stimulant hormone, fetal birth weight, hypothyroidism.

Özet: Maternal ilk trimester tiroid stimülan hormon düzeylerinin miadında doğan fetüslerin doğum ağırlıklarına etkisi

Amaç: Normal sınırlarda saptanmış serum tiroid stimülan hormon (TSH) sonuçları olan gebelerde, ilk trimester maternal TSH düzeyi ile fetal doğum ağırlığı arasında ilişki olup olmadığını araştırmayı amaçladık.

Yöntem: Çalışma şartlarını sağlayan toplam 193 hasta, birinci trimesterde saptanan TSH seviyesine göre 0.4–2.5 mU/L arasında olanlar ve 2.5–4.2 mU/L arasında olanlar olarak iki gruba ayrıldı. Birinci grupta (Grup 1) TSH seviyesi 0.4–2.5 mU/L arasında olan 162 hasta, ikinci grupta (Grup 2) ise TSH seviyesi 2.5–4.2 mU/L arasında olan 31 hasta yer aldı. Doğum ağırlıkları da üç ayrı gruba ayrıldı (<2500 g, 2500–3500 g ve >3500 g). Bu üç fetal ağırlık grubu ile ilk trimester ölçümlerine göre oluşturulan iki TSH grubu karşılaştırıldı.

Bulgular: Her iki grup demografik veriler ve fetal ağırlık yönünden karşılaştırıldığında bakılan parametreler açısından iki grup arasında anlamlı fark saptanmadı. Her iki TSH grubunda da, fetal doğum ağırlığına göre yapılan gruplarda yer alan hastaların dağılım yüzdeleri istatistiksel olarak benzer bulundu.

Sonuç: Normal TSH düzeylerinin fetal doğum ağırlığına etkisi olmadığı tespit edilerek fetal ağırlığın etkilenmesi açısından ilk trimesterde normal sınırlarda bir TSH tespit edildiğinde tiroid fonksiyonları açısından ileri bir tetkike gerek olmayabileceğini söyleyebiliriz.

Anahtar sözcükler: Tiroid stimülan hormon, fetal doğum ağırlığı, hipotiroidi.

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Introduction

During pregnancy, significant changes occur in thyroid physiology and function.[1] One of the most significant reasons is human chorionic gonadotrophin (hCG) within glycoprotein structure produced by placenta at first trimester. hCG increasing in serum is attached to TSH receptor in the thyroid cell membrane and causes T4 and T3 secretion to increase.[2] Due to this thyrotropic activity of hCG, lower TSH levels are found in the first trimester of pregnancy compared to non-pregnant women.[3] Despite some differences between different resources and clinics, normal reference range of TSH is generally accepted between 2.5 and 97.5 percentiles and given between 0.03 and 4.04 MU/L.[4]

Severe and sub-clinic hypothyroidism is the most frequent endocrine disorder, and its prevalence is reported as 2–5%.[5] Hypothyroidism is reported with lower rate, and its prevalence is between 0.1% and 0.04%.[1]

The incidence of thyroid dysfunction increased in the last decade and it was reported that this was associated with poor maternal and fetal outcomes.[1,6,7] In different studies, there is a consensus that maternal thyroid hormones are effective on the fetal development.[8,9–12] It is considered that severe maternal thyroid dysfunctions secondary to the suboptimal transplacental transition of maternal thyroid hormone are associated with low birth weights.[13]

This brought up the discussion for scanning maternal thyroid hormones during pregnancy. There are different opinions on this matter.[14,15] Although it is clear that certain maternal and fetal thyroid dysfunctions are associated with low birth weight, the effects of thyroid function tests within normal ranges on fetal development is still unclear.[16] Therefore, we aimed in this study to investigate if there is any relationship between first trimester maternal TSH level and fetal birth weight in pregnant women who have no severe pregestational thyroid dysfunction, do not have any treatment for any thyroid dysfunction during pregnancy and have serum TSH results within normal ranges.

Methods

The patients who referred to our clinic and had their all follow-ups and deliveries in our clinic between January 2013 and January 2014 were included in our retrospective study. Those with multiple pregnancies, develop fetal preeclampsia and gestational diabetes during pregnancy and gave birth before 37 weeks of gestation were excluded from the study. In our study, we included both vaginal and cesarean deliveries. The deliveries of all our patients who had elective cesarean were done between 39 and 40 weeks of gestation.

The data of 193 patients, who met all these criteria, had no thyroid dysfunction history and found to have TSH values within normal ranges in the first examination were included in the analysis. All data of the patients were obtained from electronic medical record system and patient file archives of the hospital.

In our clinic, maternal TSH levels are checked as a routine procedure in the first examination of patient. If abnormal values are found, free T3 and free T4 hormones are also checked, and patients are consulted with endocrinology department, if required. TSH values between 0.4 and 4.2 mU/L are considered normal in our clinic.

A total of 193 patients meeting study criteria were separated into two groups according to their TSH levels found at first trimester as those between 0.4 and 2.5 mU/L, and those between 2.5 and 4.2 mU/L. The cases were separated into three groups according to the fetal birth weight (<2500 g, 2500–3500 g and >3500 g), and they were compared according to their TSH levels as above.

The approval of Clinical Research Ethics Committee, Faculty of Medicine, Kahramanmaraş Sütçü İmam University was obtained for our study.

Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA) was used for the analysis of the data. Parametric methods were used for the analysis of variables with normal distribution and non-parametric methods were used for the analysis of variables without normal distribution. For the comparison of demographic data between groups, Independent-Samples T test and Mann-Whitney U (Exact) test were used, and mean ± SD (standard deviation) was found by median ± IQR (Interquartile Range). In the comparison of the groups in terms of TSH and birth weight, Pearson Chi-Square Test (Exact), Fisher Exact Test (Exact) and Linear-by-Linear Association Test were used. Categorical data were expressed as n (number) and percentage (%). The data were analyzed via 95% confidence interval, and p value less than 0.05 was considered significant.

Results

The patients included in the study were separated into two different groups according to their TSH levels. There were 162 patients in the first group (Group 1) with TSH level between 0.4 and 2.5 mU/L, and 31 patients in the second group (Group 2) with TSH level between 2.5 and 4.2 mU/L.

The groups were compared in terms of age, gravida, parity, week of gestation, fetal birth weight and maternal hemoglobin (Hb) level, and no significant difference was found in terms of these parameters (**Table 1**). Since the patients who were at 42 weeks of gestation according to their last menstrual periods were delivered vaginally or by cesarean section, we had no pregnancy older than 42 weeks.

Later, the cases were distributed into three different groups according to their fetal birth weights (<2500 g, 2500–3500 g and >3500 g). The patients in these three groups were compared according to their TSH levels. In both TSH groups, distribution percentages of the patients were found similar according to fetal birth weights and no significant difference was observed (p=1) (**Table 2**).

Table 1. Comparison of demographic data of the groups with TSH levels between 0.4 and 2.5 mU/L and between 2.5 and 4.2 mU/L.

	TSH [0.4–4.2] (N=193)		
	<2.5	2.5<	p value
Fetal birth weight*	3174.9±524.10	3169.2±649.25	0.958
Birth week**	39.00±1.00	39.00±1.00	0.546
Age*	29.5±6.40	30.0±6.77	0.660
Gravida (G)**	3.00±1.00	2.00±2.00	0.066
Parity (P)**	2.00±1.00	2.00±2.00	0.127
Maternal Hb at birth	9.40±2.80	8.70±3.10	0.242

Independent T test – Mann-Whitney U test (exact) . *Mean±SD (standard deviation), **Median±IQR (interquartile range), **Hb:** Hemoglobin

Table 2. TSH düzeyi 0.4–2.5 mU/L arasında ve 2.5–4.2 mU/L arasında olan grupların fetal doğum ağırlıklarının kilo gruplarına göre karşılaştırılması.

	TSH [0.4–4.2] (N=193)		
	<2.5	2.5<	p value
	n(%)	n(%)	
Fetal birth weight			
<2500	16 (9.9%)	4 (12.9%)	
[2500–3500]	106 (65.4%)	19 (61.3%)	1
>3500	40 (24.7%)	8 (25.8%)	

Pearson chi-square test (*exact*) – Fisher exact test (*exact*) – Linear-by-linear association test

Discussion

Maternal thyroid dysfunctions and especially hypothyroidism and autoimmune problems affect gestational outcomes and fetal development negatively. However, no program is implemented for screening women in reproductive period in terms of thyroid functions. There is still no consensus on this matter.[17]

While there are some differences among clinics, upper limit of TSH is 2.5 mU/L in the first trimester and 3 mU/L in the second trimester.[18] In our study, TSH values between 0.4 and 4.2 mU/L in our clinic were considered normal.

In our study, we investigated the effects of TSH values being under or above 2.5 mU/L on gestational outcomes and birth weight in asymptomatic patients with TSH values within normal ranges and had no treatment for thyroid disorders. We found that maternal TSH levels did not affect fetal birth weight as long as they are within normal ranges.

Thyroid hormone concentration is one of the most effective biochemical markers to have a healthy fetal development.[19] On the other hand, it has been shown in animal studies that thyroid hormones may have a direct role in fetal development and there may be abnormal skeletal development in those with thyroid hormone deficiency.[20,21]

The relationship between maternal thyroid dysfunction during pregnancy and birth weight was investigated in a series of studies.[8–10] In normal pregnancies, indirect effects of thyroid hormones on fetal growth were shown in previous studies as the low birth weight in babies of mothers with iodine deficiency in their diets compared to the babies of mothers who have sufficient iodine in their diets.[22]

Most of the studies performed on thyroid dysfunctions during pregnancy were interested in the effects of sub-clinical or clinical hypothyroidism on gestational outcomes.[23] In a study carried out for this purpose reported that mothers with hypothyroidism have the risk to deliver babies with low birth weight[22] and to labor prematurely.[24,25]

In some other studies investigating thyroid functions and birth weights analyzed free T4 (FT4) in

maternal serum.[26] The study of Shields et al. including 905 pregnant women investigated the relationship between FT4 levels and birth weight at 28 weeks of gestation and found negative correlation.[27] In another similar study, Medici et al. found that high maternal FT4 levels at early weeks of gestation were associated with low birth weight.[16]

In the studies investigating the effects of gestational thyroid functions on fetal and maternal outcomes, thyroid functions were checked in fetal cord blood in addition to maternal serum and their gestational outcomes and association with fetal development were investigated.

Medici et al. showed significant relationship between birth weight and FT4 levels checked in the fetal cord blood of normal healthy pregnant women. Also in this study, no significant relationship was found between fetal weight and FT3 or TSH results checked in cord blood. A positive correlation was found between birth weight and TSH levels in cord blood.[16]

It can be argued in our study that why FT4 and FT3 were not evaluated together with TSH levels in our patients in terms of their association with fetal birth weight. However, as a routine procedure, FT3 and FT4 levels are not checked in our clinic in addition to TSH in the first examination. Yet, in patients found to have TSH levels outside the normal ranges, these tests were carried out for evaluation. Also, not considering heights and weights of mothers and fathers, BMI score of mother at the beginning of pregnancy, dietary habits of mother, smoking and alcohol use habits as the factors affecting fetal birth weight are the weakness of our study. In addition, TSH levels at other periods of pregnancy could be checked in terms of their effects on fetal birth weight; however, when TSH levels were found within normal ranges in the first examination, they were not checked again in our clinic during the other periods of pregnancy. Our study is not a study investigating maternal thyroid levels and poor perinatal outcomes but the first study investigating the relationship between fetal weight and maternal TSH levels within normal ranges as far as we know in the literature.

Conclusion

In conclusion, previous studies investigated and presented the abnormal serum TSH levels and thyroid dysfunctions requiring treatment on fetal birth weight. Our study investigated the effect of serum TSH levels on birth weight in patients with normal TSH values and had no thyroid dysfunction history. We found that TSH levels within normal ranges and at different levels have no effect on fetal birth weight and that a further examination is not required in terms of thyroid functions when TSH level is found within normal ranges at first trimester in terms of affecting fetal weight.

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Conflicts of Interest: No conflicts declared.

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