Clinical Research

Thyroid Elastography Findings in Pregnant Women: A Single-Centre Study

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ABSTRACT

Objective: Thyroid elastography has recently become one of the main techniques of thyroid imaging. During pregnancy, physiological or pathophysiological changes occur with the effect of different hormones. In this study, we investigated the thyroid gland elasticity findings of pregnant women.
Material and Method: The study was carried out with 192 pregnant women and 66 healthy control group. All participants were first evaluated by thyroid US and then thyroid elastography was performed. Two separate ROIs in the range of 3-7 mm2 were placed in the thyroid tissue and strep muscle. Measurements were made twice for the right and left thyroid tissue, and the mean values were used for statistical analysis.
Results: Thyroid stimulating hormone (TSH) values were 1.84±0.92 mIU/L for the normal group and 1.38±0.91 mIU/L for the pregnant women group and were lower in pregnant women (p =0.001). The elastography values of the control group were calculated as 1.17±0.62 for the right lobe, 1.04±0.43 for the left lobe, and 1.11±0.42 for the mean of both lobes. The values in the pregnant group were 1.80±1.18 for the right lobe, 1.58±0.97 for the left lobe and 1.69±0.89 for the mean of both lobes, and all values were higher than the control group (p <0.001). There was a borderline inverse correlation between β-human chorionic gonadotropin (β-hCG) values and TSH values (p =0.053). No significant correlation was found in the comparison of β-hCG and strain elastography (SE).
Conclusion: In our study, we found that there is a significant decrease in thyroid elasticity during pregnancy, with or without a disorder in thyroid functions.

Keywords: *Strain Elastography, Pregnancy, Thyroid Gland, Chorionic Gonadotropin.*

ÖZ

Gebe Kadınlarda Tiroid Elastografi Bulguları; Tek Merkezli Bir Çalışma

Amaç: Tiroid elastografisi son zamanlarda tiroid görüntülemenin ana tekniklerinden biri haline gelmiştir. Hamilelik sırasında farklı hormonların etkisiyle fizyolojik veya patofizyolojik değişiklikler meydana gelir. Bu çalışmada gebe kadınların tiroid bezi elastikiyet bulgularını araştırdık.
Gereç ve Yöntem: Yüzdoksaniki gebe ve 66 sağlıklı kontrol grubu ile gerçekleştirildi. Tüm katılımcılara öncelikle tiroid USG ile değerlendirme yapıldı ve ardından tiroid elastografisi yapıldı. Tiroid dokusuna ve strep kasına 3-7 mm2 aralığında iki ayrı ROI yerleştirildi. Ölçümler sağ ve sol tiroid dokusu için iki kez yapıldı ve istatistiksel analiz için ortalama değerler kullanıldı.
Bulgular: Tiroid uyarıcı hormon (TSH) değerleri normal grupta 1,84±0,92 mIU/L, gebe grupta 1,38±0,91 mIU/L olup gebelerde daha düşüktü (p =0,001). Kontrol grubunun elastografi değerleri sağ lob için 1,17±0,62, sol lob için 1,04±0,43 ve her iki lob ortalaması için 1,11±0,42 olarak hesaplandı. Gebe grupta değerler sağ lob için 1,80±1,18, sol lob için 1,58±0,97 ve her iki lob ortalaması için 1,69±0,89 olup tüm değerler kontrol grubuna göre yüksekti (p <0,001). β-insan koryonik gonadotropin (β-hCG) değerleri ile TSH değerleri arasında sınırda ters korelasyon mevcuttu (p =0,053). β-hCG ve gerinim elastografisi (SE) karşılaştırıldığında anlamlı bir korelasyon bulunamadı.
Sonuç: Çalışmamızda tiroid fonksiyonlarında bozukluk olsa da olmasa da gebelikte tiroid elastikiyetinde anlamlı azalma olduğunu tespit ettik.

Anahtar Sözcükler: *Gerinim Elastografi, Gebelik, Tiroid Bezi, Korionik Gonodotropin Hormonu.*

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Human chorionic gonadotropin hormone and TSH are hormones with the same subunits responsible for the common molecular mechanism (1-4). The thyroid stimulating effect of hCG has been demonstrated in humans and experimental animals (2). Therefore, due to the peak of hCG in the 1st trimester of pregnancy, hyperthyroidism is not an unusual condition. hCG can mimic TSH effects by binding to TSH receptors (4, 5). Studies show that the increase in hCG levels leads to suppression in TSH levels. It is thought that for every 10000 U/L increase in HCG levels, TSH levels decrease by 0.1 IU/L and free thyroxine (FT4) levels increase by 0.1 ng/dL (5). hCG production reaches its highest value in the 8th-12th weeks of pregnancy (6). Some changes that occur during pregnancy affect the thyroid gland. These;

1. Increase in thyroid binding globulin (TBG) levels due to estrogen

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2. Increased hCG levels lower TSH levels by stimulating the thyroid
3. Altered peripheral metabolism of thyroid hormones due to placental enzymes
4. It is the decrease in plasma iodine levels with fetal use, and increased renal function (7-9).

Thyroid elastography has been one of the main methods in recent years of thyroid imaging (10). SE is the most commonly found method in commercial units. In addition to direct imaging of the thyroid, it is an module used for stiffness evaluation and can be incorporated in standard ultrasound devices (11). Many studies using elastography method to evaluate the differences of diffuse thyroid diseases from normal thyroid tissue have been conducted and significant differences have been found (12-17)

In this study, we evaluated whether normal physiologic thyroid function values and thyroid tissue stiffness of pregnant women are different from thyroid function values and thyroid tissue stiffness of other healthy (non-pregnant) individuals.

MATERIAL AND METHOD

Patients

The prospective study, which was conducted between May 2021 and May 2022, was approved by Fırat University Ethics committee (date: 22.04.2021, issue: 2021/06-31) and all participants signed the informed consent form.

We interviewed 717 pregnant women who applied to the obstetrics outpatient clinic of our hospital, were at 11 weeks 0 days - 13 weeks 6 days of gestation, and were referred to our ultrasonography (US) polyclinic for nuchal translucency (NT) measurement. Pregnant women who accepted to have elastography measurement, dual screening test and thyroid function tests (TFT) were included in the study. A working group was formed with 192 pregnant women who met the appropriate conditions.

Exclusion criteria; those with known thyroid disease before pregnancy, those with thyroid nodules and diffuse thyroid disease on B-mode US, women with twin pregnancies, pregnant women with structural anomalies, and those with risky results from the double screening test were excluded from the study. Pregnant women were divided into groups as those with and without normal laboratory according to TFT results.

The control group consisted of non-pregnanat volunteer women of childbearing age, no known thyroid disease, and normal US findings and TFT values.

Data including age, gestational age, number of pregnancies, TSH, free triiodothyronine (FT3), FT4, β-hCG values and NT measurements were recorded.

Becman Coulter Access laboratory kits were used to measure thyroid function tests. Access HYPERsensitive hTSH for TSH, Access Free T4 for T4 and Access Free T3 for T3 kits were used.

Ultrasound and SE examinations were performed in the same session by the same specialist radiologist with 10 years of experience in thyroid ultrasound and 2 years of experience in SE, using the same device (Philips EPIQ 7G) and eL18-4 MHZ linear probe. First, crown-rump length (CRL) and NT values of the fetus were measured and recorded. Thyroid dimensions and parenchyma structure were evaluated with routine B-mode before SE.

Strain Elastography Protocol

SE examination was performed by applying light pressure with free hand technique. Compression was made so that the entire of color indicator on the screen is green. Tissue elasticity was calculated and the results were shown in a color map generated on the B-mode image. The color range representing the uncertain stiffness of the tissue ranged from blue (soft) to red (stiff). In B-mode and elastography images, the imaging area was adjusted to include thyroid tissue and surrounding strep muscles. The carotid artery was kept out of the measurement area to prevent artifacts. From the recorded images, the optimal interval for measurement was selected. Two separate regions of interests (ROI) in the range of 3-7 mm^2 were placed in the thyroid tissue and strep muscle (Figure 1).

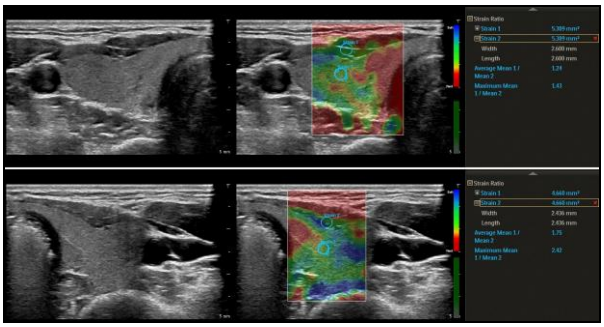

Figure 1. *US elastography image of a control group of 34 years old, healthy, not pregnant, Right lobe (a), left lobe (b).*

Mean strain index (SI) were automatically measured by the device and evaluated semi-quantitatively. This measurement was performed twice for the right and left thyroid tissue, and the mean values were used for statistical analysis.

Statistical Method

The IBM SPSS version 22 package program was used for data analysis. The Mann-Witney U test was used to examine whether the data showed a normal distribution. The descriptive statistics of the data are expressed as mean ± standard deviation for variables with normal distribution and median (minimum-maximum) for those without normal distribution in continuous (quantitative) data. In quantitative data, independent sample t-test was used to compare the means of variables showing normal distribution between two independent groups, and Kruskal Wallis H test was used to compare the means of variables not showing normal distribution between two or more independent groups. Post-hoc Dunn test was then used in pairwise comparisons.

These groups were tested with Pearson correlation analysis for group 1, and Spearman correlation analysis for groups 2 and 3 according to whether they showed normal distribution or not. GPower is above 90%. The significance threshold is set at 0.05.

RESULTS

The study was carried out with two groups of 192 pregnant women and 66 non-pregnant women. The mean age was 31.2±6.8 years in the control group and 27.2±6.1 in pregnant women. The mean number of pregnancies was 1 (range 0-3) in the control group and 2 (range 1-7) in the pregnant group. Mean gestational age was 89.5±5.5 days, mean NT was 1.16±1.1 mm. The mean β-hCG values were 51.37±75.72.

TSH values were 1.84±0.92 mIU/L for the normal group and 1.38±0.91 mIU/L for the pregnant group and were lower in pregnant women (p =0.001). TFT values of 43 pregnant women were determined to be outside the reference range. TSH values of 26 pregnant women were low and FT3 and FT4 values of 3 of them were high. FT3 or FT4 values of 9 pregnant women were high and FT3 or FT4 values of 8 pregnant women were low. TFT values of 149 pregnant women were within the normal range.

The elastography values of the control group were calculated as 1.17±0.62 for the right lobe, 1.04±0.43 for the left lobe, and 1.11±0.42 for the mean of both lobes. The values in the pregnant group were 1.80±1.18 for the right lobe, 1.58±0.97 for the left lobe and 1.69±0.89 for the mean of both lobes, and all values were greater than in the control group (p <0.001) (Table 1) (Figure 2-3).

Table 1. *Elastography values of the groups and comparison.*

	Control group (n =66)	Pregnant group (n =192)	p value
Right lobe	1.17±0.62	1.80±1.18	<0.001
Left lobe	1.04±0.43	1.58±0.97	<0.001
Average of two lobes	1.11±0.42	1.69±0.89	<0.001

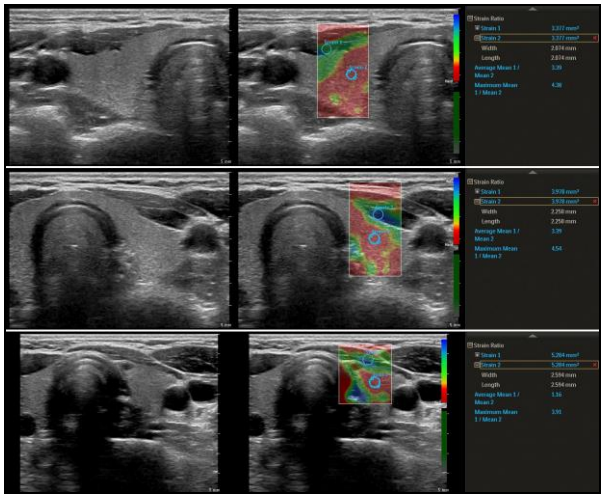

Figure 2. *US elastography images of a 32-year-old, 12 weeks 1day healthy pregnant. Right lobe (a), left lobe (b). US elastography view of a 24-year-old, 11 weeks 2 days of healthy pregnant (c).*

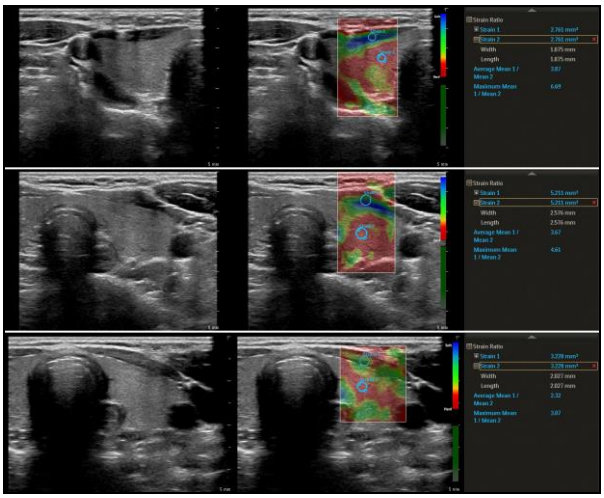

Figure 3. *US elastography images of pregnant women whose TFT values are outside normal limits. (a) 22 years old, 13 weeks 1 day pregnant, TSH<0.015 mIU/L, FT4 1.37 ng/dL . (b) 27 years old, 13 weeks and 2 days pregnant, TSH=0.11 mIU/L. (c) 24 years old, 12 weeks 0 day pregnant, TSH=0.02 mIU/L , FT3= 5.17 ng/L, FT4= 1.2 ng/dL.*

The correlation between TSH levels and SE levels of the groups was investigated. No significant correlation was found between TSH levels and SE levels in the control group. In the pregnant group, no significant correlation was found with the right lobe. However, when the correlation coefficient was 0.15, a strong negative correlation was found with the left lobe (p =0.027) and a weak negative correlation with the average value (p =0.05).

We divided the pregnant women into two groups according to their TFT values. We formed three separate groups as the control group (Group 1), normal pregnant women (Group 2) and pregnant women with abnormal TFT values (Group 3). The statistical data of the groups are shown in table 2.

Table 2. *Elastography and TSH data obtained after dividing the pregnant group into two.*

	TSH (mIU/L)	Right lobe	Left lobe	Average of two lobes
Control group (G1) (n =66)	1.84±0.92	1.17±0.62	1.04±0.43	1.11±0.42
Normal pregnant (G2) (n =149)	1.57±0.84	1.83±1.26	1.57±0.98	1.70±0.93
Pregnant women with abnormal TFT values (G3) (n =43)	0.71±0.81	1.69±0.85	1.62±0.95	1.65±0.73

TSH; Thyroid stimulating hormone, TFT; Thyroid function tests.

We compared the TSH values and elastography values of these groups (Table 3, Figure 4).

Table 3. *Comparison of TSH and elastography values of the groups.*

	p value
Right lobe	
G1-G2	p <0.001
G1-G3	p =0.001
G2-G3	p =0.866
Left lobe	
G1-G2	p <0.001
G1-G3	p <0.001
G2-G3	p =0.652
Average of two lobes	
G1-G2	p <0.001
G1-G3	p <0.001
G2-G3	p =0.620
TSH	
G1-G2	p =0.069
G1-G3	p <0.001
G2-G3	p <0.001

TSH; Thyroid stimulating hormone, G1; Group 1 control group, G2; Group 2 normal pregnant, G3; Group 3 Pregnant women with abnormal TFT values.

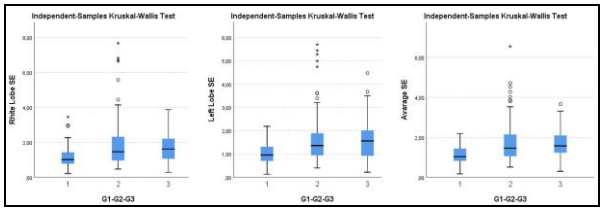

Figure 4. *Graphical presentation of the comparison of thyroid SE values of the three groups.*

Accordingly, there was a marked difference in the SE values between the control group and the two pregnant groups. However, there was no significant difference between the pregnant groups. TSH and SE values were compared. No correlation was found in G2, but an inverse correlation was observed between left lobe SE values and TSH values in G3 (p =0.018).

When the correlation coefficient was 0.17, there was a borderline negative correlation between β-hCG values and TSH values (p =0.053). There was no significant correlation between β-hCG and SE.

DISCUSSION

The normal function of the thyroid is necessary to ensure that a baby is born normally and to prevent complications that may develop. Thyroid disorders are the second most common endocrine disorder during pregnancy (8). So far, the relationships of TSH, free β-hCG and Pregnancy-Associated Plasma Protein-A (PAPP-A) levels with Trisomy-21, Trisomy-18, hyperemesis gravidarum, choriocarcinoma and molar pregnancy have been investigated (2, 4, 6, 18). There is no study done so far on elastography findings of the thyroid gland in pregnancy.

For our study, we selected pregnant women at 11-14 weeks of gestation. Because free β-hCG levels peak at 8-14 weeks (4, 6, 9, 18-21) and the first controls of all pregnant women are usually performed during these weeks. The thyrotropic effects of hCG are limited to the first trimester (20, 22). This is the most appropriate period for screening for thyroid disease (19).

The validity of thyroid-specific laboratory reference ranges for pregnant women is controversial. This is because thyroid function changes during pregnancy. There have been several studies on the determination of these reference ranges and the results have been inconsistent (23-27). An upper limit of 2.5 mU/L for TSH in pregnant women has been recommended until trimester-specific reference ranges are established (28). In 2011, the upper limit for trimester-specific TSH was set at 2.5 mIU/L in the first trimester and 3.0 mIU/L in the second and third trimesters by the American Thyroid Association (ATA) (29). In 2017, the lower limit of the TSH reference range in the first trimester of pregnancy has been lowered by about 0.4mU/L and the upper limit by 0.5mU/L (22). To test thyroid function during pregnancy, trimester-specific reference ranges are needed in each region (30). Since there are no TFT reference intervals specifically for pregnant women specific to our region, diagnosis and treatment are made according to standard reference intervals. We grouped our patients according to the standard reference intervals. The reference ranges of our biochemistry laboratory are 0.34-5.33 mIU/L for TSH, 2.6-4.37 ng/L for FT3, 0.6-1.16 ng/dL for FT4.

Strain elastography consists of color maps or gray-scale maps showing tissue stiffness. There are different classification systems created according to colors and grading tissue stiffness. In the Tsukaba scoring used for thyroid nodules:

Score 1: the entire nodule is elasticity

Score 2: much of the nodule is elasticity

Score 3: only the peripheral parts of the nodule are elasticity

Score 4: Nodule has no elasticity

Score 5: Nodule and acoustic shadow are not elasticity (31).

Normal thyroid tissue is softly observed on elastography. Homogeneous green (score 1) or green/red/yellow (score 2). In the case of parenchymal hyperplasia or involution, changes occur in normal elastography findings (11, 32). There are not many studies that talk about the stiffness values of the normal thyroid. In several acoustic radiation force impulse (ARFI) articles, the stiffness values of the normal thyroid gland have been calculated as an average of 2±0.40m/s and 1.98m/s (range 1.20-3.63). In a study of 42 patients using shear wave elastography (SWE), normal thyroid values were reported as 20.8 ± 10.4 kPa (11).

In the study performed by Kumar et al. on SE, the elastography values of the normal thyroid were 1.05±0.42 (range 0.63-1.47), 1.06±0.45 (range =0.61-1.51), 1.14±0.47 (range =0.67-1.61) for the right lobe, left lobe and isthmus, respectively. Their measurements in people with diffuse thyroid enlargement were significantly higher than normal thyroid tissue values. There were no significant differences observed between the levels of the isthmus (16).

Menzilcioglu et al. (33) compared the thyroid elastography findings of patients with chronic autoimmune thyroiditis (CAT) and healthy individuals. The SI value of patients with CAT was 1.39±0.72, which was significantly higher than the SI value of the normal thyroid (0.76±0.55).

In the study conducted by Yang et al. (17), normal thyroid SI value was found to be 1.76±0.54 (range 0.66-2.70).

In our study, the SE values of the control group were 1.17±0.62, 1.04±0.43 for the right and left lobes, respectively, and 1.11±0.42 for the mean of both lobes. These values are in line with the results of a study in the literature (16), but incompatible with some of them (17, 33). Among these studies, the SE values of the patient group of Menzilcioğlu et al. were lower than the healthy control group of Yang et al. The SE values of the patient groups were also significantly different (CAT) (Menzilcioğlu et al. mean 1.39±0.72; Yang et al. 7.04±7.744) (17, 33).

Although TFT values and US of normal pregnant women (G2) were within normal limits, SE values were higher than the control group.

Although TSH levels did not differ significantly between G1 and G2, between the elastography values was found to be statistically significant.

Although statistically significant differences were found between G2 and G3 TSH levels, no significant differences were found between elastograms. In this case, is it correct to say that TSH values have no effect on elasticity? Is there another condition that causes this in pregnant women?

Differences in the elasticity of the thyroid parenchyma depend on the histological changes caused by the previous disease. These can be summarized as lymphocyte infiltration, follicle cell hyperplasia, changes in the amount of colloids, fibrosis and an increase in vascularity (10-12). It is the structural features of the tissue matrix that determine the elasticity of the thyroid gland. Elastography creates an image reflecting the histological structure (11). The reason for the decrease in thyroid tissue elasticity during pregnancy is unknown. There are no pathophysiological studies on this. There are no studies showing whether this situation is temporary or not, including post-pregnancy.

Estrogen hormone causes a 1.5 to 2-fold increase in total T4 during pregnancy (30). β-hCG has a weak thyroid-stimulating effect (4). Studies are needed to explain which of the hormonal and physiological changes that occur during pregnancy change thyroid elasticity.

Conclusion

In our study, we found that there is a significant decrease in thyroid elasticity during pregnancy, with or without a disorder in thyroid functions. The available data were not strong enough to hold TSH or β-hCG responsible for this result. Our study had several limitations. These; the absence of other hormonal data of the pregnancy period and the absence of post-pregnancy measurements to show whether the decrease in elasticity is temporary. In order to explain this result more clearly, detailed pathophysiological studies should be performed with larger pregnant groups.

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