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Original Article

Radiology Section

# Ultrasonographic Evaluation of Thyroid Gland Volume and Nodularity in Pregnant versus Non Pregnant Females: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Continuous stimulation of thyroid gland occurs during pregnancy in order to meet the demands of growing foetus. This might result in variations in thyroid gland morphology which may be misdiagnosed if not assessed accurately. Ultrasonography can measure these variations during pregnancy in the form of change in volume, echotexture, nodularity etc.

**Aim:** To compare the thyroid volume and nodules using ultrasound, amongst different trimesters of pregnancy and with non pregnant women of similar age and find the correlation with different factors.

**Materials and Methods:** A time-bound, hospital-based, cross-sectional observational study was done in the Department of Radiodiagnosis, Maharaja Yeshwantrao (MY) Hospital, Indore, Madhya Pradesh, India, from April 2021 to August 2022 on 240 patients. All subjects were divided into groups of 60 women each, which included non pregnant women in group 1 and pregnant women during each trimester in rest three groups, as group 2, 3 and 4, respectively. Thyroid volume and nodules were measured in each group. The descriptive data was calculated using mean and standard deviation and then compared using Analysis of Variance (ANOVA) test. Linear regression analysis was also used to assess the correlation.

**Results:** Most 125 (52%) of the women belonged to the younger age group i.e., 21-25 years. Majority i.e., 114 (47.5%) of pregnant women were primigravida. Mean total thyroid volume in non pregnant group, 1st trimester group, 2nd trimester group and in 3rd trimester group were 5.44±0.82 mL, 5.85±0.64 mL, 6.25±0.67 mL and 7.24±1.16 mL, respectively, with up to 24% increase of thyroid volume during the course of pregnancy (p-value=0.001). Thyroid nodule incidence was 12.2% in pregnant women and 5% in non pregnant women.

**Conclusion:** With pregnancy, there is an increase in thyroid gland size along with a small increase in thyroid nodularity. Also, the interplay of a few factors such as Body Mass Index (BMI), parity, age etc., was noted.


**Keywords:** Colour doppler, Pregnant women, Thyroid nodules, Ultrasound

## INTRODUCTION

Thyroid dysfunctions are commonly seen in the fertile period for the reproductive age group, subclinical hypothyroidism being the most common. Pregnancy is a natural physiological state characterised by various hormonal and metabolic alterations. The thyroid gland is the second most common gland affected in pregnancy and any dysfunction can impair the foetal neurodevelopment [1]. These changes, though prudent may at times result in potentially serious outcomes if left untreated.

It is believed that pregnancy has a goitrogenic effect on the thyroid gland [2]. Females residing in iodine deficient areas are more susceptible to such effects rather than those living in iodine supplement areas, as iodine deficiency results in enhanced thyroid stimulation causing thyroid enlargement. Apart from pregnancy various other factors such as iodine status, age, gender, Body Mass Index (BMI), Thyroid Stimulating Hormone (TSH) levels, smoking and genetic factors impact the size of thyroid gland [3,4]. A number of physiological conditions such as pregnancy or pathological conditions such as iodine deficiency goitre, thyroiditis can be easily distinguished from each other if one has an inquisitive knowledge of thyroid gland size, volume, and other characteristics. Variable conclusions are found related to the thyroid nodule status in pregnancy where in some studies it is established as a common finding in iodine deficient pregnant women while in others it is seen in a normal population of iodine sufficient areas also [3,5,6].

Although the visual inspection and palpation of the thyroid gland are the accepted methods to evaluate thyroid size as part of a physical examination. However, the results of such examinations are often inaccurate and may lead to an incorrect diagnosis of a goiter. High resolution ultrasonography apart from being safe, cost-effective and a non invasive modality, has a unique advantage of visualising superficial structures with more precision, and owing to the superficial location of thyroid gland, it can be easily employed in the evaluation of pregnant females. The aim behind this study was to estimate the volume and nodularity of thyroid gland using high frequency ultrasound during different trimesters of pregnancy and to compare it with non pregnant females. Also, these findings are to be correlated with factors such as age, parity and BMI.

## MATERIALS AND METHODS

A time-bound, hospital-based, cross-sectional observational study was conducted in the Department of Radiodiagnosis, Maharaja Yeshwantrao (MY) Hospital, Indore, Madhya Pradesh, India, from April 2021 to August 2022 comprising 240 females. Study was conducted after approval from the Institutional Ethics and Scientific Review Committee (EC/MGM/ June-21/23). These were then categorised into four different groups each comprising 60 females. Group 1 included non pregnant women and pregnant women were divided as per their respective trimesters in three groups as group 2, 3 and 4, respectively. The non pregnant group was selected randomly from the patients coming to the department for ultrasonography apart from obstetrics ultrasound while the pregnant group were selected from the patients who came for routine antenatal scan.

**Inclusion criteria:** Pregnant women with clinically euthyroid status and non pregnant women of similar age group were included in the study.

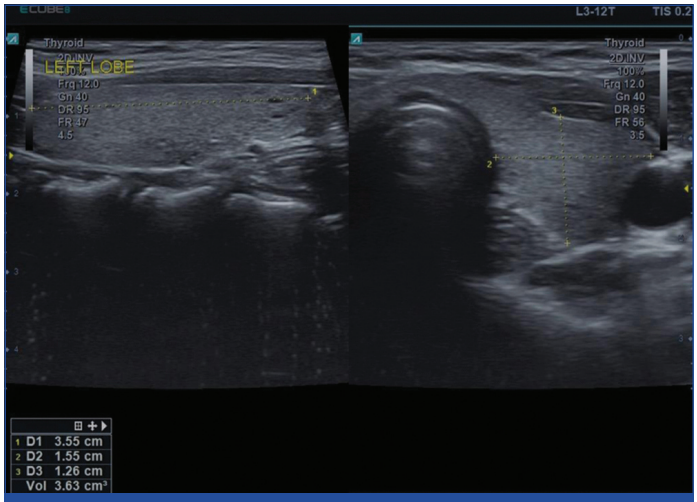
**Exclusion criteria:** Previous history of thyroid disease or thyroid surgery or any systemic illness at present, patient on antithyroid medications and patients who refused to give consent were excluded from the study.

## Study Procedure

Females were explained about the procedure and demographic data was recorded. BMI was calculated as weight in kilograms divided by height in meter squared. They were then examined in a supine position with the hyperextended neck. A high frequency linear array transducer (7-13 MHz) that provides adequate penetration and high resolution image was used. Scanning of thyroid gland was done both in transverse and longitudinal planes. Thyroid gland was evaluated for its volume, parenchymal echogenicity, and any nodule present within thyroid gland. Thyroid volume was calculated using Brunn expression as shown in [Table/Fig-1] [7]:

$V_{US}$=0.479 *L*W*T

Volume for each lobe was calculated and then thyroid lobes volume was added together: $V_{Thyroid}=V_{RL}+V_{LL}$. Isthmus was excluded from the thyroid gland volume estimation. Parenchymal echogenicity was assessed by comparing it with the adjacent muscles. Thyroid gland vascularity was demonstrated using Colour Flow Doppler Sonography (CFDS) where the patterns were graded as Pattern-0, with absent or minimal intraparenchymal flow; Pattern-I, uneven distribution; Pattern-II, mildly increased flow with patchy distribution; Pattern-III, marked increase in blood flow with diffuse homogenous pattern [8].




**[Table/Fig-1]:** Ultrasonographic measurements for volume of left lobe of thyroid gland.

## STATISTICAL ANALYSIS

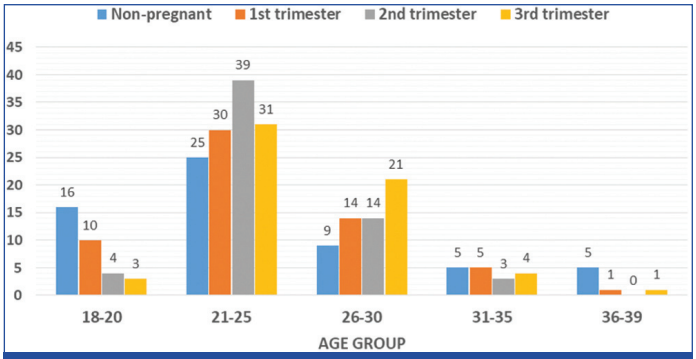
Variables such as BMI or thyroid volume etc., were expressed using mean and standard deviation. Correlation was evaluated using Analysis of Variance (ANOVA) and Pearson correlation. Data is considered significant at 5% level of significance (p-value <0.05). Statistical Package for the Social Sciences (SPSS) software version 25.0 was used for statistical analysis.

## RESULTS

Out of the total 240 patients, 125 (52%) patients belonged to 21-25 year age group. Mean age was 24.5±5.49 years in non pregnant group and 24.7±3.83 years in pregnant groups [Table/Fig-2].

Most of the patients overall in the study 114 (47.5%) were primigravida followed by 110 (45.9%) multipara and 16 (6.6%) nulliparous patients. On comparing BMI, 197 (82%) females were found to have normal BMI followed by 22 (9.16%) overweight, 20 (8.3%) in underweight and 1 (0.4%) in obese category.

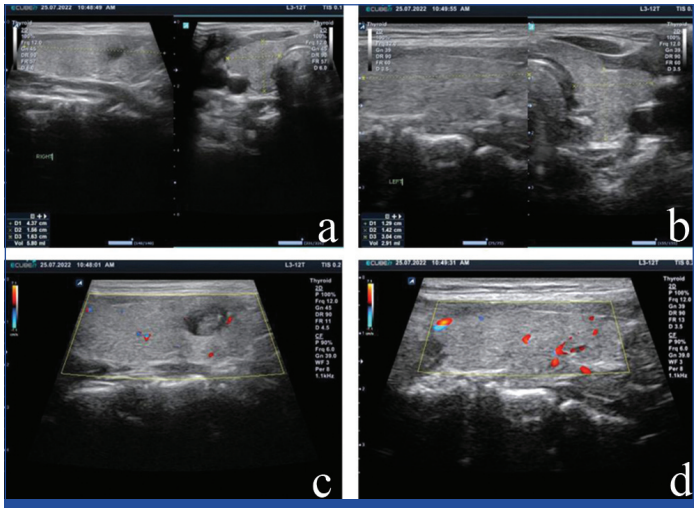
The mean total thyroid volume was 5.44±0.82 mL in non pregnant group and 7.24±1.16 mL in 3rd trimester group [Table/Fig-3,4]. On comparing right lobe, left lobe and total volume of thyroid gland amongst groups, significant difference was found between non pregnant with 2nd trimester and 3rd trimester; between 1st and 3rd trimester group and between 2nd and 3rd trimester group [Table/Fig-5-7]. Using linear regression analysis, correlation of age, parity and BMI was studied with thyroid volume. All three showed positive correlation but only BMI was found to be independent predictor of thyroid volume during pregnancy [Table/Fig-8].




**[Table/Fig-2]:** Figure showing distribution of females according to age (years).

| Parameter | Non pregnant | 1st trimester | 2nd trimester | 3rd trimester | p-value* |
|---|---|---|---|---|---|
| Right lobe thyroid volume | 3.13±0.57 | 3.26±0.44 | 3.45±0.44 | 3.98±0.75 | **0.001** |
| Left lobe thyroid volume | 2.30±0.52 | 2.58±0.39 | 2.80±0.39 | 3.26±0.67 | **0.001** |
| Total thyroid volume | 5.44±0.82 | 5.85±0.64 | 6.25±0.67 | 7.24±1.16 | **0.001** |
| BMI | 20.6±2.47 | 21±1.94 | 22.17±2.27 | 23.01±2.36 | **0.001** |

**[Table/Fig-3]:** Table depicting thyroid gland volume and BMI in non pregnant, 1st, 2nd and 3rd trimester group.
Results were presented in mL as mean±SD. p-value in bold font indicates statistically significant value (ANOVA test was used)




**[Table/Fig-4]:** A 33-year-old pregnant female in her 2nd trimester came for a routine ultrasound scan. a,b) shows total thyroid volume of 8.71 mL; c,d) shows a solid cystic nodule with CFDS Pattern-I vascularity of thyroid parenchyma.

| (I) Trimester | (J) Trimester | Mean difference (I-J) | Standard error | p-value |
|---|---|---|---|---|
| Non pregnant | 1st trimester | -0.135 | 0.104 | 1.000 |
| | 2nd trimester | -0.322 | 0.104 | **0.014** |
| | 3rd trimester | -0.851 | 0.104 | **0.001** |
| 1st trimester | Non pregnant | 0.135 | 0.104 | 1.000 |
| | 2nd trimester | -0.187 | 0.104 | 0.445 |
| | 3rd trimester | -0.716 | 0.104 | **0.001** |
| 2nd trimester | Non pregnant | 0.322 | 0.104 | **0.014** |
| | 1st trimester | 0.187 | 0.104 | 0.445 |
| | 3rd trimester | -0.529 | 0.104 | **0.001** |
| 3rd trimester | Non pregnant | 0.851 | 0.104 | **0.001** |
| | 1st trimester | 0.716 | 0.104 | **0.001** |
| | 2nd trimester | 0.529 | 0.104 | **0.001** |

**[Table/Fig-5]:** Table depicting comparison of mean right lobe thyroid gland volume in non pregnant, 1st, 2nd and 3rd trimester group.

| (I) Trimester | (J) Trimester | Mean difference (I-J) | Standard error | p-value |
|---|---|---|---|---|
| Non pregnant | 1st trimester | -0.279 | 0.093 | 0.069 |
| | 2nd trimester | -0.492 | 0.093 | **0.001** |
| | 3rd trimester | -0.956 | 0.093 | 0.001 |
| 1st trimester | Non pregnant | 0.279 | 0.093 | 0.069 |
| | 2nd trimester | -0.213 | 0.093 | 0.139 |
| | 3rd trimester | -0.677 | 0.093 | **0.001** |
| 2nd trimester | Non pregnant | 0.492 | 0.093 | **0.001** |
| | 1st trimester | 0.213 | 0.093 | 0.139 |
| | 3rd trimester | -0.464 | 0.093 | **0.001** |
| 3rd trimester | Non pregnant | 0.956 | 0.093 | **0.001** |
| | 1st trimester | 0.677 | 0.093 | **0.001** |
| | 2nd trimester | 0.464 | 0.093 | **0.001** |

**[Table/Fig-6]:** Table depicting comparison of mean left lobe thyroid gland volume in non pregnant, 1st, 2nd and 3rd trimester group.

| (I) Trimester | (J) Trimester | Mean difference (I-J) | Std. Error | p-value |
|---|---|---|---|---|
| Non pregnant | 1st trimester | -0.413 | 0.155 | 0.052 |
| | 2nd trimester | -0.813 | 0.155 | **0.001** |
| | 3rd trimester | -1.806 | 0.155 | **0.001** |
| 1st trimester | Non pregnant | 0.413 | 0.155 | 0.052 |
| | 2nd trimester | -0.400 | 0.155 | 0.065 |
| | 3rd trimester | -1.390 | 0.155 | **0.001** |
| 2nd trimester | Non pregnant | 0.813 | 0.155 | **0.001** |
| | 1st trimester | 0.400 | 0.155 | 0.065 |
| | 3rd trimester | -0.993 | 0.155 | **0.001** |
| 3rd trimester | Non pregnant | 1.806 | 0.155 | **0.001** |
| | 1st trimester | 1.393 | 0.155 | **0.001** |
| | 2nd trimester | 0.993 | 0.155 | **0.001** |

**[Table/Fig-7]:** Table depicting comparison of mean total thyroid gland volume in non pregnant, 1st, 2nd and 3rd trimester group.

| Group | Variable | Coefficients | p-value | R |
|---|---|---|---|---|
| Control group | Age | 0.052 | 0.180 | 0.364 |
| | Parity | 0.370 | 0.367 | |
| | BMI | 0.167 | 0.042 | |
| 1st trimester | Age | 0.057 | 0.299 | 0.371 |
| | Parity | 0.063 | 0.047 | |
| | BMI | 0.201 | 0.020 | |
| 2nd trimester | Age | 0.022 | 0.630 | 0.36 |
| | Parity | 0.094 | 0.046 | |
| | BMI | 0.185 | 0.009 | |
| 3rd trimester | Age | 0.049 | 0.215 | 0.344 |
| | Parity | 0.181 | 0.040 | |
| | BMI | 0.150 | 0.013 | |

**[Table/Fig-8]:** Table depicting thyroid gland volume and other factors in non pregnant, 1st, 2nd and 3rd trimester group.

All the pregnant and non pregnant females showed normoechogenicity of thyroid gland in all the groups. A 12.2% of females in pregnant group and 5% in non pregnant group showed nodules in thyroid gland. Amongst pregnant women maximum number were found to be in 3rd trimester group [Table/Fig-9]. Most of the nodules were spongiform in nature seen in 17 (8%) pregnant females, 3 (1.4%) had colloid nodules and 2 (0.9%) females in the third trimester showed solid-cystic nodule.

Thyroid gland parenchymal vascularity was found to be Pattern-0 or I in majority of patients [Table/Fig-10]. Pattern-II was seen in 11 (4.5%) pregnant women.

| Nodules | Non pregnant n (%) | Pregnant n (%) |
|---|---|---|
| Present | 3 (5) | 22 (12.2) |
| Absent | 57 (95) | 158 (87.8) |
| Total | 60 (100) | 180 (100) |

**[Table/Fig-9]:** Table showing thyroid nodules in non pregnant group and pregnant group.

| Parameter | Non pregnant (n) | 1st trimester (n) | 2nd trimester (n) | 3rd trimester (n) | Total n (%) |
|---|---|---|---|---|---|
| Pattern-0 | 29 | 28 | 20 | 14 | 91 (37.9%) |
| Pattern-I | 31 | 32 | 37 | 38 | 138 (57.5%) |
| Pattern-II | - | - | 3 | 8 | 11 (4.5%) |
| Pattern-III | - | - | - | - | - |
| Total | 60 | 60 | 60 | 60 | 240 (100%) |

**[Table/Fig-10]:** Table showing distribution as per thyroid intraparenchymal vascularity on colour doppler.
Percentage is given in parenthesis ()

## DISCUSSION

In this study, age distribution of females was between 18-40 years with maximum number of females (52%) belonging to younger age group of range 21-25 years. Similar demographic results were obtained in the study done by Mehran L et al., where 69.5% females were in younger age group with a mean age of 25.3±5 years in pregnant group [9].

In the present study, majority of females were primigravida (47.5%), followed by multipara (45.9%) and very few (6.6%) females were nullipara. However, in the study done by Fister P et al., 67.7% females were found to be multiparous [10].

Mean BMI is increasing with each trimester and shows a significant increase in BMI from non pregnant and 1st trimester group to 3rd trimester group. The rising trend of BMI with trimester was in concordance with the findings in study done by Fister P et al., [11]. Study done by Kumar S et al., also showed similar results and found a significant increase in BMI with each trimester (p-value <0.05) [12].

On comparing volume of both lobes of thyroid gland amongst groups, significant difference was found between non pregnant with 2nd trimester and 3rd trimester; between 1st and 3rd trimester group and between 2nd and 3rd trimester group. Also, in the present study authors found that right thyroid lobe mean volume in each group was higher than left thyroid lobe mean volume in each group. These results are comparable with study findings of Sahin SB et al., where mean volume of right lobe of thyroid gland was 6.48±1.84 mL and mean volume of left lobe of thyroid gland was 5.61±1.58 mL with the difference being statistically significant [13]. Özdikici M (Özdikici M has only mentioned that right lobe volume was greater than left lobe volume however, no values were mentioned in their study) and Agrawal N et al., (mean right thyroid lobe volume was 3.89±1.28 mL and left lobe thyroid volume was 3.59±1.09 mL) demonstrated similar findings of right thyroid lobe volume being higher than the left thyroid lobe volume [14,15].

Mean total thyroid volume in non pregnant group, 1st trimester group, 2nd trimester group and in 3rd trimester group were 5.44±0.82 mL, 5.85±0.64 mL, 6.25±0.67 mL, and 7.24±1.16 mL, respectively. On comparing mean total thyroid volumes amongst all groups, difference of non pregnant group with 2nd trimester group (p-value <0.05) and 3rd trimester group (p-value <0.05) was significant. These findings were in accordance with the results observed by Özdikici M where increase in total thyroid volume was seen from non pregnant group (mean thyroid volume of 11.95±1.90 mL) to 3rd trimester group (mean thyroid volume of 17.20±1.2 mL) which was statistically significant (p-value <0.05) [14].

Also, in the present study significant difference in total volume of thyroid gland was noted between 1st trimester group and 3rd trimester

group (p-value <0.05) 2nd trimester group and 3rd trimester group (p-value <0.05). However, the difference between non pregnant and 1st trimester group, 1st trimester and 2nd trimester group were non significant. These results were in concordance with the findings observed in Brander A and Kivisaari L study who observed the mean volumes in 1st, 2nd and 3rd trimester as 11.5 mL, 11.6 mL and 12.6 mL, respectively [16]. Thus, Brander A and Kivisaari L observed that the total thyroid gland volume was increasing in each trimester and found significant association between 1st and 3rd trimester group only [16]. Similarly, Fister P et al., observed the significant difference in thyroid volume of pregnant women with mean volume of 8.7±2.5 mL in 1st trimester to 11.3±3.1 mL in 3rd trimester (p-value<0.05) [10]. Comparable results were demonstrated by Sahin SB et al., where volume of thyroid gland in 3rd trimester (14.2±7.9 mL) was significantly greater than in 1st trimester [13].

The increase in thyroid volume can be attributed to the increase in blood volume and the extracellular fluid during pregnancy causing hyperemia of thyroid gland [17]. In literature, mixed opinions are there on goitrogenic effect of pregnancy, being more pronounced in iodine deficient areas rather than iodine sufficient areas [2,18]. However, few studies reported the increase in thyroid gland volume even in iodine sufficient areas [5,16]. An increase of up to 24% in volume of thyroid during the course of pregnancy was reported in this study. The results were comparable with the study conducted by Sahin SB et al., and Brander A and Kivisaari L where the increase in thyroid volume from 1st trimester to 3rd trimester was found to be 19.3% and 10%, respectively [13,16].

With age and as the number of pregnancies increase, a small increase in total thyroid volume was seen amongst each group though the correlation was statistically insignificant. This correlated well with the observations made by Fister P et al., and Rotondi M et al., respectively [10,19]. Another factor assessed was BMI. Significant positive correlation between thyroid volume and body mass index in pregnant women was found in the current study. These findings of this study corroborated with the study done by Fister P et al., [10]. Karger S et al., also concluded similar observations in their respective studies [20].

The correlation of independent factors such as age, parity and BMI with the thyroid volume was studied by a linear regression analysis and it was found that BMI is a significant independent predictor for thyroid volume during pregnancy. These findings are in concordance with the study done by Fister P et al., showing a significant BMI correlation with thyroid volume during pregnancy (p-value <0.05) [10].

The echogenicity of thyroid gland was found to be always higher than the surrounding adjacent muscles. No appreciable difference was found in pregnant and non pregnant females. Similar results were obtained in the study done by Brander A and Kivisaari L [16].

Thyroid nodules were detected in 26 (12.2%) women out of 210 pregnant women. Out of these 26 pregnant women, 13 (59%) pregnant females were in 3rd trimester group. However, nodules were seen only in 3 (5%) non pregnant females. Thus, nodularity was found to be increased in our study in pregnant females as compared to non pregnant females. This was comparable with the study conducted by Kung AW et al., and Shokri S et al., where 15% and 16.4% incidence of thyroid nodules was found in pregnancy [21,22].

On colour doppler analysis, mild increase in vascularity was found on comparing non pregnant group to the 3rd trimester group demonstrating the hyperaemia of thyroid gland during pregnancy. Fister P et al., found significant majority of patients in 3rd trimester with CFDS Pattern-II and even CFDS III and on follow-up in postpartum period there was decrease in CFDS pattern confirming that blood flow must have increased during pregnancy [11]. The difference in the results could be attributed to the fact that Fister P et al., did a follow-up study whereas in our study different sets of patients were taken in each trimester. Interobserver variation could also have played a role [11].

In the present study, most appreciable effect of pregnancy on ultrasound was seen on thyroid gland volume. Moreover, the incidence and characteristics of nodule can be determined on ultrasonography, governing the further management, if needed.

### Limitation(s)

The study was done in different sets of groups (heterogenous sample) i.e., same patient was not followed-up in each trimester hence the data could not be generalised. Also, no blood tests were performed to check the euthyroid status of the patient thus some patients with subclinical thyroid disorders with no symptoms or signs might be included in the study.

## CONCLUSION(S)

Despite being an iodine sufficient area, changes in the thyroid gland during pregnancy have been well appreciated in this study. The interplay of several different factors takes part in these changes; among which the significant role of BMI was confirmed. Though the various changes as documented on ultrasonography of the thyroid gland were not pathological, they provide proof of change in thyroid characteristics with pregnancy.

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