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Assessment of thyroid functions and thyroid volume in normal pregnant Egyptian females

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ABSTRACT
The normal range of thyroid functions during pregnancy differs between ethnic groups. This study assessed the thyroid functions in normal pregnant Egyptian females. Thyroid peroxidase antibodies (TPO Abs) and thyroid volume were also assessed. The study included 150 normal pregnant Egyptian females, recruited from Cairo University Hospital Antenatal Care Clinic (50 in each trimester), with 40 age-matched non-pregnant females, as a control group. Serum thyroid stimulating hormone (TSH) and TPO Abs were measured. Thyroid volume was assessed by ultrasonography. TSH ranges were 0.21–1.7, 0.52–3.2 and 0.72–2.6 mIU/L during first, second and third trimesters, respectively. The mean TSH level in pregnant females was significantly lower than that of non-pregnant women (1.2 ± 0.7 vs 2.7 ± 0.9 mIU/L, p < .001). TPO Abs were significantly higher in the first trimester compared to both second and third trimesters (p < .001 for both).

Introduction
Thyroid gland size and hormone production increases during pregnancy. Pregnancy represents a state of excessive thyroid stimulation leading to an increase in thyroid size by 10% in iodide-sufficient areas and 20–40% in iodide-deficient regions [1].

Because of increased thyroid hormone production, increased renal iodine excretion and fetal iodine requirements, dietary iodine requirements are higher in pregnancy than they are for non-pregnant adults [2]. Maternal dietary iodine deficiency results in impaired maternal and fetal thyroid hormone synthesis. Low thyroid hormone values stimulate increased pituitary TSH production, and the increased TSH stimulates thyroid growth, resulting in maternal and fetal goiter [3]. In an iodine-sufficient area these thyroid adaptations during pregnancy are well tolerated; however, in iodide deficient areas these physiological adaptations lead to significant changes during pregnancy [4].

Approximately 2–3% of pregnant women will have an elevated serum TSH level at the time of routine screening. Of the screened women, 0.3–0.5% will have overt hypothyroidism (OH) and 2–2.5% will have subclinical hypothyroidism (SCH) [5]. The prevalence of both OH and SCH increases with patient age and is also likely to be higher in iodine-deficient regions. Hyperthyroidism is less common, occurring in approximately 0.1–0.4% of pregnant women [6]. Moreover, about 10–20% of all euthyroid pregnant females are positive for thyroid antibodies [7]. Thyroid size is influenced by different factors, including iodine supply, genetics, gender, age, TSH, anthropometric parameters and pregnancy [8]. About 11–20% of women with a thyroid nodule detected in the first trimester of pregnancy developed a second nodule through the course of pregnancy [9]. Pregnancy was considered a risk factor for growth of thyroid nodules; however, it is still unclear if thyroid nodules are more commonly diagnosed in pregnant than in non-pregnant women [10]. The aim of this study was to assess the thyroid functions in normal pregnant Egyptian females in order to establish a population-specific reference range. Thyroid peroxidase antibodies (TPO Abs) and thyroid volume (by ultrasonography) were also assessed.

Materials and methods
The study included 150 normal pregnant Egyptian females recruited from Cairo University Hospital Antenatal Care Clinic, 50 in each trimester of pregnancy (mean ages 27.5 ± 6.5, 28.9 ± 6.1, 27.1 ± 6.1 years in first, second and third trimesters, respectively) and 40 age-matched non-pregnant females (confirmed by normal beta human chorionic gonadotropin test), as a control group. Both the study and control group subjects were on iodine sufficient-diet. Females with any history suggestive of thyroid disease (including medical or surgical treatment or family history), malignancy, neck surgery or irradiation, history of...
liver or kidney diseases or diabetes mellitus, history of amiodarine or lithium therapy or recent administration of iodinated radiographic contrast were excluded. The study was approved by Cairo University ethical committee and review board. All participants provided written informed consents.

The study population was subjected to thorough history (including calculation of the gestational age) and clinical examination. Gestational age <14, 14–27 and >28 weeks comprised the first, second and third trimesters of pregnancy, respectively. Body mass index (BMI) was calculated as weight/height². All participants were clinically euthyroid. Serum samples were taken in all three trimesters for assessment of TSH by ELISA kit (using the quantitative sandwich immunoassay technique). TPO Ab level was measured by ELISA reader (ORGENTEC Diagnostika GmbH, Germany).

Thyroid volume was assessed using ultrasound (HDI 5000) portable instrument with color Doppler ultrasound scanner and a 7.4-MHz linear transducer. The thyroid volume was the sum of the volume of both lobes.

Statistical analysis was performed using SPSS, Version 23. Chi-square test was used to compare between the groups with respect to categorical data. Comparisons between two groups for normally distributed numeric variables were done using the Student’s t-test while for non-normally distributed numeric variables, comparisons were done by Mann–Whitney U test. Comparisons between more than two groups was performed by the analysis of variance (ANOVA) for normally distributed and Kruskal-Wallis for non-normally distributed variables.

Pearson’s correlation coefficients were used to measure the strength of association between the normally distributed measurements. Spearman’s correlation coefficient was calculated for non-normally distributed variables. Logistic regression analysis was done to give adjusted odds ratio and magnitude of the effect of different risk factors. p ≤ .05 was considered significant.

Results

TSH ranges normal pregnant Egyptian females were 0.21–1.7, 0.52–3.2 and 0.72–2.6 mIU/L during first, second and third trimesters, respectively. The mean TSH level in pregnant females was significantly lower than that of non-pregnant women (1.2 ± 0.7 vs 2.7 ± 0.9 mIU/L, p < .001). The mean TPO Ab level was significantly higher in the first trimester as compared with both second and third trimesters (117.8 ± 39.7 vs 80.4 ± 32.0 and 71.1 ± 31.9 IU/mL, respectively, p < .001 for both). The mean TPO Ab level was significantly higher in pregnant females as compared with the control group (89.8 ± 40 vs 20.5 ± 14.4 IU/mL, p < .001). TPO Ab levels in pregnant females also showed a negative correlation with TSH (r = −0.68, p < .001).

Thyroid volume of pregnant females was non-significantly higher than that of non-pregnant control (8.6 ± 2.9 vs 7.9 ± 2.5 mL, p = .126). The percent of pregnant females with increased thyroid volume was higher than that of non-pregnant females; however, the difference was insignificant (p = .060). In pregnant females, thyroid volume showed a significant positive correlation between thyroid volume and BMI (p < .001).

The study results are summarized in Tables 1–3.

Discussion

The range of normal thyroid functions during pregnancy differs between ethnic groups. In view of the absence of a published reference range of thyroid functions in normal pregnant Egyptian females, this study aimed to establish that population-specific reference range. In our study, we found that TSH was significantly lower in pregnant women compared with non-pregnant females, in agreement with Yan et al. [11] who reported similar findings in their cross-sectional study on pregnant Chinese women.

In our cross-sectional study TSH reference range (5th to 95th percentile) in normal pregnant Egyptian females were 0.21–1.7, 0.52–3.2 and 0.72–2.6 mIU/L during first, second and third trimesters, respectively, with median (50th percentile) values of 0.61, 1.08 and 1.4 mIU/L in the first, second and third trimesters, respectively. Our study showed narrower reference range with lower upper limit compared with the study done by Marwaha et al. [12] who reported TSH reference ranges for normal pregnant Indian females to be 0.6–5.0, 0.44–5.78 and 0.74–5.70 mIU/L during first, second and third trimesters, respectively, and using also the 5th and 95th percentiles as the reference limits. But their study included a larger sample size of 331 pregnant females. Again, our reference range was narrower and with a lower upper limit compared with the study done by Yu et al. [13], who reported TSH reference ranges for normal pregnant Chinese females to be 0.02–3.65, 0.36–3.46 and 0.44–5.04 mIU/L during first, second and third trimesters, respectively. But their sample size of 538 pregnant females was also larger than ours. Xing et al. [14] also studied the thyroid functions in 2540 Chinese women with normal pregnancies. They reported TSH reference ranges to be 0.07–3.96, 0.27–4.53 and 0.48–5.40 mIU/L during first, second and third trimesters, respectively. Those ranges were much wider and with higher upper limits than ours. The difference could be explained by the significantly larger sample size and different ethnic background. These differences also emphasize the importance of establishing trimester-specific reference ranges for every population.

Our study showed that the mean TPO Ab level was significantly higher in pregnant females as compared with the control group. TPO Ab levels in pregnant females also showed a significant negative correlation with TSH. Glinoer et al. [15] and Negro et al. [16] also reported an increase in TSH levels with progression of gestation in TPO Ab positive euthyroid women. This is due to the limited ability of the thyroid gland to increase its hormone production during gestation especially in situations of limited thyroid hormone reserve like thyroid autoimmunity and iodine deficiency which cause imbalance between supply and demand.

In our study, TPO Ab was significantly higher in the first trimester compared to both second and third trimesters (p < .001 for both). Glinoer et al. [15] also found that anti-thyroid antibody titers were highest in the first trimester, although they decreased by about 60% over the course of gestation. Negro et al. [16] 2006 reported similar results. Balucan et al. [17] also

| Table 1. Clinical and laboratory criteria of the study and control groups. |
|-----------------------|-----------------------|-----------------------|-----------------------|
|                       | Control              | 1st trimester         | 2nd trimester         | 3rd trimester         |
| Age (year)            | Mean SD              | Mean SD               | Mean SD               | Mean SD               |
| 29.3 ± 6.6            | 27.4 ± 6.4           | 28.9 ± 6.1            | 27.1 ± 6.1            | 6.1 ± 0.26            |
| BMI (kg/m²)           | 26.6 ± 5.2           | 28.1 ± 6.7            | 29.0 ± 6.7            | 31.2 ± 6.9            | 0.007                |
| TSH (mIU/L)           | 2.7 ± 0.9            | 0.8 ± 0.5             | 1.3 ± 0.8             | 1.5 ± 0.6             | <0.001               |
| TPO Ab (IU/mL)        | 20.5 ± 14.4          | 117.8 ± 39.7          | 80.4 ± 32.0           | 71.1 ± 31.9           | <0.001               |
| Thyroid volume (mL)   | 7.9 ± 2.5            | 8.3 ± 3.4             | 8.7 ± 3.1             | 8.9 ± 2.2             | 0.340                |

BMI: body mass index; TSH: thyroid stimulating hormone; TPO Ab: thyroid peroxidase antibody; SD: standard deviation.

Values p ≤ .05 is considered significant.

Bold values are statistically significant.
Our study showed that Thyroid volume of pregnant females was non-significantly higher than that of non-pregnant control subjects. No significant difference was found between the three trimesters groups as regard thyroid volume, noddularity and vascularity as compared with each other and the control group. Correlation between thyroid volume with different clinical and laboratory variables in pregnant females showed a significant positive correlation between thyroid volume and BMI, but there was no significant correlation between thyroid volume and age, TSH or TPO Ab. Fister et al. [18] reported that in iodine-sufficient republic of Slovenia, thyroid volume increases during pregnancy and decreases after delivery. They also found that the changes in volume are associated with changes in BMI and TSH. Berghout et al. [19] found no significant differences regarding thyroid volume in different trimesters of pregnancy in areas which known to be iodide-sufficient. Okafor et al. [20] reported an increase in mean thyroid volume in pregnant compared to non-pregnant control in iodide-sufficient regions in Nigeria. They also found that the thyroid volume increased progressively across trimesters of pregnancy. Rasmussen et al. [21] also reported a progressive increase in thyroid volume from the second trimester to the end of pregnancy. Glinoer et al. [22] observed an increase in thyroid volume during pregnancy in iodine-deficient Belgium. In Italy, an iodine-deficient region as well, a progressive increase in thyroid volume throughout the pregnancy was observed in 18 subjects, but not in 17 pregnant controls who were treated with iodide salt [23]. The results of these studies support the hypothesis that the observed increase in thyroid size in areas with less than acceptable iodine supplementation is related to a further increase in iodine deficiency during pregnancy. This increase can partly be prevented by supplying extra iodine (at least 100 mg/day) as suggested by Glinoer et al. [24]. We also found a significant positive correlation between thyroid volume and BMI. But no significant correlation was found between thyroid volume and other clinical or laboratory parameters. Fister et al. [18] reported that BMI is an independent predictor of thyroid volume during pregnancy.

Lack of iodine status evaluation and the small sample size are important limitations of our study. The cross-sectional nature of the study could not enable us to follow the dynamic changes in the thyroid functions and volume in the pregnant females throughout the whole period of pregnancy. Further longitudinal studies with higher number of cases are required to provide more information about changes in thyroid functions and volume in pregnant Egyptian females during pregnancy. Also, a larger population-based study would help to confirm the trimester-specific reference ranges for thyroid hormone levels during pregnancy.

The reference ranges in this study are different from previous studies done in other countries. These differences can be explained by variations in assays as well as population-specific factors, such as ethnic background as well as nutritional and environmental factors. Accordingly, it is necessary to use trimester specific reference ranges for every population.

**Disclosure statement**

The authors declare no conflicts of interest.

**References**


