

Fluctuation of Thyroid Stimulating Hormone (TSH) During Pregnancy

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Abstract: Pregnancy causes a decrease in the upper and lower limits of maternal TSH levels compared to the typical reference range for non-pregnant TSH levels. This changes in the thyroid glands physiology and common complications in pregnancy with serious consequences for the mother and adverse maternal outcome associated with abnormal maternal thyroid function. utilizing population-based trimester reference intervals (RIs) for thyroid testing is one of the recommendations suggested by international standards. This study aims to identify an optimal RI for thyroid-stimulating hormone (TSH) in pregnant Iraqi women.

Methods: A total of 80 women visiting primary health care centers in Babylon province aged 19 to 35 years (20 non pregnant women, 20 pregnant women in first trimesters: T1 (1-12 weeks), 20 pregnant women in second trimesters: T2 (13-25 weeks), and 20 pregnant women in third trimesters: T3 (26-41 weeks) were used in the study. Women from Babil Governorate's primary health care centers participated in a reference interval study after exception certain medical and prenatal history criteria.

Results: The results upper limits of the TSH reference range of pregnant groups were all lower than that of non pregnant group reference of upper limits. The results of TSH reference range was 0.42 to 1.94 mIU/L, 0.30 to 1.71 mIU/L, 0.12 to 3.00 mIU/L in the first, second and third trimesters respectively. Also in the second trimester there was lowest level of the upper limit for TSH and T3 whereas in the third trimester was the lowest value of the lower limit for TSH and T3.

Conclusions: To diagnose thyroid conditions during pregnancy it is necessary to establish pregnancy-specific and laboratory RIs, especially for TSH. during pregnancy, the function of the thyroid gland changes in women, especially TSH and free T3.

Key words: TSH, T3, Fluctuation, Pregnancy

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Introduction

The thyroid gland, located in the inferior, anterior neck, produces and secretes thyroid hormones and maintains iodine levels in the human body. The thyroid gland produces approximately ninety percent inactive thyroid hormone or thyroxine (T4) as well as ten percent active thyroid hormone, or triiodothyronine (T3). Inactive thyroid hormone undergoes peripheral conversion to activated or alternative thyroid hormone. Inactive thyroid hormone. [1]

Thyroid disease is the second most frequent endocrine problem during pregnancy, after diabetes. Thyroid diseases affects pregnant women's physiology and has serious maternal and fetal consequences. Research indicates that adequate iodine stores increase thyroid gland size by 10% during pregnancy in countries with adequate iodine stores, and increases by 20% to 40% in countries with iodine deficiency. During pregnancy, thyroid hormone production and daily iodine requirements increase by around 50%. Pregnant women with thyroid disorders, including hypothyroidism and hyperthyroidism, require ongoing monitoring and medication as needed. Thyroid nodules and malignancy can cause complications during pregnancy, necessitating additional care.[2,3]

Thyroid stimulating hormone (TSH) is a glycoprotein hormone secreted from the anterior lobe of the pituitary gland. The thyroid gland produces thyroid hormones primarily in response to this stimuli. Additionally, it promotes thyroid follicular cell development, resulting in thyroid hypertrophy. The hypothalamic-pituitary axis controls TSH secretion. Neurons in the hypothalamus release TRH, which encourages thyrotrophs in the anterior pituitary to produce TSH. TSH induces thyroid follicular cells to generate thyroid hormones (T3 or T4). [4,5].

During pregnancy, the TSH reference range shifts downward, reducing both the bottom and upper limits of TSH in pregnant women compared to The standard nonpregnant range. Additionally, utilizing population-based, trimester-specific RIs for thyroid tests that were generated from local populations has been recommended by national guidelines around the world due to racial and geographic variances in population, data representing a provider's laboratory. [6].

Since the recommendation statements, data on population-based gestational RIs has increased significantly. "The American Thyroid Association and the American Endocrine Association recommend fixed reference limits (RIs) for TSH in the first, second, and third trimesters: 0.1-2.5 mIU/L in the first trimester, 0.2-3.0 mIU/L in the second trimester, and 0.3-3.0 mIU/L in the third trimester" [7]. In 2017, the ATA guideline recommended a revised upper reference limit of TSH 4 mIU/L in early pregnancy [6]. The ATA guideline recommends defining population-based trimester-specific reference ranges for serum TSH using data from a health care provider's practice. This study aims to create gestation and laboratory-specific RIs for TSH and evaluate its trend during pregnancy.

Materials and Methods

A total of 80 women visiting primary health care centers in Babylon province aged 19 to 35 years (20 non pregnant women, 20 pregnant women in first trimesters: T1 (1-12 weeks), 20 pregnant women in second trimesters: T2 (13-25 weeks), and 20 pregnant women in third trimesters: T3 (26-41 weeks) were used in the study.

The current study excluded women with chronic disease (hypertension, diabetes) and autoimmune disorders as (psoriasis, cancer and rheumatoid, arthritis) and pregnancy issues as (gestational hyperglycemia, hypertension, spontaneous abortion).

Body mass index (BMI) was determined by using the formula which dividing weight in kilograms by height in square meters. The BioTek 800 TS absorbance reader and CALBIOTECH Triiodothyronine (T3) ELISA Kit were used to evaluate blood pressure and serum levels of TSH and T3. Disposable syringes were used to collect approximately 5 mL of maternal venous blood for testing. The serum sample has been separated and kept for later analysis.

Statistical analysis

Statistical Package for Social Science (SPSS) version 23.0 (SPSS, Chicago, USA) was used for statistical analysis of the data. Data was given in the form of arithmetic mean values and standard deviations. Also the median, lower limits of the reference intervals and upper limits of the reference intervals were determined.

Results

As described in the table (1), figure (1) and figure (2) the demographic data concerning women visiting primary health care centers in Babylon province, the median maternal age of non pregnant group was 24.50 years (range: 18-32 years). Group T1 women in first trimesters the median maternal age was 26.50 years (range: 16-35 years), whereas T2 group women in second trimesters the median maternal age was 25.50 years (range: 18-32 years) and the median maternal age in T3: women in third trimesters was 26.50 years (range: 27-33 years).

The median gestational age of group T1 was 8.50 weeks (range: 4-12 weeks), group T2 was 21.50 weeks (range: 16-24 weeks) and 26.50 weeks (range: 27-33 weeks).

The median blood pressure in the non-pregnant group was 8/12 mm Hg (range: 7/9-11/13 mm Hg), while in the T1 group it was 8/11 mm Hg (range: 5/9-10/13 mm Hg), in the T2 group it was 8/12 mm Hg (range: 5/9-8/14 mm Hg), and in the T3 group it was 8/12 mm Hg (range: 7/11-8/12 mm Hg).

The median maternal body mass index of non pregnant group was 27.30 kg/m² (range: 22.3-30.10 kg/m²), T1 group body mass index median was 23.75 kg/m² (range: 20.60-31.50 kg/m²), T2 group body mass index median was 25.65 kg/m² (range: 19.50-30.20 kg/m²) and T3 group body mass index median was 27.00 kg/m² (range: 20.70-39.80 kg/m²).

Table 1. Demographic details in a Sample of Pregnant Women visiting Primary Health Care Centers in Babylon Province.

Groups	Maternal age years*	Gestational age, weeks*	LP	HP	BMI
Non pregnant	24.80±4.68		8.2±1.13	11.60±1.07	24.88±2.49
	24.50(18-32)	-	8.00 (7-11)	12.00 (9-13)	27.30 (22.3-30.10)
T1	25.50±5.4	8.60±2.50	7.40±1.42	11.00±1.24	24.96±3.22
	26.50(16-35)	8.50(4-12)	8.00(5-10)	11.00(9-13)	23.75(20.60-31.50)
T2	25.30±5.71	21.30±2.31	7.50±0.97	11.8±1.39	25.24±3.60
	25.50(17-34)	21.50(16-24)	8.00 (5-8)	12.00(9-14)	25.65(19.50-30.20)
T3	25.80±5.65	31.40±1.17	7.90±0.31	11.9±0.31	27.95±4.88
	26.50(27-33)	31.50(30-33)	8.00(7-8)	12.00(11-12)	27.00(20.70-39.80)

Data are presented in first row for each group as mean ± SD and second row Median (lower limit- upper limit). T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters; LP: Low pressure; HP: High pressure; BMI: Body Mass Index.

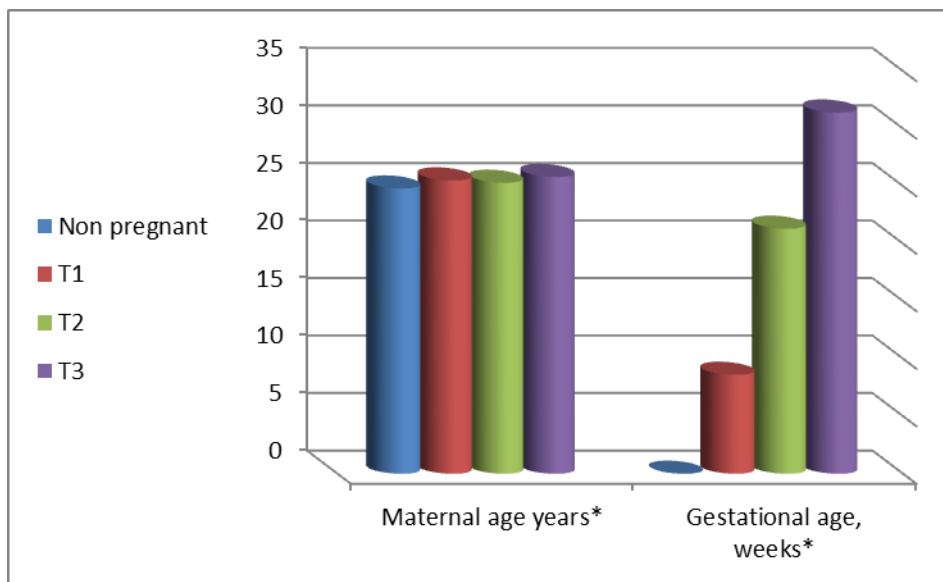


Figure (1) comparative of Maternal's age by years* and Gestational age by weeks* between groups. T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters.

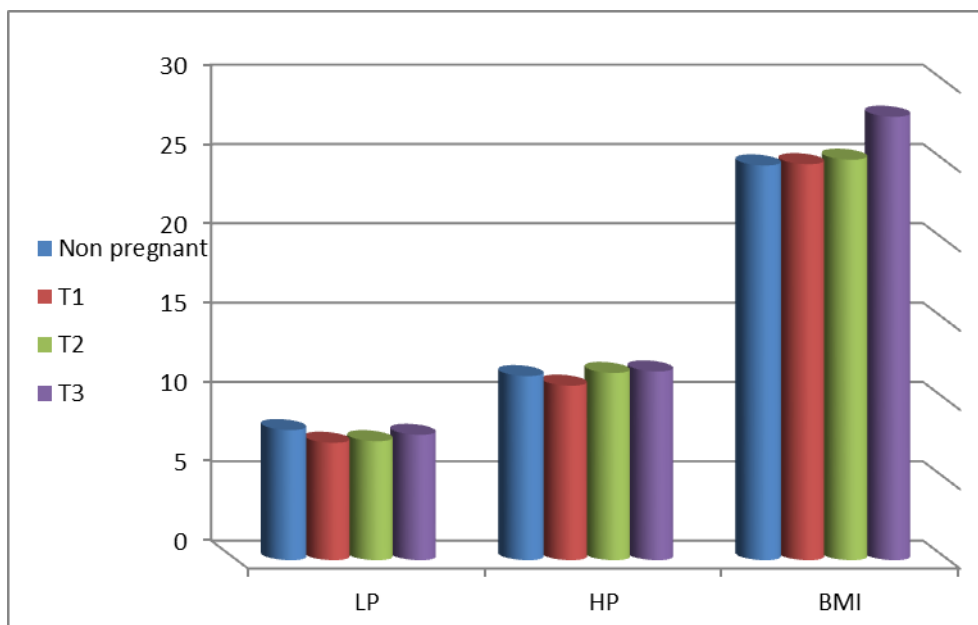


Figure (2) comparative of Maternal's blood pressure (mm Hg) and body mass index (kg/m²) between groups. T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters; LP: Low pressure; HP: High pressure; BMI: Body Mass Index.

The results of Thyroid-Stimulating Hormone TSH as shown in table (2) and figure (3) exposed TSH level variation for the first, second, and third trimesters was 0.42 to 1.94 mIU/L, 0.30 to 1.71 mIU/L, and 0.12 to 3.00 mIU/L, respectively (Table 2). The TSH reference range upper limits were lower than the ATA suggested upper limits (2.5 mIU/L in the first trimester and 3 mIU/L in the second and third trimesters). Also, the TSH reference range had lower upper limits compared to the non-pregnant group (0.40-3.01 mIU/L). The lowest upper limit for TSH was identified in the second trimester, whereas the lowest lower limit was detected in the third trimester.

Table 2. Trimester-specific reference intervals for Thyroid-Stimulating Hormone TSH (mIU/L) details in a Sample of Pregnant Women visiting some Primary Health Care Centers in Babylon Province comparing with American Thyroid Association (ATA) Guidelines.

Trimester	Mean \pm SD	Median	Lower limit	Upper limit	ATA maternal recommendatin*
Non pregnant	1.30 \pm 0.78	1.0580	0.40	3.01	-
T1	0.81 \pm 0.45	0.70	0.42	1.94	0.1 to 2.5
T2	0.67 \pm 0.49	0.50	0.30	1.71	0.2 to 3.0
T3	0.62 \pm 0.84	0.38	0.12	3.00	0.3 to 3.0

T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters; * “ The Guidelines from 2011 of ATA recommends maternal TSH levels between 0.1 and 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.0 mIU/L in the third trimester”

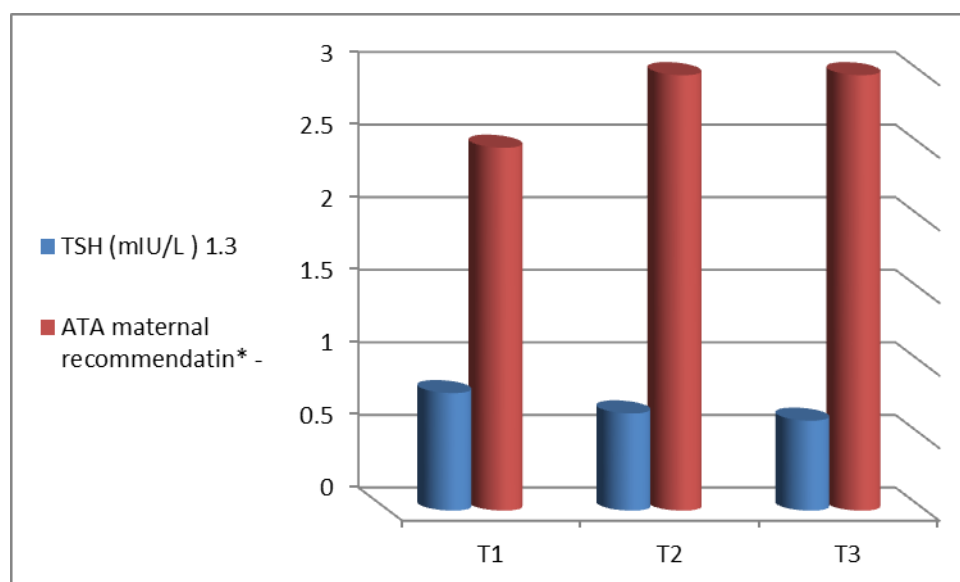


Figure (3) Trimester-specific reference intervals for Thyroid-Stimulating Hormone TSH (mIU/L) comparing with American Thyroid Association (ATA) Guidelines .. T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters. * “ The Guidelines from 2011 of ATA recommends maternal TSH levels between 0.1 and 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.0 mIU/L in the third trimester”

The results of FreeTriiodothyronine (T3) pg/mL as shown in table (3) and figure (4) the median of free T3 in non pregnant womens was 1.05 pg/mL (range: 0.95-4.07 pg/mL) , The median of T1 group was 3.63 pg/mL (range: 2.85-5.62 pg/mL), The median of T2 group was 3.32 pg/mL (range: 099-5.40) and The median of T3 group was 3.23 pg/mL (range: 093-10.52 pg/mL). Despite the lowest level of upper limit for freeT3 was observed in the second trimester and the lowest value of the lower limit for free T3 was detected in the third trimester. These results are identical to the results of the TSH in the lowest value of the upper limit and the lowest value of the lower limit.

Table 3. Free Triiodothyronine levels details in a Sample of Pregnant Women visiting Primary Health Care Centers in Babylon Province

Trimester	Mean \pm SD	Median	Lower limit	Upper limit
Non pregnant	2.46 \pm 1.13	1.05	0.95	4.07
T1	3.90 \pm 3.07	3.63	2.85	5.62
T2	3.12 \pm 1.18	3.32	0.99	5.40
T3	3.72 \pm 2.70	3.23	0.93	10.52

T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters.

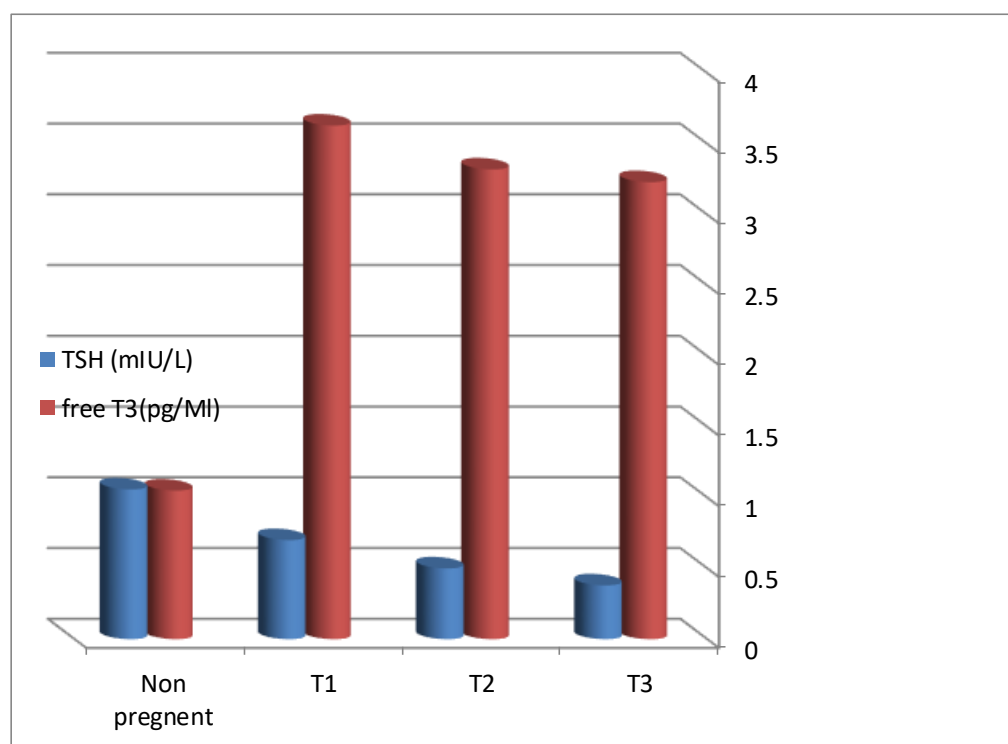


Figure (4) Thyroid-Stimulating Hormone (TSH) and Free Triiodothyronine levels in a Sample of Pregnant Women visiting Primary Health Care Centers in Babylon Province. T1: women in first trimesters; T2: women in second trimesters; T3: women in third trimesters.

Discussion

Thyroid-Stimulating Hormone (TSH) is largely acknowledged as the universal screening method for thyroid dysfunction in patients, including pregnant women (8). TSH levels decreased significantly during the first, second, and third trimesters. During the first trimester, higher levels of serum hCG stimulate the TSH receptor and increase thyroid hormone synthesis, leading to a reduction in serum TSH levels [6]. Serum TSH levels remain lower in the second and third trimesters compared to non-pregnant women, this result agree with previous studies [9, 10].

The lower limit of TSH in the first, second and third trimesters was higher than ATA lower limit but lower than in non-pregnant lower limit .The difference may be due to different analysis methodologies, even though this variation not clinically significant. [11]. To reduce variability must be utilize the Multiple of Medians calculation to compare values across assays. The formula divides an individual's value by the population median [12].

The results of maternal body mass index reveals an increases with the progression of pregnancy, and this is a logical and acceptable maternal weight gain during pregnancy might provide valuable insight into the mother's well-being. [13] this result agree with [14].

The assessment of blood pressure is fundamental to the provision of safe obstetrical care [15]. The blood pressure results of this study reveals there was non significant increase in maternal blood pressure when compared with non pregnant womens. This result indicates that the decrease in the TSH level does not affect blood pressure. Thyroid hormones and TSH, have an essential effect on cardiovascular function, perhaps contributing to the development of high blood pressure [16].

Thyroid hormones play many roles in glucose metabolism and homeostasis, with a well-established correlation between thyroid malfunction and glucose abnormalities. T3 has been ignored, despite its crucial function in glucose control [17]. The results of this study exposed gradually increasing inT3 concentration with increasing gestational age this result agree with [18]. The results of the current study displays that there is a relationship between the decreasing of TSH and the rising of free T3 hormone in the first ,second and third trimester of pregnancy this result agree with [19,20].

Conclusions:

Considering the lack of local data regarding thyroid function testing in pregnant Iraqi women as population-based reference intervals for thyroid functiontests , using the reference limits recommended by ATA.Maternal thyroid function, especially TSH and free T3, fluctuated during pregnancy.Hormone levels tend to be high TSH and low free T3 during the first trimester, and high free T3 and low in TSH in the third trimester.

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