Thieme

Reference Intervals for Thyroid Hormones During the First Trimester of Gestation: A Report from an Area with a Sufficient Iodine Level

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ABSTRACT

The physiological changes during pregnancy modulate the endocrine system. Therefore, both the American and the European thyroid associations recommend the use of local trimester-specific reference intervals. The purpose of this study was to establish the first trimester reference intervals for thyroid function tests in the central area of Iran. We examined 436 pregnant women in their first trimester of pregnancy, and 444 non-pregnant women in a cross sectional study. Serum levels of thyroid stimulating hormone (TSH), free thyroxin (FT_4), free triiodothyronine (FT_3), thyroid peroxidase antibody, urinary iodine concentration (UIC), and thyroid volume were measured for all subjects. The first trimester-specific reference intervals (2.5th–97.5th percentile) were determined for 185 pregnant women and 256 non-pregnant women with negative TPOAb, adequate iodine level (UIC ≥ 150 µg/l in pregnant and UIC ≥ 100 µg/l in non-pregnant women), and normal thyroid examination. We calculated multiples of the median (MoM) for TFTs to normalize the obtained data. The first trimester-specific reference intervals of serum TSH, FT_4, and FT_3 for pregnant women were 0.20–4.60 mIU/l, 9.0–18.02 pmol/l, and 3.40–5.64 pmol/l, respectively, while the corresponding figures for non-pregnant women were 0.59–5.60 mIU/l, 9.52–19.30 pmol/l, and 3.70–5.55 pmol/l, respectively. The first and 99th percentile MoM of TSH in pregnant women in their first-trimester was 0.026–4.61. The local normal reference ranges for the first trimester of pregnancy in central region of Iran were different from the ranges suggested by the ATA.

ABBREVIATIONS

TFTs	Thyroid function tests
TSH	Thyroid stimulating hormone
FT_4	Free thyroxin
FT3	Free triiodothyronine
TPOAb	Thyroid peroxidase antibody
UIC	Urinary iodine concentration
HCG	Human chorionic gonadotropin
TBG	Thyroid-binding globulin
ATA	American Thyroid Association
LMP	The first day of the last menstrual period
MoM	Multiples of the median
SD	Standard Deviation
NACB	National Academy of Clinical Biochemistry
NHANES	National Health and National Examination Survey

Background

Pregnancy makes dynamic changes in several systems in the body, including the thyroid [1], mainly affected by the thyroid stimulating effect of human chorionic gonadotropin (HCG), secreted from placental syncytiotrophoblast, which has structural similarity with thyroid stimulating hormone (TSH) [2–4]. The highest concentration of β-HCG is observed in the first trimester of pregnancy, when thyrotropine decreases [3] and the concentration of serum thyroid-binding globulin (TBG) rises due to high levels of maternal estradiol (E_2) [5]. Furthermore, the maternal iodine requirement increases as a result of higher renal clearance of this essential element and fetal use of iodine [6].

The importance of maternal thyroid malfunction on pregnancy and fetal development is well known, with potential adverse prenatal outcomes, such as miscarriage, pre-eclampsia, placental abruption, preterm birth, post-partum hemorrhage, low birth weight, increased neonatal respiratory distress syndrome, and decreased cognitive function [6, 7]. Many factors such as iodine intake [8, 9], ethnicity, gestational age [10, 11], laboratory assay methods [12], the study design method, and selection of the reference population [13, 14] can affect the reference ranges of thyroid function tests (TFTs) and lead to inconsistent reported values. Due to the diversity exists in TSH concentrations during pregnancy, the guidelines of the Endocrine Society, the American Thyroid Association (ATA), and the European Thyroid Association (ETA) recommend that trimester-specific reference ranges should be established and used for each region separately [15–17].

Due to limited data available for the trimester-specific reference intervals in Iranian pregnant women, we conducted this study to establish specific reference ranges for thyroid function tests in healthy pregnant women during their first trimester of gestation at the central area of Iran. We have also calculated the multiple of the median (MoM) values [18].

Subjects and Methods

In this cross sectional study, 880 women, who were referred to antenatal care clinics for mother and child health care, and private clinics for the first prenatal care visit, were enrolled from September 2015 to January 2017. The samples were selected from 25 urban health centers affiliated to the Isfahan University of Medical Science and 30 private gynecology and midwifery clinics in different areas of the city. In order to obtain a representative sample group, we randomly selected health centers and private clinics; this was followed by random selection of women from the list of eligible participants in each center and clinic. In each included center or clinic in our study, a pair matching was performed between pregnant and non-pregnant women based on age and gravida; eventually 436 pregnant and 444 non-pregnant women were enrolled in the study.

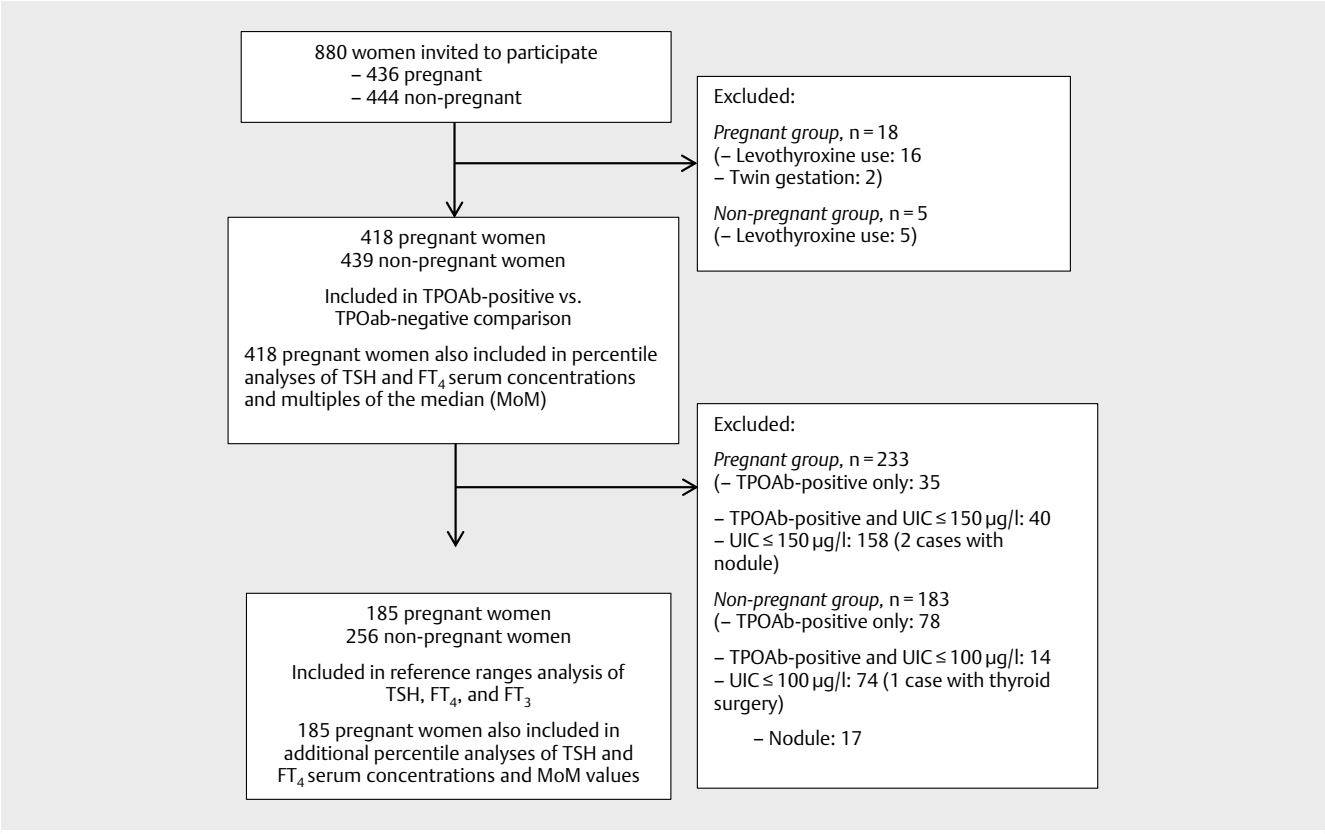
Women aged 15–45 were included in the study and the gestational age was calculated based on the first day of their last menstrual period (LMP); if the woman was unsure about her LMP, the ultrasound report was considered as the beginning of pregnancy to the completion of 14th week of gestation [19]. We excluded women with multiple gestation, goiter or thyroid nodules, autoimmune, acute or chronic diseases, positive thyroid peroxidase antibody, and known thyroid disease. Women who were taking levothyroxine, propylthiouracil, methimazole, or any other medications, which could affect TFTs were excluded from the study. Pregnant women with UIC less than 150 µg/l and non-pregnant women with UIC less than 100 µg/l were also excluded from the study (233 pregnant and 188 non-pregnant women). Finally, the reference ranges were determined for 185 pregnant and 256 non-pregnant women. For the flow chart of the study design, ▶ **Fig. 1**.

Each woman was visited individually and signed the informed consent form after receiving complete verbal explanation about the study objectives.

Five milliliter venous blood sample was obtained from each participant, centrifuged and the serum was stored at −70 °C for 2 days. Serum concentrations of TSH, free thyroxin (FT_4), free triiodothyronine (FT_3), and TPOAb were measured in the laboratory of Isfahan Endocrine and Metabolism Research Center of Isfahan University of Medical Sciences. Urine samples were collected and frozen in falcon tubes and transmitted to Isfahan Health Center Laboratory to measure the urinary iodine concentration. Urinary iodine concentration was measured by chloric acid digestion method [20]. All samples were taken within 7:30–10:30 AM. Thyroid volume was measured using ultrasound scanning by Philips affinity 70, superficial probe, 4–12 MHz (Made in the Netherlands), for all women by an expert sonographer (S.Sh.). The volume of each lobe (ml) was calculated by 0.000479 × length × width × thickness (mm). TPOAb values higher than 60 IU/ml were considered as positive according to the manufacturer's cut-off values.

Serum concentrations of TSH, FT_4, FT_3, and TPOAb were measured by chemiluminescence immunoassay sys-ADVIA centaur CP/SIMENS 2010-American. TSH Intra-assay and inter-assay coefficient of variation (CV) were 2.8–3.1 % and 2.9–3.5 %, respectively. FT_4 intra-assay was 1.68–2.22 % and interassay CV was 1.42 % and 3.48 %; the intra-assay and interassay CV for FT_3 were 1.7–4.0 % and 3.1–3.4 %, respectively. The intra-assay and interassay CV values for TPO-Ab were 1.7–7.8 % and 2.0–7.3 %, respectively.

The ethics committee of the Isfahan University of Medical Sciences approved the design and protocol of the present study and all steps were aligned with the principles of Declaration of Helsinki on human studies.



▶ **Fig. 1** Flow chart of the study design.

Statistical analysis

The data were statistically analyzed using Statistical Package for Social Science (SPSS), version 16.0 (IBM statistic software, 2009, NY; USA). The results of TFT were examined for normality by Kolmogorov–Smirnov test and Q-Q plot. Positive skewed data were subjected to logarithmic and square root transformations. The data with normal distribution were reported by mean and standard deviation (SD). In pregnant women, the distribution of square root for TSH, log base 10 for FT_3 and Ln (le Logarithme Naturel) for FT_4 were used for approximation of Gaussian normality, while in non-pregnant women Ln approximation was used for TSH, FT_4, and FT_3.

The manufacturer's values were as follows: TSH: 0.35–5.50 mIU/l, FT_4: 11.45–22.65 pmol/l, and FT_3: 3.1–6.5 pmol/l. For each TFT, median, 2.5th, 5th, 10th, 90th, 95th, 97.5th percentile, first and third quartiles were calculated. The 2.5th and 97.5th percentiles were determined as limits of the reference ranges. Comparisons between different groups were performed using Student's t-test and Chi-square test, where appropriate. Median test and binomial test were used to compare differences in median and selected percentiles between pregnant and non-pregnant women. p-Values less than 0.05 were considered statistically significant.

We have also calculated multiples of medians (MoMs) for TSH and FT_4. MoMs have been calculated by dividing the results of TFTs by the median value of each test in that population [18].

Results

The mean ± SD of age for 185 pregnant and 256 non-pregnant women was 28.7 ± 5.11 and 29.3 ± 4.87 years, respectively (p = 0.21). Median, minimum, and maximum gravida in pregnant and non-pregnant women were 2, 1, and 6, respectively. More details about the basic and clinical characteristics of participants in both groups are presented in ▶ **Table 1**.

Reference ranges for TSH, FT_4 and FT_3 values in the first trimester of gestation were 0.2–4.60 mIU/l, 9.0–18.02 pmol/l, and 3.40–5.64 pmol/l, respectively, and in non-pregnant women were 0.59–5.60 mIU/l, 9.52–19.30 pmol/l, and 3.70–5.55 pmol/l, respectively.

The first quartile (25th percentile) of TSH, FT_4, and FT_3 concentrations in pregnant women were 1.0 mIU/l, 11.60 pmol/l and 4.10 pmol/l, respectively, and the corresponding figures for non-pregnant women were 1.40 mIU/l, 12.87 pmol/l, and 4.20 pmol/l, respectively, and the third quartile (75th percentile) of TSH, FT_4, and FT_3 concentrations were 2.10 mIU/l, 14.15 pmol/l, and 4.70 pmol/l, respectively, in pregnant women, and 2.90 mIU/l, 15.44 pmol/l, and 4.70 pmol/l in non-pregnant women.

TPOAb was positive in 17.9 % of pregnant (75/418) and 21.9 % of non-pregnant (96/438) women; comparing the TFTs between participants with positive and negative TPOAb indicated that pregnant women with positive TPOAb had a higher median and 97.5th percentiles of TSH than pregnant women with negative TPOAb. The same results were obtained for non-pregnant women (▶ **Table 2**).

▶ **Table 1** Participants' basic characteristics and thyroid hormone levels.

Variables	Pregnant women (n = 185)	Non-pregnant women (n = 256)	p-Value
Age (years) *	28.7 ± 5.11	29. 3 ± 4. 87	0.212
TSH Median (2.5th–97.5th) (mIU/l) **			
Age < 25 years	1.6 (0.3–4.1)	1.9 (0.71–5.8)	
Age 25–29.99 years	1.35 (0.2–4.6)	2.1 (0.6–7.8)	
Age 30–34.99 years	1.6 (0.13–5.22)	1.95 (0.5–4.8)	
Age ≥ 35 years	1.5 (0.2–4.9)	2.1 (0.8–4.5)	
Gestational age (week/day) *	9.6 ± 2.6	–	
Gestational age (week/day) **	10w/3d (5w–14w/1d)		
Urinary iodine concentration (Min-Max) (mg/l) ***	209.0 (150–549)	194.0 (100–533 (	0.135
Thyroid volume (ml) *	6. ± 2.5 *	6.4 ± 2.1 *	0.245
TSH Median (Min-Max) (mIU/l) ***	1.50 (0.03–5.30)	2.10 (0.5–9.7)	0.001
2.5th percentile of TSH	0.20	0.59	
5th percentile of TSH	0.40	0.80	
10th percentile of TSH	0.60	1.00	
90th percentile of TSH	2.85	3.80	
95th percentile of TSH	4.10	4.30	
97.5th percentile of TSH	4.60	5.60	
FT_4 Median (Min-Max) (pmol/l) ***	12.87 (9.0–22.65)	14.15 (9.0–27.02)	0.001
2.5th percentile of FT_4	9.0	9.52	
5th percentile of FT_4	10.30	10.30	
10th percentile of FT_4	11.58	11.60	
90th percentile of FT_4	15.44	18.01	
95th percentile of FT_4	16.73	18.01	
97.5th percentile of FT_4	18.02	19.30	
FT_3 Median (Min-Max) (pmol/l) ***	4.40 (2.50–6.90)	4.50 (2.70–7.50)	0.356
2.5th percentile of FT_3	3.40	3.70	
5th percentile of FT_3	3.53	3.80	
10th percentile of FT_3	3.80	3.90	
90th percentile of FT_3	5.10	5.10	
95th percentile of FT_3	5.27	5.20	
97.5th percentile of FT_3	5.64	5.55	

* Data is presented as mean ± SD; ** Median (2.5th–97.5th); *** Median (Min-Max).

MoM values for different percentiles of serum TSH and FT_4 in pregnant women are summarized in ▶ **Table 3.1** and ▶ **Table 3.2**; MoM values of 1st and 99th percentiles for TSH were 0.026 and 4.61 in total sample and in healthy pregnant women were 0.05 and 3.41. MoM values for FT_4 at the 2.5th and 99th percentiles were 0.70 and 1.40 in total sample and in healthy pregnant women were 0.70 and 1.45, respectively.

Discussion

In the present study, we measured concentrations of TSH, FT_4, FT_3, and TPOAb in pregnant women during their first trimester and compared the results with a non-pregnant control group to determine the first trimester reference range of TFTs. A longitudinal and cross-sectional study from China [13] measured TSH concentration in pregnant women with negative TPOAb during their first trimester of gestation. Our results for the 2.5th percentile of TSH in pregnant women with negative TPOAb was similar to their values in the cross-sectional study (0.2 mIU/l vs. 0.19 mIU/l for cross sectional and 0.02 mIU/l for longitudinal studies), while the 97.5th percentile of TSH concentration in our study was higher than their similar percentile in both longitudinal and cross sectional studies (4.60 mIU/l vs. 3.54 mIU/l for cross sectional and 3.65 mIU/l for longitudinal studies).

Previous studies reported the 2.5th and 97.5th percentiles of TSH in Brazilian [21], Swiss [22] and Indian [23] pregnant women during the first trimester as 0.14–3.68 mIU/l, 0.0878–2.829 mIU/l,

▶ **Table 2** Median and 2.5th and 97.5th percentiles of thyroid function test values for participants with positive and negative thyroid peroxidase antibody (TPOAb) in both groups of pregnant and non-pregnant women, including women with and without iodine deficiency.

Variable	Pregnant women		P value	Non-pregnant women		P value
	TPOAb-positive (n = 75)	TPOAb-negative (n = 343)		TPOAb-positive (n = 96)	TPOAb-negative (n = 343)	
TSH						
Median (min–max) mIU/l	1.70 (0.001–9.80)	1.50 (0.01–7.10)	0.049	3.05 (0.006–113)	2.10 (0.008–10.70)	0.001
2.5th percentile	0.09	0.20		0.24	0.50	
97.5th percentile	8.81	4.65		23.54	5.74	
FT4						
Median (min–max) pmol/l	12.8(9.009–28.31)	12.78 (9.009–22.56)	0.03	14.16 (5.15–24.50)	14.16 (9.009–33.50)	0.069
2.5th percentile	9.009	9.009		7.46	10.30	
97.5th percentile	19.303	16.73		18.14	19.30	
FT3						
Median (min–max) pmol/l	4.50 (3.50–10.50)	4.50 (2.30–6.90)	0.232	4.40 (2.20–7.70)	4.50 (2.70–9.80)	0.023
2.5th percentile	3.59	3.46		3.00	3.70	
97.5th percentile	6.18	5.90		5.25	5.54	

▶ **Table 3.1** The serum TSH concentrations and multiples of the median (MoM) values at various percentiles in pregnant women (n = 418), and in the healthy pregnant women (TPOAb-negative and urinary iodine concentration [UIC] > 150 µg/l; n = 185) whose data were used to determine the reference range.

Percentile	Pregnant group * * n = 418		Healthy pregnant group n = 185	
	TSH(mIU/l)	MoM TSH	TSH(mIU/l)	MoM TSH
1st	0.04	0.026	0.081	0.05
2nd *	–	–	–	–
2.5th	0.20	0.133	0.20	0.133
5th	0.30	0.20	0.40	0.266
10th	0.50	0.33	0.60	0.40
50th	1.50	1.00	1.50	1
90th	3.40	2.26	2.85	1.89
95th	4.41	2.93	4.10	2.73
97.5th	5.10	3.40	4.60	3.06
98th	5.55	3.70	4.68	3.12
99th	6.91	4.61	5.13	3.41

* Available data did not permit assignment of values at these percentiles. * * Including those with TPOAb-positivity and/or UIC ≤ 150 µg/l

▶ **Table 3.2** The serum FT_4 concentrations and multiples of the median (MoM) values at various percentiles, in pregnant women (n = 418), and in healthy pregnant women (TPOAb-negative and urinary iodine concentration [UIC] > 150 µg/l; n = 185) whose data were used to determine the reference range.

Percentile	Pregnant group * * (n = 418)		Healthy pregnant group (n = 185)	
	FT_4 (pmol/l)	MoM FT_4	FT_4 (pmol/l)	MoM FT_4
1st *	–	–	–	–
2nd *	–	–	–	–
2.5th	9.00	0.70	9.00	0.70
5th *	–	–	10.30	0.80
10th	10.30	0.80	11.58	0.90
50th	12.87	1.00	12.87	1.00
90th	15.44	1.20	15.44	1.20
95th *	–	–	16.73	1.30
97.5th *	16.73	1.30	–	–
98th *	–	–	18.02	1.40
99th	18.02	1.40	18.66	1.45

* Available data did not permit assignment of values at these percentiles in one or both groups. * * Including those with TPOAb-positivity and/or UIC ≤ 150 µg/l.

0.09–6.65 mIU/l, respectively. Another study [24] defined the 2.5th and 97.5th percentiles of TSH in pregnant women with negative TPOAb at 4–13 weeks of gestation at 0.06–8.3 mIU/l, 0.04–9.3 mIU/l, and 0.12–7.4 mIU/l in United Arab Emirates, other Arab nations, and Asians, respectively.

The results of a large multi-ethnicity population-based cohort study from the Netherlands [25] on Dutch, Turkish, Moroccan, and Surinamese pregnant women showed higher levels of TSH in Dutch women, although it was lower than our findings (0.11–4.18 vs. 0.2–4.60 mIU/l).

The highest values for 2.5th and 97.5th percentiles of TSH concentration in pregnant women have been reported for Arab pregnant women residing in United Arab Emirates [24], and the lowest values have been reported for white Swiss women [22]. Evidence also suggests higher TSH concentration levels in the Middle Eastern and Asian pregnant women, compared to the European [22] and South American [21] pregnant women. These regional discrepancies might also originate from differences such as gestational age at sampling, ethnicity and racial differences of maternal HCG levels [26], genetic characteristics [14], study design [11], assay methods, iodine intake status [27], and inclusion criteria for the determination of reference population and sample size [28]. Our results show slight differences in the 5th and 95th percentile of TSH concentration with previous reports from Tehran, Iran [29, 30] (5th percentile: 0.4 vs. 0.2 mIU/l and 95th percentile: 4.10 vs. 3.9 mIU/l). The similarity of our findings with previous reports [29, 30] from another large region in Iran, suggests that the same reference interval can be implemented for the first trimester of gestation in Iranian pregnant women.

In the present study, 2.5th and 97.5th percentiles of pregnant women with positive TPOAb were 0.190–8.830 mIU/l, higher than that in pregnant women with negative TPOAb 0.01–7.10 mIU/l, consistent with previous studies [9, 31]. Women with positive TPOAb were treated by levothyroxine in Italy, which reduced the negative pregnancy outcomes [32], supporting the negative impact of positive TPOAb on pregnancy. This suggests that women with positive TPOAb should be excluded from the studies that aim to define the reference ranges for TSH concentration [27].

We have shown that the reference range of TSH concentration in the first trimester of pregnancy (0.2–4.60 mIU/l) for Iranian women was lower and narrower than manufacturer's reference values (0.35–5.50 mIU/l); the reference range derived for non-pregnant women was 0.59–5.60 mIU/l.

The reference ranges of TFTs for pregnant and non-pregnant women are incomparable due to the physiological changes during pregnancy. The thyrotrophic effect of HCG is associated with lower serum TSH concentration, especially during early stage of pregnancy [1, 33]. Therefore, the reference ranges for TSH and other TFTs of the general population should not be used to interpret the TFTs during pregnancy. Moreover, our TSH reference range (0.2–4.60 mIU/l) is wider and higher than the ATA recommendation for Americans and Europeans in the first trimester of pregnancy (0.1–2.5 mIU/l) in 2017 [15]. However, recent studies in Asia, India, and the Netherlands, have shown only a modest reduction in the upper reference limit [25, 34–37]. A study from China [35] showed a downward shift in the TSH reference range at 7–12 weeks of gestational age; the upper reference interval was decreased from 5.31 to 4.34 mIU/l.

Previous report [15] showed that both the lower and upper limits of maternal TSH were reduced during pregnancy by about 0.1–0.2 mIU/l and 0.5–1.0 mIU/l respectively, relative to the non-pregnant reference interval of TSH. According to the reference interval of TSH for non-pregnant women, derived from our study (0.59–5.60 mIU/l), the lower and upper limits of reference interval for TSH should change to 0.39–0.49 mIU/l, and 4.60–5.10 mIU/l, respectively, for the first trimester of pregnancy in Iranian population.

In the present study, the 2.5th–97.5th percentile range for FT_4 concentration was determined as 9.0–18.02 pmol/l, which was lower and narrower than that found for non-pregnant women (9.52–19.30 pmol/l) and manufacture's reference values (11.45–22.65 pmol/l). Whereas, the calculated reference ranges for FT_3 concentration in pregnant women (3.40–5.64 pmol/l) was marginally wider than that for non-pregnant women (3.70–5.55 pmol/l); and the reference ranges for FT_3 concentration in pregnant and non-pregnant women were narrower than manufacturer's values (3.1–6.5 pmol/l). Factors such as exclusion criteria, population characteristics, immunometric assay method and iodine sufficiency status might have led to different values of such markers [38].

Previous studies [39–41] suggested the transformation of the results to multiples of median (MoM) in order to unitize different laboratories reports. This method is universally used for antenatal screening of Down syndrome and neural tube defects [41]. MoM is usually used for screening test results, specifically when the results of each test show considerable variations [42].

We reported MoM values of TSH and FT4 concentrations to overcome the effect of maternal weight and gestational age on the hormonal values. The 1st–99th percentiles of TSH MoM were 0.026–4.61 and the 2.5th–99th percentiles of FT_4 MoM were 0.70–1.40.

In the UK and Italian pregnant women with gestational ages less than 16 weeks, the lower and upper limit of TSH MoM (1st–99th percentiles) were 0.02–4.57 and 0.01–4.10, respectively, and their similar percentiles for free thyroxine MoM were 0.75–1.38 and 0.76–1.46, respectively [39]. A study from the USA [41] reported 97.5th percentile of TSH concentration in the first trimester singleton and twin pregnancies as 4.0 and 3.5 MoM, respectively. Based on these results, the upper limit was defined as 2.5 MoM in singleton and twin pregnancies [41]. Our results showed that the upper limit (99th percentile) for TSH concentration at 4.61 MoM covers approximately 96.5 percentile points of TSH concentration, during the first trimester of pregnancy (5th–14th weeks of pregnancy). According to our findings, the upper value for FT_4 MoM in pregnant women was 1.4, which can cover 99 percentile points of FT_4 concentration in the pregnant population.

With regard to the national protocol of maternal care in Iran, TSH is measured in the first prenatal care visit. Based on manufacturer's recommended reference ranges, 7.89 % of women could have been diagnosed with hypo- and hyperthyroidism and 9.75 % with isolated hypothyroxinemia. According to the ATA reference range, 22.78 % of our pregnant women had hypo- or hyperthyroidism and 6 % had isolated hypothyroxinemia, while, by using our determined reference range, only 5.50 % of pregnant women had thyroid dysfunction and none had isolated hypothyroxinemia.

The strength of the present study was the measurement of TPOAb, urine iodine, and determination of thyroid gland size through ultrasound scanning. A combination of inclusion criteria, suggested by National Academy of Clinical Biochemistry (NACB) [43] and the National Health and National Examination Survey (NHANES) [44], were used to define the exclusion criteria. This resulted in a more clear definition of normal population for reference ranges. In addition, each participant was examined separately for thyroid gland scanning and full clinical examination was performed. A major limitation of this study was measuring UIC only once for each participant. Another limitation was the geographical restriction of sampling to the central area of Iran, which restrains the generalization of findings to the whole country.

Conclusions

In the present study, reference ranges of serum TSH, FT_4, and, FT_3 concentrations were determined for singleton pregnant Iranian women with negative TPOAb (TSH: 0.2–4.60 mIU/l, FT_4: 9.0–18.02 pmol/l and FT_3: 3.40–5.64 pmol/l), and non-pregnant women (TSH: 0.59–5.60 mIU/l, FT_4: 9.52–19.30 pmol/l, and FT_3: 3.70–5.55 pmol/l) with adequate level of iodine after being matched for age and gravidity. These values were different from the reference ranges, recommended by the ATA and the reference ranges, determined for non-pregnant women (TSH: 0.70–5.60 mIU/l vs. TSH: 0.35–5.50 mIU/l) in our study. Therefore, we suggest the use of reference ranges obtained from this study for Iranian women, as recommended by guidelines.

Authors' Contributions

All authors were contributed to the design the study. A. A, A. H, and M. F supervised the findings of this work and M. K. and S. S. implementation of the research. A. F. and M. K. analyzed the data. A. A. and M. K. wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of it. All authors are accountable for all aspects of the work. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Notice
This article was changed according to the erratum on August 12, 2021.

Erratum
In the above-mentioned article Fig. 1, Tables 1, 2 and 3 were incorrect. This has now been corrected.