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Maternal Thyroid Function at 11–13 Weeks of Gestation

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Key Words

Thyroid function · Pregnancy · Hypothyroidism · Anti-thyroid antibodies · Thyroid-stimulating hormone · Thyroxine, free · Triiodothyronine, free

Abstract

Objective: To establish normal ranges of maternal serum thyroid-stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) at 11–13 weeks of gestation. ***Methods:*** Maternal serum concentrations of FT3, FT4, TSH, anti-thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies were measured at 11–13 weeks. Normal ranges were constructed from the data of singleton pregnancies with no anti-thyroid antibodies resulting in live births after 34 weeks of phenotypically normal neonates with birth weight above the 5th percentile. Adjustments were made for maternal characteristics found by multiple regression analysis to affect the levels of TSH, FT3 and FT4. ***Results:*** 3,592 of the 4,318 pregnancies examined were antibody negative, and in this group serum TSH increased whereas FT3 and FT4 decreased with gestation, and all three were lower in black than in white women. Serum FT3 and FT4 decreased but TSH did not change significantly with maternal age; TSH and FT3 increased whereas FT4 decreased with body mass index; TSH decreased whereas FT3 and FT4 increased with serum free β-hCG. In the antibody-positive group, compared to the negative group, median TSH was higher and median FT3 and FT4 were lower. ***Conclusion:*** The study established normal ranges for maternal thyroid function at 11–13 weeks.

Introduction

Thyroid disease during pregnancy may be associated with an increased risk of miscarriage, fetal death, preterm delivery and preeclampsia [1–3]. There is also some evidence that subclinical hypothyroidism, defined by an increased serum concentration of thyroid-stimulating hormone (TSH) in the presence of normal levels of thyroxine (T4) and triiodothyronine (T3), is associated with an increased risk for some of these pregnancy complications and adverse neuropsychological development of the child [1–4]. However, there is controversy concerning routine screening for hypothyroidism during pregnancy and treatment of subclinical hypothyroidism [5–9]. The controversy can be resolved by firstly demonstrating that disturbed maternal thyroid function in early pregnancy is indeed associated with specific adverse pregnancy outcomes, and secondly by showing through randomized

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studies that early treatment can improve pregnancy outcome.

Screening for thyroid disease in early pregnancy is hindered by the lack of appropriate reference ranges of thyroid function. Ranges derived from non-pregnant individuals are inappropriate because pregnancy is associated with profound changes affecting thyroid function. Human chorionic gonadotropin (hCG), whose levels increase during the first 10 weeks of pregnancy and subsequently decrease, has thyrotropic properties causing an increase in serum T4 and decrease in TSH [10]. The concentration of thyroid-binding globulins increases with gestation as a result of estrogen stimulation and therefore measurement of the total amount of thyroid hormones does not provide an accurate reflection of active free (F) fraction of these hormones [11, 12]. Previous studies reporting reference ranges of thyroid function in early pregnancy examined a small number of patients, or the gestational range was wide, maternal history of thyroid disease was not recorded, anti-thyroid antibodies were either not measured or patients with such antibodies were not excluded, or they did not examine serum TSH with both FT3 and FT4 [13–27].

The aims of this study are firstly to establish reference ranges of serum TSH, FT3 and FT4 at 11–13 weeks in a large number of singleton pregnancies with no known thyroid disease and in the absence of anti-thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies, and secondly to examine the effect of maternal characteristics and serum anti-TPO, anti-Tg and free β-hCG on the levels of TSH, FT3 and FT4.

Materials and Methods

This was a prospective screening study for adverse obstetric outcomes in women attending for their routine first hospital visit in pregnancy. In this visit, which is held at 11^{+0}–13^{+6} weeks of gestation, we recorded maternal characteristics and performed an ultrasound scan to confirm gestational age from the measurement of the fetal crown-rump length, to diagnose any major fetal abnormalities, and to measure fetal nuchal translucency thickness and maternal serum free β-hCG and pregnancy-associated plasma protein-A (PAPP-A) as part of screening for chromosomal abnormalities [28, 29]. Additionally, blood was collected for research and the separated plasma and serum were stored at –80°C for subsequent biochemical analysis. Written informed consent was obtained from the women agreeing to participate in the study, which was approved by the King's College Hospital Ethics Committee.

Maternal characteristics recorded were age, racial origin (White, Black, South Asian, East Asian and mixed) and method of conception (spontaneous or assisted conception requiring the use of ovulation drugs). The maternal weight and height were measured and the body mass index (BMI) was calculated in kg/m^2. Maternal serum PAPP-A and free β-hCG were measured using the Delfia Express analyzer (PerkinElmer, Waltham, Mass., USA) and the measured concentration was converted to multiples of the expected normal median (MoM) as previously described [29].

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women.

Study Population

During the study period (March 2006 to December 2006) we examined 4,852 singleton pregnancies with a live fetus at 11^{+0}–13^{+6} weeks. Included in the study were 4,318 pregnancies resulting in live birth of phenotypically normal neonates. We excluded 69 because the mothers reported that they had hypothyroidism or hyperthyroidism, 44 because there were major fetal abnormalities, 87 because the pregnancies resulted in miscarriage or fetal death, 91 because they developed preeclampsia, 49 because delivery occurred before 34 weeks, and 194 because the birth weight was less than the 5th percentile.

Sample Analysis

The maternal serum concentrations of FT3, FT4, TSH, anti-TPO and anti-Tg were measured by immunoassay using direct, chemiluminometric technology (Siemens Advia Centaur assays, Siemens Healthcare Diagnostics Ltd., Surrey, UK). The minimum detectable concentrations of FT3, FT4, TSH, anti-TPO and anti-Tg were 0.3 pmol/l, 1.3 pmol/l, 0.003 mIU/l, 15 and 30 U/ml, respectively. The intra-assay coefficients of variation were 3.08, 2.35 and 2.47% at FT3 concentrations of 2.9, 6.6 and 14.2 pmol/l, respectively; 4.69, 2.31 and 2.22% at FT4 concentrations of 6.1, 13.9 and 39.9 pmol/l, respectively; 2,48, 2.44 and 2.41% at TSH concentrations of 0.74, 5.65 and 18.98 mIU/l, respectively; 7.93, 4.54 and 6.26% at anti-TPO concentrations of 1.70, 10.01, 14.95 U/ml, respectively, and 5.5 and 2.9% at anti-Tg concentrations of 62 and 333 U/ml, respectively. If the serum concentration of anti-TPO and anti-Tg was <60 U/ml, which was the manufacturer's reference limit, the patients were considered to be antibody negative.

Statistical Analysis

The characteristics of the antibody-positive and -negative groups were compared by the Mann-Whitney test for continuous variables and Fisher's exact test or χ^2 test for categorical variables. In the antibody-negative group, serum TSH, FT3 and FT4 were logarithmically transformed. However, $\log_{10}$ TSH remained negatively skewed, therefore square root transformation was applied. Multiple regression analysis was then used to determine if gestational age at screening, maternal age, BMI, racial origin and method of conception were significant predictors of square root TSH, $\log_{10}$ FT3, $\log_{10}$ FT4. The observed values of TSH, FT3 and FT4 were then expressed as MoM. Regression analysis was also used to determine the significance of the inter-relations between serum TSH, FT3 and FT4 and free β-hCG. Comparison of TSH MoM, FT3 MoM and FT4 MoM between the antibody-positive and antibody-negative groups was done by the Kruskal-Wallis test with post hoc Bonferroni correction (critical statistical significance $p < 0.0167$). The proportion of cases with serum TSH above the 97.5th percentile and serum FT3 and FT4 below the

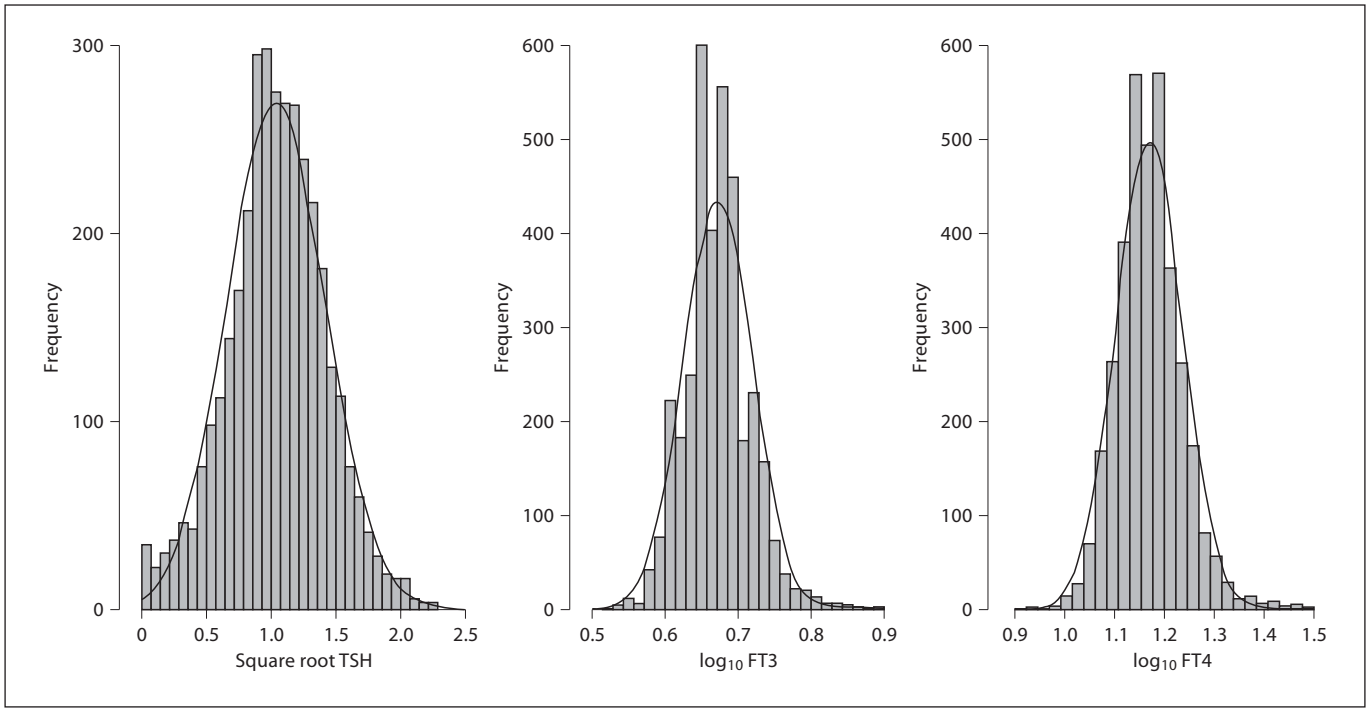

Fig. 1. Frequency distribution of square root TSH, $\log_{10}$ FT3 and $\log_{10}$ FT4.

2.5th percentile in the antibody-positive and -negative groups were compared using the χ^2 test with post hoc Bonferroni correction.

The statistical software package SPSS 16.0 (SPSS Inc., Chicago, Ill., USA), Medcalc for Windows, version 9.6.2.0 (MedCalc Software, Mariakerke, Belgium) and XLSTAT-Pro 2008 (Addinsoft, USA) were used for data analyses.

Results

In 3,592 of the 4,318 pregnancies examined the serum concentration of anti-TPO and anti-Tg was <60 U/ml and in 726 (16.8%) the concentration of one or both antibodies was 60 U/ml or more. The patient characteristics of the antibody-negative and antibody-positive groups are compared in table 1. In the antibody-positive group the mean maternal age was increased and there was a higher proportion of white and South Asian women.

Reference Range of Serum FT3, FT4 and TSH

In the antibody-negative group the distribution of square root TSH, $\log_{10}$ FT3 and $\log_{10}$ FT4 approximated a Gaussian normality (fig. 1). Multiple regression analysis demonstrated that there were significant contributions to the level of TSH, FT3 and FT4 from maternal characteristics (table 2). Serum TSH increased whereas FT3 and FT4 decreased with gestational age and all three were lower in black than in white women (fig. 2). Serum FT3 and FT4 decreased but TSH did not change significantly with maternal age. Serum TSH and FT3 increased whereas FT4 decreased with BMI. The 50th, 95th, 97.5th, 5th and 2.5th percentiles of serum TSH, FT3 and FT4 are shown in table 3.

There were significant associations between TSH MoM and FT4 MoM ($r = -0.176$, $p < 0.0001$) and FT3 MoM ($r = -0.107$, $p < 0.0001$) and between FT3 MoM and FT4 MoM ($r = 0.547$, $p < 0.0001$). There were significant associations between free β-hCG MoM and TSH MoM ($r = -0.156$, $p < 0.0001$), FT3 MoM ($r = 0.135$, $p < 0.0001$) and FT4 MoM ($r = 0.134$, $p < 0.0001$).

Serum TSH, FT3 and FT4 in the Antibody-Positive Group

In 726 (16.8%) of the 4,318 pregnancies the concentration of one or both anti-TPO and anti-Tg was 60 U/ml or more. In 308 (7.1%) both antibodies were positive, in 133 (3.1%) only anti-TPO was positive and in 285 (6.6%) only anti-Tg was positive. The prevalence of antibody positivity was higher in white (582 of 3,125, 18.6%) than black women (51 of 759, 6.7%; $p < 0.0001$).

Table 1. Comparison of maternal characteristics in the antibody-negative and -positive groups

Maternal characteristics	Antibody negative (n = 3,592)	Antibody positive (n = 726)
Median maternal age, years (IQR)	32.2 (27.9–36.0)	33.2 (29.3–36.7)*
Median body mass index (IQR)	24.7 (22.2–27.9)	24.5 (22.3–28.2)
Median crown-rump length, mm (IQR)	63.5 (59.0–68.7)	63.6 (58.9–68.8)
Racial origin		
White, n (%)	2,543 (70.8)	582 (80.2)*
Black, n (%)	708 (19.7)	52 (7.0)*
South Asian, n (%)	148 (4.1)	63 (8.7)*
East Asian, n (%)	57 (1.6)	13 (1.8)
Mixed, n (%)	136 (3.8)	17 (2.3)
Conception		
Spontaneous, n (%)	3,491 (97.2)	699 (96.3)
Ovulation drugs, n (%)	101 (2.8)	27 (3.7)

IQR = Interquartile range.
* Comparisons by χ^2 test with post hoc Bonferroni correction for categorical variables ($p < 0.0167$) and by Mann-Whitney test for continuous variables ($p < 0.05$).

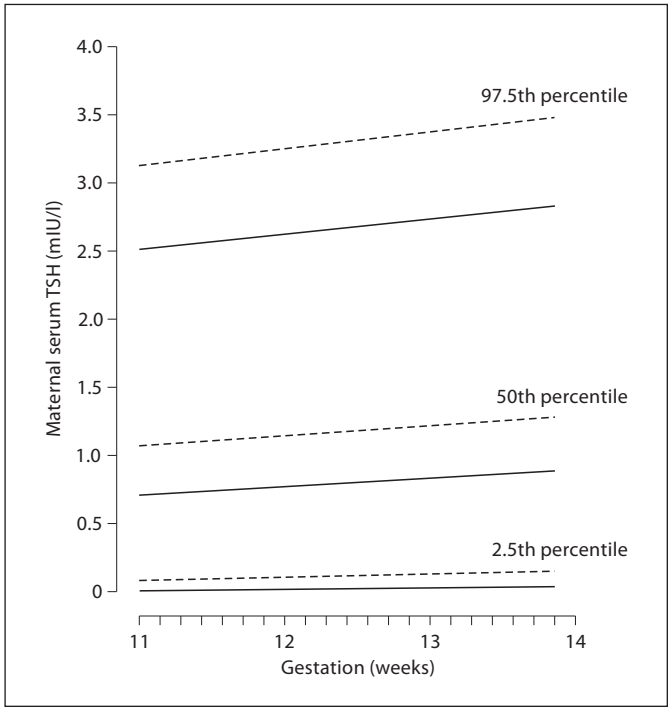

Fig. 2. Reference range of maternal serum TSH with gestational age in white (– – – –) and black (——) women.

Table 2. Contribution of maternal and fetal characteristics to square root TSH, $\log_{10}$ FT4 and $\log_{10}$ FT3 demonstrated by multiple regression analysis

Characteristics	Coefficient	Standard error	p value
Square root TSH			
Gestational age, weeks	0.034864	0.012	0.0042
Body mass index	0.002811	0.001	0.0002
Black racial origin	–0.182494	0.016	<0.0001
Asian racial origin	–0.133563	0.032	<0.0001
Oriental racial origin	–0.162253	0.050	0.0013
$\log_{10}$ FT4			
Gestational age, weeks	–0.006395	0.002	0.0026
Maternal age, years	–0.000518	0.0002	0.005
Body mass index	–0.001280	0.0002	<0.0001
Black racial origin	–0.010828	0.003	<0.0001
Asian racial origin	0.011146	0.004	<0.0001
Oriental racial origin	0.018198	0.009	0.038
$\log_{10}$ FT3			
Gestational age, weeks	–0.004332	0.002	0.032
Maternal age, years	–0.001165	0.0001	<0.0001
Body mass index	0.001138	0.0002	<0.0001
Black racial origin	–0.009081	0.002	<0.0001

In the antibody-positive group, compared to the antibody-negative group, the median TSH was higher and the median FT3 and FT4 were lower (table 4). Serum TSH was above the 97.5th percentile in 2.5% of the antibody-negative group and increased to 5.3% (3 of 57) in the group with anti-TPO of 60–100 IU/ml, 15.1% (28 of 186) in the group with anti-TPO of 101–500 IU/ml and 31.3% (62 of 198) in the group with anti-TPO of >500 IU/ml. The respective values in the anti-Tg group were 10.4% (27 of 259), 21.1% (64 of 303) and 32.3% (10 of 31).

Table 3. Maternal serum concentration of TSH, FT4 and FT3 at 11–13 weeks

Race	GA weeks	BMI	TSH, mIU/l					Age years	FT4, pmol/l					FT3, pmol/l				
			2.5th	5th	50th	95th	97.5th		2.5th	5th	50th	95th	97.5th	2.5th	5th	50th	95th	97.5th
White	11	<25	0.08	0.16	1.05	2.69	3.09	<30	11.64	12.21	15.64	20.04	21.02	3.90	4.04	4.82	5.75	5.95
								>30	11.53	12.09	15.49	19.85	20.82	3.82	3.95	4.72	5.63	5.82
		>25	0.09	0.18	1.08	2.75	3.15	<30	11.44	11.99	15.37	19.69	20.65	3.96	4.10	4.89	5.84	6.04
								>30	11.33	11.88	15.22	19.51	20.46	3.88	4.01	4.79	5.72	5.92
	12	<25	0.10	0.19	1.12	2.81	3.22	<30	11.47	12.03	15.41	19.75	20.71	3.86	4.00	4.77	5.69	5.89
								>30	11.36	11.92	15.27	19.56	20.52	3.78	3.91	4.67	5.57	5.77
		>25	0.11	0.21	1.15	2.86	3.28	<30	11.27	11.82	15.14	19.41	20.35	3.92	4.06	4.85	5.78	5.98
								>30	11.16	11.71	15.00	19.22	20.16	3.84	3.97	4.74	5.66	5.86
	13	<25	0.13	0.23	1.19	2.93	3.34	<30	11.30	11.85	15.19	19.46	20.41	3.82	3.96	4.72	5.64	5.83
								>30	11.20	11.74	15.05	19.28	20.22	3.74	3.87	4.62	5.52	5.71
		>25	0.14	0.24	1.23	2.98	3.41	<30	11.11	11.65	14.92	19.12	20.05	3.88	4.02	4.80	5.73	5.92
								>30	11.00	11.54	14.78	18.94	19.86	3.80	3.93	4.70	5.60	5.80
Black	11	<25	0.01	0.05	0.71	2.13	2.49	<30	11.36	11.91	15.26	19.55	20.50	3.82	3.95	4.72	5.63	5.83
								>30	11.25	11.79	15.11	19.37	20.31	3.74	3.87	4.62	5.51	5.70
		>25	0.01	0.06	0.73	2.18	2.54	<30	11.16	11.70	14.99	19.21	20.14	3.88	4.01	4.79	5.72	5.92
								>30	11.05	11.59	14.85	19.03	19.95	3.80	3.93	4.69	5.60	5.79
	12	<25	0.02	0.07	0.77	2.23	2.60	<30	11.19	11.73	15.04	19.27	20.20	3.78	3.91	4.67	5.58	5.77
								>30	11.08	11.62	14.89	19.08	20.01	3.70	3.83	4.57	5.46	5.65
		>25	0.02	0.08	0.80	2.28	2.65	<30	10.99	11.53	14.77	18.93	19.85	3.84	3.98	4.75	5.66	5.86
								>30	10.89	11.42	14.63	18.75	19.66	3.76	3.89	4.64	5.54	5.74
	13	<25	0.03	0.09	0.83	2.33	2.71	<30	11.03	11.56	14.82	18.98	19.91	3.75	3.87	4.62	5.52	5.71
								>30	10.92	11.45	14.67	18.80	19.72	3.67	3.79	4.53	5.40	5.59
		>25	0.04	0.10	0.86	2.39	2.77	<30	10.83	11.36	14.56	18.65	19.56	3.80	3.94	4.70	5.61	5.80
								>30	10.73	11.25	14.42	18.47	19.37	3.72	3.85	4.60	5.49	5.68

GA = Gestational age.

Table 4. Comparison of the antibody-positive and antibody-negative groups for median TSH, FT3 and FT4 and proportion of cases with TSH above the 97.5th percentile of the reference range and FT3 and FT4 below the respective 2.5th percentile

Thyroid function	Antibody negative (n = 3,592)	Antibody positive		
		anti-TPO only (n = 3)	anti-Tg only (n = 5)	both (n = 308)
Serum TSH				
Median MoM	1.01	1.53*	1.30*	1.80*
>97.5th percentile, n (%)	89 (2.5%)	17 (12.8%)*	24 (8.4%)*	76 (24.7%)*
Serum FT4				
Median MoM	0.99	0.98	1.01	0.96*
<2.5th percentile, n (%)	89 (2.5%)	5 (3.8%)	9 (3.2%)	14 (4.5%)
Serum FT3				
Median MoM	0.99	0.98*	0.98	0.97*
<2.5th percentile, n (%)	89 (2.5%)	9 (6.8%)*	14 (4.9%)	17 (5.5%)*

Comparisons between each antibody-positive group with the antibody-negative group by χ^2 test with post hoc Bonferroni correction for categorical variables and by Kruskal-Wallis with post hoc Bonferroni correction for continuous variables.

* $p < 0.0167$.

Table 5. Summary of previous studies reporting on thyroid function in pregnancy

Author	n	Gestation	Ethnic and/or racial origin	Assay	TSH mIU/l	FT4 pmol/l	FT3 pmol/l
Smith and Bold [13], 1983	56	4–11 weeks	UK	Amersham International	4.9 (2.7–7.1)	15.2 (11.9–18.5)	
Chan and Swaminathan [14], 1988	25	1st trimester	China	Abbot Diagnostics	0.7 (0–1.6)	13.7 (8.6–18.8)	3.9 (2.2–5.6)
Leylek et al. [15], 1996	20	<13 weeks	Turkey	Immulite 2000	2.4 (0.4–4.4)	32.3 (19.4–45.2)	3.4 (1.9–4.9)
Panesar et al. [16], 2001	55	11 weeks	China	Chiron Diagnostics	0.8 (0.03–2.3)	16.2 (11.1–22.9)	4.0 (3–5.7)
Haddow et al. [17], 2004	1,005[a]	8–13 weeks	USA: mainly White	Immulite 2000	0.94 (0–3.1)	–	–
Kurioka et al. [18], 2005	119	<14 weeks	Japan	Roche Diagnostics	1.1 (0–3.0)	18.1 (12.9–23.2)	5.5 (4.0–7.1)
Dashe et al. [19], 2005	2,326	11–13 weeks	USA: 84% Hispanic, 12% Black	Immulite 2000	0.8 (0.01–3.7)	–	–
Stricker et al. [20], 2007	575[b]	7–12 weeks	Switzerland	Abbot Diagnostics	0.95 (0.07–2.8)	13.9 (10.5–18.5)	4.7 (3.5–6.3)
Casey et al.[21], 2007	17,298	6–20 weeks	USA: 86% Hispanic, 10% Black	Immulite 2000	– (0.08–3.0)	– (11.6–24.5)	
Cotzias et al. [22], 2008	307 at 6–40 weeks	1st trimester	UK: 45% White, 36% South Asian	Bayer Diagnostics	– (0–5.5)	– (10.0–16.0)	– (3.0–7.0)
Gilbert et al. [24], 2008	1,817[b]	9–13 weeks	Australia	Abbot Diagnostics	0.7 (0.02–2.2)	13.5 (10.4–17.8)	4.4 (3.3–5.7)
Lambert-Messerlian et al. [23], 2008	8,351[b]	11–13 weeks	USA: mainly White	Immulite 2000	1.0 (0–3.0)	14.2 (10.3–18.4)	
McElduff and Morris [25], 2008	218[a]	10–14 weeks	Australia	Immulite 2000	0.8 (0–1.8)	15.7 (10.4–21.0)	5.5 (3.0–8.1)
Marwaha et al. [26], 2008	107	1st trimester	India	Roche Diagnostics	2.1 (0.3–5.6)	14.5 (11.5–20.1)	4.4 (1.4–6.1)
Pearce et al. [27], 2008	585[a]	5–13 weeks	USA: 77% White, 10% Black	Bayer Diagnostics	1.1 (0.04–3.6)	–	–

The values are medians or means with reported or estimated 95% confidence intervals.
[a] Anti-TPO-positive excluded; [b] anti-TPO- and/or anti-Tg-positive excluded.

Discussion

This study has established normal ranges of maternal serum TSH, FT3 and FT4 at 11–13 weeks of gestation. We excluded pregnancies complicated by miscarriage or fetal death, fetal growth restriction, preeclampsia and preterm delivery because of the reported association between these pregnancy complications and clinical or subclinical hypothyroidism [1–3]. We also excluded pregnancies with known thyroid disease and those with anti-thyroid antibodies. We chose 11–13 weeks because this is the gestational age at which pregnant women attend maternity units for their first antenatal visit. At this visit an ultrasound scan is carried out to determine the number of fetuses, confirm the gestation, exclude major defects and measure the fetal nuchal translucency thickness which in combination with maternal serum free β-hCG and PAPP-A is used for effective screening of aneuploidies. Consequently, this is the likely gestational age for screening for thyroid disease in pregnancy should such screening be accepted as a necessary part of routine antenatal care because it would be important to identify and treat hypothyroidism as early in pregnancy as possible.

Multiple regression analysis demonstrated that in our anti-thyroid antibody-negative normal pregnancies maternal characteristics and gestational age affect the serum concentrations of TSH, FT3 and FT4. Consequently, in establishing normal ranges we made adjustments for these factors by using the same MoM approach as in the analysis of other metabolites, such as serum free β-hCG [29]. Previous studies on maternal thyroid function in pregnancy have not made such adjustments and the observed differences in reported results (table 5) may be a consequence of differences in maternal characteristics of the study populations, such as racial origin, age and BMI. Other possible factors contributing to the differences in results are the inclusion of patients with or without anti-thyroid antibodies, gestational age distribution of the pregnancies and reagents used for the assays.

Serum TSH increased and FT3 and FT4 decreased with gestational age within the narrow range of 11–13 weeks, and this is likely to be the consequence of the

thyrotropic properties of hCG whose concentration decreases with gestation. The finding that serum FT3 and FT4 decrease with maternal age suggests that the function of the thyroid gland declines with age. A large study in non-pregnant individuals reported an age-related increase in both the mean serum TSH concentration and in the percentage of people with high serum TSH concentration (>4.5 mIU/l) [30]. The finding that serum TSH increases and FT4 decreases with BMI is compatible with the association between clinical and subclinical hypothyroidism with increased insulin resistance and the metabolic syndrome [31, 32]. We cannot offer an explanation for the finding that FT3 increases with BMI.

In black women the serum concentration of both TSH and the thyroid hormones is lower than in white women. The results suggest that the pituitary-hypothalamus-thyroid gland axis in Blacks is set at a different level than in whites but the underlying mechanism is uncertain. The finding of lower serum TSH in Blacks compared to Whites has also been reported in previous studies in both pregnant women and in non-pregnant individuals [30, 33].

In about 10% of our population there were detectable anti-TPO antibodies and this prevalence is similar to the 5–15% rate reported in previous studies in the first trimester of pregnancy [17, 20, 23, 25–27]. In 14% of our population there were anti-Tg antibodies and this prevalence is higher than the 3–9% rate reported in previous studies [23, 25, 26]. The finding of lower antibody positivity in Blacks compared to Whites has also been reported in previous studies in both pregnant women and non-pregnant individuals [30, 33]. In the antibody-positive group compared to the antibody-negative group, the median TSH was higher and the median FT3 and FT4 were lower. This effect was observed for both anti-TPO and anti-Tg antibodies in contrast to a report in non-pregnant individuals that anti-Tg antibodies in the absence of anti-TPO do not affect thyroid function [30]. In the antibody-positive group the percentage of cases with TSH values above the 97.5th percentile increased with the serum antibody concentration. A previous study reported that the majority of antibody-positive women with subclinical hypothyroidism during pregnancy will develop clinical hypothyroidism within the subsequent 10 years [4]. Consequently, in establishing normal ranges of thyroid function it is necessary to exclude antibody-positive patients.

Conclusion

The study established normal ranges for maternal thyroid function at 11–13 weeks after adjustment for maternal characteristics which affect the measured serum concentrations of TSH, FT3 and FT4. These ranges will form the basis for the study of thyroid function in pathological pregnancies and the investigation of the consequences of subclinical hypothyroidism.

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