Thyroid Testing during Pregnancy at an Academic Boston Area Medical Center

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Context: Gestational hypothyroidism leads to adverse obstetric outcomes and intellectual impairment in offspring. Pregnancy thyroid screening is controversial.

Objective: Our objective was to determine thyroid function testing and thyroid dysfunction rates in pregnant women at Boston Medical Center (BMC).

Methods: We retrospectively enrolled 1000 pregnant women aged 18–46 yr seen in BMC's Obstetrics/Gynecology (OB/GYN) or Family Medicine (FM) Clinics for their initial prenatal visit during 2008. Age, race, insurance, gestational age (GA), medical history (thyroid or other autoimmune disorders), obstetric history, and thyroid function tests were ascertained.

Results: A total of 983 women were included (17 excluded for coding error). Median maternal age was 28 yr and GA 9.4 wk. Thyroid testing rates were similar in the 918 (93%) followed by OB/GYN and 65 (7%) followed by FM (84 *vs.* 86%). Thirty-nine women had previous thyroid disease, of whom 19 took thyroid medications. Four had type 1 diabetes, and nine had other autoimmune diseases. Serum TSH was obtained in 832 women (84.6%) at median GA 9.7 wk (range, 0.1–39.7). The majority were tested during their first trimester (65.5%). Of the 832 tested, 56 (6.7%) had trimester-specific elevated TSH, of whom nine had a previous history of thyroid disease, two had type 1 diabetes, and one had dyschromia. Based on current case-finding guidelines, 45 of 56 women (80.4%) with an elevated TSH in pregnancy might not have been tested.

Conclusion: BMC has a high rate of thyroid function testing in pregnancy. Targeted thyroid testing in only high-risk patients would have missed 80.4% of pregnant women with hypothyroidism. **(*J Clin Endocrinol Metab* 96: E1452–E1456, 2011)**

The prevalence of hypothyroidism during pregnancy in the United States is estimated at approximately 2–3%, of which most (2–2.5%) is subclinical (1, 2). Some studies suggest that undetected and untreated subclinical hypothyroidism leads to maternal and fetal risks (1) and leads to intellectual impairment in the offspring (3–5). However, others have not found adverse obstetrical outcomes in subclinically hypothyroid pregnant women (6, 7). In a single study, L-T_4 therapy for subclinically hypothyroid pregnant women did not affect intellectual development of their offspring (8).

Currently, the need for universal thyroid screening in pregnant women is controversial. The 2002 practice guidelines from the American College of Obstetricians and Gynecologists (ACOG) recommend thyroid testing only in high-risk pregnant women who are symptomatic or have a personal history of thyroid disorders, personal history of type 1 diabetes, or other autoimmune disorders (9). The ACOG guidelines do not recommend testing in asymptomatic women or women with small goiters. The Endocrine Society recommends case finding in pregnant women or those who wish to become pregnant if they have symptoms or physical exam findings suggestive of a goiter or hypothyroidism, a history of type 1 diabetes, a personal or family history of thyroid disease, a personal history of

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Abbreviations: FM, Family Medicine; GA, gestational age; OB/GYN, Obstetrics/Gynecology.

autoimmune disorder, recurrent miscarriages or infertility, or previous head or neck irradiation (10). The American Association of Clinical Endocrinologists (AACE) recommends routine thyroid function screening before pregnancy for all patients who wish to become pregnant or during their first trimester (11).

A recent study examined the efficacy of targeted high-risk case finding in identifying women with thyroid dysfunction during early pregnancy (12). In addition to screening blood tests, a detailed questionnaire was used to screen for personal or family history of thyroid and autoimmune disorders and current or past thyroid treatments. Of these women, 2.6% had a TSH greater than 4.2 mIU/liter, and the prevalence was higher in the high-risk *vs*. the low-risk group. However, 30% of the women with an elevated TSH were in the low-risk population, suggesting that current case-finding guidelines would miss about one third of pregnant women with hypothyroidism. Recent studies also suggest conflicting guidelines can lead to variability in testing rates among practitioners (13, 14).

The purpose of the present study was to examine current rates of thyroid function testing and thyroid dysfunction in pregnant women at Boston Medical Center (BMC).

Subjects and Methods

The Boston University Medical Campus Institutional Review Board Committee approved this study for Institutional Review Board exemption. We conducted a retrospective study of 1000 consecutive pregnant women between the ages of 18–46 yr old who presented to BMC's Obstetrics/Gynecology (OB/GYN) or Family Medicine (FM) clinics for their initial prenatal visit during 2008. Women were excluded if they were under 18 yr of age or if the visit was improperly coded.

We collected demographic data (including age, race, and insurance), pregnancy history (preterm delivery and abortions), medical history (including thyroid medications, history of thyroid disease, and/or autoimmune disorders), and serum TSH values. Gestational age (GA) at the first visit was estimated from the time of last menses or from ultrasound dating when available. Serum TSH levels were measured by a chemiluminescence assay (Centaur; Bayer, Fernwald, Germany; normal range, 0.35–5.50 mIU/liter). We used trimester-specific ranges for our analyses, with a reference range of 0.1–2.5 mIU/liter in the first trimester and 0.1–3 mIU/liter in the second and third trimesters (10).

Results

Demographic data

One thousand patient charts were evaluated, but 17 were excluded due to miscoding. Of the 983 women in the study, the median maternal age was 28 yr and the median gestational age was 9.4 wk (Table 1). The women were predominantly minorities and from socioeconomically disadvantaged backgrounds.

TABLE 1. Demographic characteristics of the patients studied

	Range (median)	n (%)	Rate of testing (%)
Age			
Maternal age (yr)	18–46 (28)		
Gestational age (wk)	0–41.1 (9.4)		
Race			
African-Americans		560 (57)	
Caucasians		218 (22)	
Hispanics		133 (14)	
Asians		50 (5)	
Others		22 (2)	
Insurance			
Medicaid		596 (61)	
Private		269 (27)	
Free care		98 (10)	
Medicare		12 (1)	
Jails		8 (1)	
Clinic visits			
OB/GYN		918 (93)	84
FM		65 (7)	86
Gravida			
One		283 (29)	
Two		276 (28)	
Three		176 (18)	
Four		117 (12)	
Five		62 (6)	
Six or more		68 (7)	

Ninety-three percent of the women were seen in OB/GYN clinics for their prenatal care and only 7% in FM (Table 1). However, the rate of thyroid testing was similar in both clinics, 84 and 86%, respectively. Approximately one third (29%) of the women were prima gravida (Table 1).

Medical history

Thirty-nine women had a history of thyroid disease, of whom 20 had hypothyroidism, nine had hyperthyroidism, seven had goiters/thyromegaly, and three had solitary thyroid nodules (Table 2). Eighteen of the 20 hypothyroid women were on thyroid replacement therapy. Only one hyperthyroid woman was on antithyroid medication (propylthiouracil).

Thirteen women had a known history of autoimmune disease, of whom four had type 1 diabetes and nine had a personal history of another autoimmune disease (including one dyschromia, one myasthenia gravis, one polymyositis, one systemic lupus erythematosus, two rheumatoid arthritis, and three melasma) (Table 2).

Thyroid function testing

Of the 983 women in the study, 832 (84.6%) had a serum TSH obtained at a median gestational age of 9.7

TABLE 2. Summary of thyroid testing in the patient population evaluated

	n	TSH obtained (n)	GA [wk (range)]	TSH range (n) <0.1	0.1–2.49[a] (0.1–2.99)	2.5–5.49[a] (3.0–5.45)	>5.5
Thyroid disease							
Hypothyroidism	20	18	9.4 (0.8–37.0)				
Hyperthyroidism	9	8	11.0 (5.4–26.9)				
Goiter/thyromegaly	7	7	9.5 (6.4–14.0)				
Nodule	3	3	5.7 (5.6–10.9)				
Total	39	36	9.9 (0.8–37.0)				
Medications							
Thyroid replacement	18	17	8.4 (0.8–33.6)				
Antithyroid	1	1	5.4				
Total	19	18	7.9 (0.8–33.6)				
Autoimmune disease							
Type 1 diabetes	4	4	8.3 (7.4–11.9)				
Other	9	9	10.0 (5.7–26.7)				
Total	13	13	8.9 (5.7–26.7)				
Trimester							
First		545	≤11.9	28	476	36	5
Second		185	12–23.9	7	169	7	1
Third		103	≥24	1	95	6	1

[a] Values are for first trimester with values for second and third trimesters in *parentheses*.

wk (range 0.1–39.7). The majority of women (65.5%, 545 of 832) had a serum TSH during their first trimester (Table 2).

All thirteen women (100%) with a personal history of autoimmune disease had a serum TSH at a median GA of 8.9 wk (Table 2), including four women with type 1 diabetes (median GA 8.3 wk) and nine women with other autoimmune diseases (median GA 10.4 wk).

Thirty-six of the 39 women (92.3%) with a personal history of thyroid disease had a serum TSH at a median GA of 9.9 wk, including 18 of 20 known hypothyroid women (90%, median GA 9.4 wk) and eight of nine known hyperthyroid women (88.9%, median GA 11.0 wk) (Table 2). Serum TSH was obtained in 94.4% (17 of 18) of the women on thyroid hormone replacement at a median GA of 8.4 wk (range 0.8–33.6) (Table 2). Three of these women presented in late pregnancy (GA of 29.4, 31.3, and 33.6 wk) for their first prenatal visit at BMC.

Of the 832 women who had a TSH, 545 women (65.5%) were tested during the first trimester, 184 (22.1%) during the second trimester, and 103 (12.4%) during the third trimester (Table 2). Based on trimester-specific reference ranges, 56 of the 932 women in the study (5.7%) had an elevated TSH in pregnancy. Of these 56 women with an elevated TSH, nine had a history of thyroid disease (seven hypothyroid, one thyromegaly and one thyroid nodule), two had a history of type 1 diabetes, and one had a history of dyschromia. Based on current Endocrine Society case-finding guidelines, only these 11 women with an elevated TSH would have undergone thyroid testing in pregnancy (one patient had a history of both hypothyroidism and dyschromia). The other 80.4% of women with an elevated TSH in pregnancy would not have been tested, assuming they were asymptomatic and did not have a palpable goiter.

Discussion

Our study of the rate of thyroid testing in pregnant women at BMC found that 80.4% of pregnant women with TSH elevation would have been missed based on current high-risk screening guidelines, compared with approximately 30% in a similar study by Vaidya *et al.* (12). The patients in the present study were predominantly from minority and socioeconomically disadvantaged backgrounds. Furthermore, there was a high rate of thyroid testing during pregnancy (84.6%), much greater than previously published reports (13, 14). Most thyroid testing was performed during the first trimester, a time when some have suggested that early detection and therapy may lead to improved outcomes (11, 15).

Thyroid hormone is essential for neurodevelopment, which occurs during fetal life and early infancy. The fetal brain develops during the first trimester when the fetal thyroid is not yet functioning, and the fetus is therefore entirely dependent on maternal thyroid hormone crossing the placenta. In addition, thyroid hormone deficiency in the newborn may lead to permanent cognitive, neurological, and developmental abnormalities if not recognized and treated promptly (3–5, 16).

Subclinical hypothyroidism in pregnancy has been shown to result in adverse outcomes including maternal anemia, myopathy, congestive heart failure, gestational hypertension and preeclampsia, placental abnormalities, low birth weight, fetal death and postpartum hemorrhage (1, 17–19), although others have not found adverse pregnancy outcomes (6, 7). Mild symptoms of hypothyroidism might be attributed to pregnancy and, therefore, subclinical hypothyroidism may not be diagnosed during early pregnancy. Some studies have shown increased intellectual impairment in children born to women with untreated subclinical hypothyroidism or hypothyroxinemia during pregnancy (3–5, 20).

In view of the conflicting results regarding the adverse effects of subclinical hypothyroidism on pregnancy outcomes and the dearth of data on whether L-T_4 therapy in subclinical hypothyroid pregnant women improves pregnancy outcomes and childhood development, screening for thyroid dysfunction in first-trimester pregnant women has been controversial. The 2002 ACOG (9) and 2007 Endocrine Society Guidelines (10) have recommended case finding, whereas AACE (11) proposed that first-trimester pregnant women should be screened for thyroid dysfunction. New guidelines from the Endocrine Society and American Thyroid Association are currently under development.

Except for one L-T_4 intervention study demonstrating improved pregnancy outcomes in subclinically hypothyroid women (15), there is currently no evidence that L-T_4 therapy would indeed improve pregnancy outcomes. Only one study to date has prospectively analyzed the effect of placebo *vs.* L-T_4 therapy in mild thyroid failure during pregnancy on offspring IQ. In preliminary analyses, the Controlled Antenatal Thyroid Screening Study (CATS) has found that L-T_4 therapy of hypothyroid pregnant women beginning in the first trimester did not affect the IQ of their 3-yr-old offspring (8). However, L-T_4 treatment was not initiated until a mean of 12.5 wk of gestation, which may be too late to affect infant neurodevelopment. A National Institutes of Health multicenter study is ongoing to address a similar question.

There are inherent limitations to our study due to the fact that this was a retrospective chart review. We were dependent on accurate physician charting and coding. We were not able to access the patients' family histories, and we did not have information about whether the women were symptomatic at presentation, both being criteria for case finding in current guidelines. If a patient had thyroid testing from an outside provider before her referral to BMC for prenatal care, we were unable to access those results through our database.

In conclusion, this study showed a high rate of thyroid testing in pregnancy and a high rate of thyroid hypofunction in our patient population. This was a serendipitous finding because there has been no formal discussion to date between the Section of Endocrinology, Diabetes, and Nutrition and the Departments of OB/GYN or FM on how or when to conduct thyroid screening in pregnancy. We have a large thyroid group at this academic institution, which may have increased awareness among the practitioners at BMC. We believe these observational results support universal screening in pregnancy. However, such screening cannot be advocated in the absence of data showing that L-T_4 treatment improves outcomes.

Thus, the question of whether to test remains controversial. However, if thyroid testing is carried out in first-trimester women, the recommendation to only obtain targeted thyroid testing early in pregnancy may not be advisable because many pregnant women who have subclinical hypothyroidism would be missed.

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