National Status of Testing for Hypothyroidism during Pregnancy and Postpartum

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Context: Hypothyroidism, overt or subclinical, is associated with adverse outcomes for pregnant women and their offspring. Knowledge of current national thyroid testing rates and positivity during pregnancy is limited.

Objective: The aim of the study was to estimate thyroid testing rate and positivity during pregnancy and postpartum, including testing and positivity rates of thyroperoxidase antibody (TPO Ab) and free T_4 tests in pregnant women with elevated TSH levels (hypothyroid), and in pregnant women having TSH within range (euthyroid).

Design and Setting: Records from a large, national sample of pregnant women screened from June 2005 through May 2008 were examined.

Participants: The study included 502,036 pregnant women, for whom gestational age information was available.

Main Measures: Testing rates and the prevalence of hypothyroidism during pregnancy and postpartum were measured using assay-specific, trimester-specific reference intervals. Screening and positivity rates of TPO Ab and free T_4 tests were also measured.

Results: Of women ages 18 to 40 yr, 23% (117,892 of 502,036) were tested for gestational hypothyroidism (defined as both subclinical and overt hypothyroidism). Of these, 15.5% (18,291 of 117,892) tested positive for gestational hypothyroidism. Twenty-four percent (22,650 of 93,312) of women with TSH within range and 33% (6,072 of 18,291) of women with elevated TSH were also tested for gestational hypothyroxinemia. Gestational hypothyroxinemia was seen in 0.2% (47 of 22,650) of the tested women with TSH within range and was seen in 2.4% (144 of 6,072) of the tested women having elevated TSH; 0.3% (276 of 93,312) of women with TSH within range received a TPO Ab test, and of these, 15% (41 of 276) tested positive; 0.66% (120 of 18,291) of women with elevated TSH received a TPO Ab test, and of these, 65% (78 of 120) tested positive. Only 20.7% (1873 of 9063) of hypothyroid women received thyroid screening within 6 months postpartum; of these, 11.5% (215 of 1873) were diagnosed with postpartum hypothyroidism.

Conclusion: Gestational hypothyroidism is more common than generally acknowledged. Testing is not common, and test selection is variable. There is a low rate of postpartum follow-up. **(*J Clin Endocrinol Metab* 97: 777–784, 2012)**

Thyroid dysfunction is the second most common endocrine disorder affecting women of reproductive age (1). The generally acknowledged rate of gestational hypothyroidism is 2 to 3% (2). In North America, autoimmune thyroiditis is the main cause of hypothyroidism during pregnancy (3). Optimal treatment for hypothyroidism during pregnancy is recommended in preventing maternal and fetal morbidity, even in the absence of interventional studies (4).

Abbreviation: TPO Ab, Thyroperoxidase antibody.

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There is controversy concerning the appropriate diagnostic approach and obstetric management of this condition. The American College of Obstetricians and Gynecologists recommends thyroid testing in pregnant women with a history or symptoms of thyroid disease but states that there are "insufficient data to warrant routine screening of asymptomatic pregnant women for hypothyroidism" (1). Organizations including the American Association of Clinical Endocrinologists, the American Thyroid Association, and The Endocrine Society have different recommendations concerning the testing of pregnant women, while maintaining the importance of the case-finding approach (5). Because 2–3% of pregnant women are estimated to have subclinical hypothyroidism, thyroid dysfunction cannot be adequately diagnosed without systematic screening (3). Two recent studies reported that targeted screening of only pregnant women considered high-risk would miss 30–80% of women with overt or subclinical hypothyroidism (6, 7). Furthermore, hypothyroidism during pregnancy has been linked to adverse neurophysiological fetal development in some studies (8), but not in other studies (9).

There are several criteria for the diagnosis of hypothyroidism during pregnancy. The American Thyroid Association supports the use of assay-specific, trimester-specific reference intervals to define subclinical hypothyroidism. In the absence of this information, trimester-specific reference intervals—*i.e.*, 2.5 mIU/liter during the first trimester and 3.0 mIU/liter during the second and third trimesters—are recommended (3, 5, 10). Individuals with TSH greater than 2.5 mIU/liter may have a higher prevalence of thyroperoxidase antibody (TPO Ab) than individuals with TSH concentrations in the 0.5 to 2.5 mIU/liter range (11). In a 2010 study, Negro *et al.* (12) found that pregnant women with first-trimester TSH levels between 2.5 and 5.0 mIU/liter and who were TPO Ab-negative were 70% more likely to have fetal loss than euthyroid women. Another approach that has been suggested is the application of a multiple of the median TSH (13).

The purpose of the current study is to provide an analysis of the status of testing for hypothyroidism during pregnancy in a large, national sample. We evaluated prenatal and antenatal testing for hypothyroidism by calculating the testing and positivity rates of gestational hypothyroidism (defined as both subclinical and overt hypothyroidism), as well as the postpartum hypothyroid testing and positivity rates, among 502,036 pregnant women. Among pregnant women with hypothyroidism, we examined testing and positivity for hypothyroxinemia and TPO Ab.

TABLE 1. Comparison of age distributions from study population and the 2006 U.S. pregnant population

Age group (yr)	Total study population, % (n)	Total U.S. pregnant population in 2006, % (n)
18 to 24	29.22 (146, 680)	34.01 (1, 376, 930)
25 to 29	30.52 (153, 206)	29.19 (1, 181, 899)
30 to 34	28.02 (140, 659)	23.47 (950, 258)
35 to 40	12.25 (61, 491)	13.33 (539, 796)
Total	100.00 (502, 036)	100.00 (4, 048, 883)

Patients and Methods

Quest Diagnostics has over 145 million patient encounters yearly with individuals from all states and the District of Columbia in the United States. Test results are stored in the largest private clinical laboratory data warehouse in the United States, referred to as the Quest Diagnostics Informatics Data Warehouse. For the present study, we extracted testing data for pregnant and postpartum women as described below; all data were deidentified before analysis. Information about ethnicity and weight was derived from data provided by ordering physicians on the maternal serum screens. Only testing performed by Quest Diagnostics was considered in this study. This study was determined to be exempt by the Western Institutional Review Board.

A pregnant woman was defined as having: 1) a rubella test [IgG, associated with the obstetric panel of testing (CPT code 80055) (14) typically ordered during the first prenatal visit]; and 2) a maternal serum screen result with both gestational age and race group recorded; and 3) any additional laboratory test performed at Quest Diagnostics between estimated weeks 30 and 45 of gestation (15). This serves to suggest that these women (a total of 502,036 pregnant women) received continued laboratory testing through Quest Diagnostics. Gestational week was based on the reported gestational age of the women based on information provided with her maternal serum screen.

Comparisons were also made of the age distributions between the study's pregnant population (during the 36-month study period of June 1, 2005 through May 30, 2008) and the age distributions of the pregnant population within the United States in 2006 (16) (Table 1). In addition, comparisons were made of race group distributions between those with a race designation (as recorded with the maternal serum screens) from the study's pregnant population and the 2006 U.S. pregnant population. For a more direct comparison, we subtracted the 2006 California pregnant population from the 2006 U.S. pregnant population because the Informatics Data Warehouse does not contain ethnicity information from patients from California (Table 2).

To calculate the TSH testing rate, results from TSH tests for women aged 18 to 40 yr were extracted from the Informatics Data Warehouse. There were no changes in the TSH testing methodology during the study period. The testing rate for TSH was calculated as the number of pregnant women who had a TSH test result divided by the total number of women identified as pregnant.

To calculate the positivity rate for gestational hypothyroidism, we employed an assay-specific, trimester-specific reference interval of "within-range" TSH concentrations as 0.10 to 2.50 mIU/liter during the first trimester, 0.55 to 2.75 mIU/liter during the second trimester, and 0.43 to 2.91 mIU/liter during the third

TABLE 2. Comparison of race group distributions from study population and the 2006 U.S. pregnant population

Race group	Total study population, % (n)	Total U.S. minus California pregnant population, % (n)	Total U.S. pregnant population, % (n)
African-American	14.53 (72, 972)	15.32 (540, 130)	14.08 (570, 113)
Asian	5.88 (29, 514)	4.41 (155, 618)	5.45 (220, 475)
Caucasian	56.46 (283, 447)	58.65 (2, 067, 657)	54.80 (2, 218, 707)
Hispanic	18.70 (93, 856)	19.76 (696, 446)	24.00 (971, 821)
Other	4.44 (22, 267)	1.86 (65, 447)	1.67 (67, 767)
Total	100.00 (502, 036)	100.00 (3, 525, 298)	100.00 (4, 048, 883)

trimester, as recommended by the American Thyroid Association and The Endocrine Society (3, 5). The positivity rate for gestational hypothyroidism was calculated as the number of pregnant women who have gestational hypothyroidism divided by the number of pregnant women tested.

We calculated the testing rate for gestational hypothyroxinemia (free T_4 concentrations less than 0.7 ng/dl or 9.0 pmol/liter) in pregnant women who had a TSH level within or above the upper limit of the assay-specific, trimester-specific reference intervals, respectively, as listed above. We employed this standard reference range that is common among clinical laboratories, realizing that this results in an underestimation of overt and subclinical hypothyroidism. The gestational hypothyroxinemia testing rate for pregnant euthyroid or hypothyroid women was calculated as the number of pregnant women who had a free T_4 divided by the number of pregnant euthyroid or hypothyroid women, respectively. To calculate the gestational hypothyroxinemia rate, we employed a reference interval of free T_4 concentrations as 0.7 to 2.0 ng/dl (9.0 to 25.7 pmol/liter). The positivity rate for gestational hypothyroxinemia was calculated as the number of pregnant women who have gestational hypothyroxinemia divided by the number of pregnant women with free T_4 testing.

The TPO Ab testing rate for pregnant euthyroid or hypothyroid women was calculated as the number of women who had a TPO Ab test during pregnancy, divided by the number of pregnant women who were euthyroid or hypothyroid (based on the definitions above), respectively.

The TPO Ab positivity rate for pregnant euthyroid or hypothyroid women was calculated as the number of women who were euthyroid or hypothyroid and had a positive TPO Ab result during pregnancy, divided by the total number of euthyroid or hypothyroid women, respectively, with a TPO Ab test during pregnancy.

To calculate the postpartum TSH testing rate, we limited the study population to women who had gestational hypothyroidism or a positive TPO Ab test result and continued to receive testing at Quest Diagnostics after pregnancy. These patients had additional laboratory testing at Quest Diagnostics during the period between the estimated delivery due date (based on the gestational age of the women reported on the maternal serum screen) and 6 months postpartum. We report the scenario for the highest postpartum testing rate (15).

A woman diagnosed with gestational hypothyroidism or having a positive TPO Ab test result during pregnancy was considered to have a postpartum testing result if we found results of a TSH test being performed within 6 months after the calculated 40th gestational week. The postpartum testing rate was calculated as the number of women with a postpartum testing result divided by the number of women who had gestational hypothyroidism or a positive TPO Ab test result and continued to receive testing at Quest Diagnostics within 6 months postpartum. The postpartum hypothyroidism rate was calculated as the number of women with postpartum hypothyroidism divided by the number of women with postpartum TSH testing.

The flowchart in Fig. 1 outlines the study design.

Statistical comparisons were made using a Pearson χ^2 test to assess the difference between proportions (with an adjusted P value <0.05 denoting statistical significance) and a multiple logistics regression to determine the odds ratio between two race, weight, or age groups. The statistical software package SAS 9.2 (SAS Institute Inc., Cary, NC) was used for all data analyses.

Results

There were 502,036 pregnant women aged 18 to 40 yr in the study population. Comparison of the age distributions from the study population with that of the 2006 U.S. pregnant population reveals a variance of less than 5% in each maternal age group category (Table 1). The study population was underrepresented relative to the U.S. pregnant population among women ages 19 to 24 yr and overrepresented relative to the U.S. pregnant population among women ages 30 to 34 yr. Comparison of the race group distributions from the study population with that of the 2006 U.S. pregnant population reveals a variance of less than 3% in each race group (Table 2).

Of the 502,036 women, 117,892 (23%) were tested for gestational hypothyroidism by measuring TSH. Testing rates increased as the maternal age increased (Fig. 2). Of the 502,036 pregnant women, Asian women had the highest testing rate, at almost 28%, whereas African-American women had the lowest testing rate, at 19% (Table 3). Multiple logistic regression analysis was performed to examine the impact of age, race group, or maternal weight on testing for gestational hypothyroidism (Table 4). Women ages 35 to 40 yr are 2.2 times as likely to be tested for gestational hypothyroidism as those ages 18 to 24 yr. In addition, women weighing over 275 pounds (125 kg) are 1.3 times as likely to be tested for gestational hypothyroidism as those weighing between 100 and 124 pounds (45.4 and 56.2 kg). Asian women are 1.8 times as likely to be tested

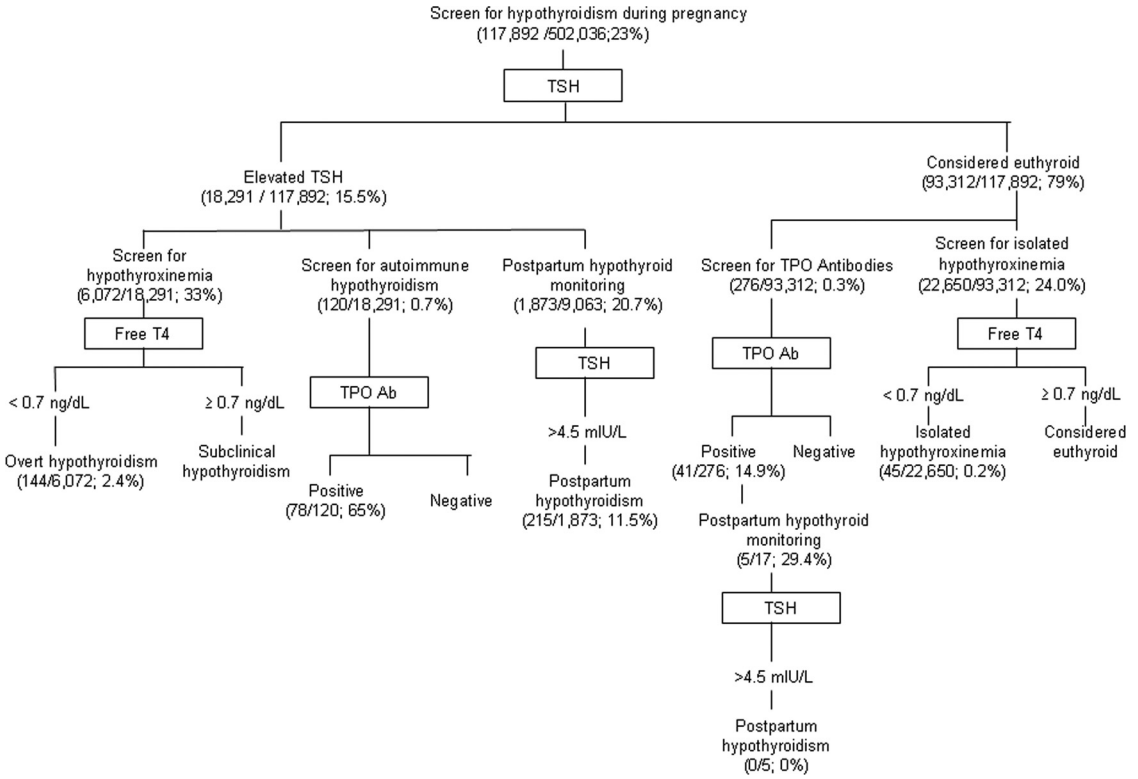

FIG. 1. Study protocol and resultant percentage positivity for gestational hypothyroidism, gestational hypothyroxinemia, autoimmune hypothyroidism, and postpartum hypothyroidism.

for gestational hypothyroidism as African-American women.

Of the 117,892 women aged 18 to 40 yr who were tested for gestational hypothyroidism, 18,291 (15.5%) tested positive. Asian women had a higher positivity rate for gestational hypothyroidism than other major ethnic groups (Table 3). The incidence of gestational hypothyroidism increases with maternal age (Fig. 2). Multiple logistic regression analysis was performed to examine the impact of age, race group, and maternal weight on a woman's risk for gestational hypothyroidism (Table 4). Women ages 35 to 40 yr are 1.8 times as likely to develop gestational hypothyroidism as those ages 18 to 24 yr. In addition, women weighing over 275 pounds (125 kg) are 2.5 times as likely to develop gestational hypothyroidism as those weighing between 100 and 124 pounds (45.4 and 56.2 kg). Asian women are almost five times as likely to develop gestational hypothyroidism as African-American women.

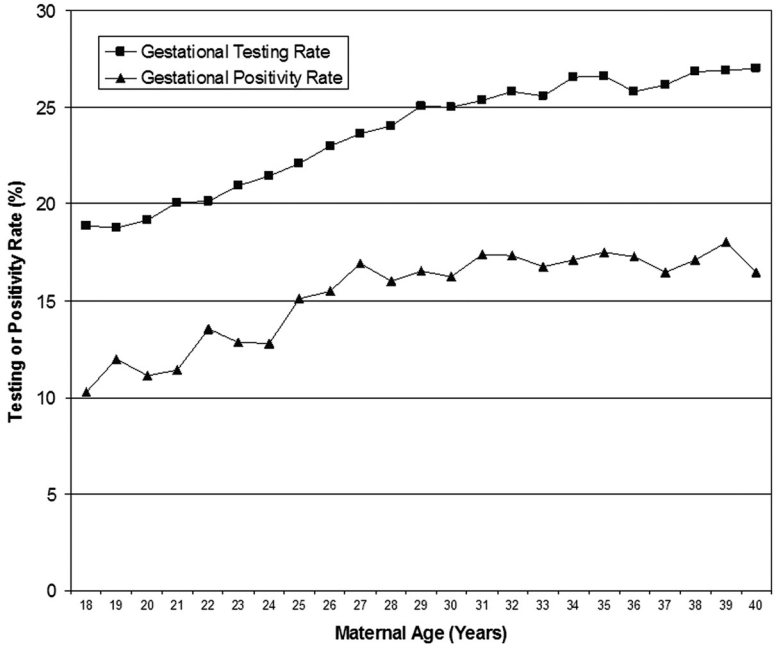

FIG. 2. TSH testing and positivity rates during pregnancy.

Of the pregnant women who were tested for gestational hypothyroidism (based on the assay-specific, trimester-specific reference intervals described in *Patients and Methods*), 79% (93,312 of 117,892) had TSH levels within range during pregnancy. Twenty-four percent (22,650 of 93,312) of women with TSH levels within range were also tested for gestational hypothyroxinemia by free T_4 testing. Of these, 0.2%

TABLE 3. Gestational and postpartum thyroid testing and positivity rates (%) of pregnant women

Rate (%)	African-Americans[a]	Asians[a]	Caucasian[a]	Hispanic[a]	Others[a]	Total
Gestational testing rate[b]	19.2 (72, 952)	27.7 (29, 514)	25.1 (283, 447)	20.1 (93, 856)	26.3 (22, 267)	23.5 (502, 036)
Gestational positivity rate[c]	6.7 (13, 982)	19.3 (8, 190)	16.4 (71, 022)	15.2 (18, 841)	22.2 (5, 857)	15.5 (117, 892)
Hypothyroid women: free T_4 testing rate[d]	30.4 (930)	35.9 (1, 577)	33.2 (11, 626)	31.0 (2, 858)	36.6 (1, 300)	33.2 (18, 291)
Hypothyroid women: free T_4 positivity rate[e]	8.5 (283)	0.9 (566)	2.1 (3, 860)	3.5 (887)	0.8 (476)	2.4 (6, 072)
Euthyroid women: TPO Ab testing rate[f]	25.2 (11, 803)	27.4 (5, 970)	24.2 (56, 307)	21.9 (14, 996)	26.2 (4, 236)	24.3 (93, 312)
Euthyroid women: TPO Ab positivity rate[g]	3.0 (2, 969)	11.1 (1, 637)	18.0 (13, 646)	9.5 (3, 288)	25.0 (1, 110)	14.9 (22, 650)
Hypothyroid women: TPO Ab testing rate[h]	0.2 (930)	0.7 (1, 577)	0.6 (11, 626)	1.1 (2, 858)	0.8 (1, 300)	0.7 (18, 291)
Hypothyroid women: TPO Ab positivity rate[i]	50.0 (2)	45.5 (11)	69.2 (65)	77.4 (31)	27.3 (11)	65.0 (120)
Euthyroid women: TPO Ab testing rate[j]	0.3 (11, 803)	0.3 (5, 970)	0.3 (56, 307)	0.4 (14, 996)	0.3 (4, 236)	0.3 (93, 312)
Euthyroid women: TPO Ab positivity rate[k]	3.0 (33)	11.1 (18)	18.0 (167)	9.5 (42)	25.0 (16)	14.9 (276)
Hypothyroid women: postpartum testing rate[l]	18.3 (460)	19.4 (747)	19.4 (5, 813)	19.1 (1, 393)	22.3 (650)	19.5 (9, 063)
Hypothyroid women: postpartum positivity rate[m]	14.7 (75)	12.2 (147)	10.4 (1, 239)	16.2 (253)	10.1 (159)	11.5 (1, 873)

Data are expressed as percentage (number).

[a] Number of pregnant women eligible for testing in each race group.

[b] Testing rates (expressed as the number of patients tested, divided by the total number of pregnant women) differed significantly across ethnicities: $\chi^2 = 2151.7$; $P < 0.001$.

[c] Positivity rates (expressed as the number of patients with a positive result, divided by the number of patients tested) differed significantly across ethnicities: $\chi^2 = 1166.1$; $P < 0.001$.

[d] Testing rates differed significantly across ethnicities: $\chi^2 = 21.2$; $P < 0.001$.

[e] Positivity rates differed significantly across ethnicities: $\chi^2 = 62.2$; $P < 0.001$.

[f] Testing rates differed significantly across ethnicities: $\chi^2 = 90.7$; $P < 0.001$.

[g] Positivity rates did not differ significantly across ethnicities: $\chi^2 = 0.60$; $P = 0.964$.

[h] Testing rates differed significantly across ethnicities: $\chi^2 = 13.3$; $P = 0.010$.

[i] Positivity rates differed significantly across ethnicities: $\chi^2 = 11.5$; $P = 0.021$.

[j] Testing rates did not differ significantly across ethnicities: $\chi^2 = 1.2$; $P = 0.878$.

[k] Positivity rates did not differ significantly across ethnicities: $\chi^2 = 7.4$; $P = 0.118$.

[l] Testing rates differed significantly across ethnicities: $\chi^2 = 18.3$; $P = 0.001$.

[m] Positivity rates did not differ significantly across ethnicities: $\chi^2 = 8.1$; $P = 0.088$.

(45 of 22,650) tested positive for isolated gestational hypothyroxinemia (defined as having TSH levels within range and low free T_4 levels). In contrast, 33% (6,072 of 18,291) of women with elevated TSH levels were tested for gestational hypothyroxinemia by free T_4 testing. Of these, 2.4% (144 of 6,072) tested positive for overt gestational hypothyroxinemia (defined as having elevated TSH levels and low free T_4 levels) (Table 3).

Of the 18,291 pregnant women who had elevated TSH, 120 (0.7%) also received TPO Ab testing. Hispanic women had the highest TPO Ab testing rate at 1.1%, whereas African-American women had the lowest TPO Ab testing rate at 0.2%. Of the 120 women who had elevated TSH and TPO Ab testing, 78 (65%) women had a positive TPO Ab result. Hispanic women had the highest TPO Ab positivity rate at 77.4%, whereas Asian women had the lowest rate at 45.5% (Table 3).

Of the 93,312 women who had TSH levels within range, 276 (0.3%) also received TPO Ab testing. Of the 276 women who had TSH levels within range and TPO Ab testing, 41 (15%) women had a positive TPO Ab result. Caucasian women had the highest TPO Ab positivity rate at 18%, whereas African-American women had the lowest rate at 3% (Table 3).

TABLE 4. Odds ratios for associations between gestational hypothyroidism testing[a]/positivity[b] rates and patient demographic variables

	Odds ratio[a] (95% CI) for testing rates	Odds ratio[b] (95% CI) for positivity rates
Age group (yr)		
18 to 24	1.000	1.000
25 to 29	1.541 (1.519, 1.563)	1.454 (1.404, 1.506)
30 to 34	1.988 (1.959, 2.016)	1.682 (1.625, 1.742)
35 to 40	2.223 (2.161, 2.287)	1.786 (1.682, 1.896)
Weight group (pounds)		
100 to 124	1.000	1.000
125 to 149	1.028 (1.010, 1.047)	1.142 (1.094, 1.191)
150 to 174	1.054 (1.034, 1.073)	1.205 (1.153, 1.260)
175 to 199	1.106 (1.083, 1.130)	1.290 (1.227, 1.355)
200 to 224	1.175 (1.146, 1.205)	1.418 (1.339, 1.501)
225 to 249	1.219 (1.181, 1.257)	1.653 (1.544, 1.769)
250 to 274	1.213 (1.163, 1.264)	1.975 (1.816, 2.148)
275 and over	1.328 (1.269, 1.390)	2.456 (2.252, 2.678)
Race group		
African-Americans	1.000	1.000
Caucasian	1.672 (1.643, 1.700)	3.470 (3.271, 3.682)
Asians	1.784 (1.734, 1.834)	4.882 (4.539, 5.250)
Hispanics	1.228 (1.203, 1.253)	2.720 (2.548, 2.903)
Others	1.883 (1.827, 1.940)	4.956 (4.600, 5.339)

CI, Confidence interval.

Of the women who had gestational hypothyroidism, 9063 women had continued laboratory care with Quest Diagnostics within 6 months after the estimated delivery due date. Of these, 1873 (20.7%) were identified as returning for postpartum hypothyroidism monitoring. Postpartum testing rates varied significantly by ethnicity (Table 3) and increased with patient age (data not shown).

There were 17 additional women with a positive TPO Ab result who had continued laboratory care with Quest Diagnostics within 6 months after the estimated delivery due date. Of these, five (29%) were identified as returning for postpartum hypothyroidism monitoring. None of these five women were diagnosed with postpartum hypothyroidism.

Of the 1873 women with gestational hypothyroidism who returned for postpartum hypothyroid testing, 215 (11.5%) had test results consistent with a diagnosis of postpartum hypothyroidism. Hispanic women had the highest rate of postpartum hypothyroidism, at 16%, whereas Caucasian women had the lowest rate, at 10% (Table 3).

The flowchart in Fig. 1 summarizes the testing and positivity rates for gestational hypothyroidism, gestational hypothyroxinemia, autoimmune hypothyroidism, and postpartum hypothyroidism.

Discussion

This study describing the testing results from a large, national population of over one-half million pregnant women provides unique insights into the use of thyroid testing in obstetrical care. Testing for gestational hypothyroidism and hypothyroxinemia is important because these conditions are associated with pregnancy-induced hypertension, gestational diabetes, preterm premature rupture of membranes, increase in the frequency of low-birth-weight infants, and abnormal fetal brain development (9, 17). In contrast, one study found that treatment of subclinical hypothyroidism in pregnant women did not affect the intellectual development of the offspring (18). Currently, routine screening for thyroid function during pregnancy is not performed in the United States. There are increasing calls for the introduction of a universal prenatal and antenatal program (10), although the benefit of universal antenatal screening is uncertain (18).

We found that only 23% were tested for gestational hypothyroidism. Among pregnant women with unrecognized hypothyroidism, the median interval to clinical diagnosis of hypothyroidism is 5 yr; therefore, earlier diagnosis may address symptoms and subclinical disease that occur during this period (8). We found that obese women and women over age 35 yr were more likely to have thyroid function testing performed. This supports the recently published case-finding criteria adopted by the American Thyroid Association in 2011, which recommends case finding for women over 30 yr of age (5).

By extrapolating our observations, an estimated additional 483,000 pregnant women could have had undetected gestational hypothyroidism in the United States (based on 4,048,883 live births in the United States in 2006, with 77% of them not tested, and with 15.5% of those positive for gestational hypothyroidism) (16). These results suggest that the current observed rate of gestational hypothyroidism testing could adversely affect a large number of women and their offspring nationwide. Our study population was slightly underrepresented among younger pregnant women and slightly overrepresented among older pregnant women. Given the higher rate of gestational hypothyroidism among older pregnant women, this bias in the study population means the overall rate of gestational hypothyroidism is slightly lower than we report (the age-adjusted positivity rate is 15.1%).

The present study used an assay-specific, trimester-specific reference interval to define gestational hypothyroidism and found that 15.5% of pregnant women tested have gestational hypothyroidism (of which 2.4% have overt hypothyroidism and 97.6% have subclinical hypothyroidism), based on TSH testing alone. This contrasts with

the commonly cited prevalence of 2 to 3% of pregnant women having subclinical hypothyroidism, with an outdated upper limit of 6.0 mU/liter (19). This striking disparity between what is observed disease prevalence among more than one-half million pregnancies and the generally cited prevalence of gestational hypothyroidism may lead to reconsideration of practice guidelines.

TPO Ab testing remains a well-documented risk factor for continued or progressive thyroid dysfunction postpartum and perinatal complications (20, 21). Therefore, it is surprising that, in pregnant women with documented hypothyroidism, a low percentage (0.7%) is tested for the presence of TPO Ab. Given the high rate of TPO Ab positivity (65%) in women with gestational hypothyroidism, TPO Ab testing should be considered for all women with gestational hypothyroidism.

In this study, we report that 20.7% of women with gestational hypothyroidism were also tested postpartum. The degree of TSH elevation during pregnancy did not predict the probability that a test would be performed postpartum. Of those tested, 11.5% tested positive for postpartum hypothyroidism. Because this is much higher than the 6% previously reported in a national Australian study, the importance of postpartum thyroid dysfunction in the United States should be investigated further (22).

Consistent with studies of healthy nonpregnant individuals, our results indicate that, among pregnant women, African-American women have the lowest rate of gestational hypothyroidism, whereas Asian women have the highest rate (23). Because TSH levels of African-Americans tend to run lower than those of other ethnic groups, clinicians caring for a large number of African-Americans might need to use slightly different TSH parameters than for other groups. In addition, researchers who perform prospective studies should make certain that they keep these ethnic differences in mind when analyzing data and relating them to perinatal/neonatal outcome.

Given that maternal hypothyroxinemia has recently been associated with an elevated risk of expression language delay and nonverbal cognitive delay (24), we estimated the rate of hypothyroxinemia among pregnant women with TSH levels within range and those with elevated TSH. Although 0.22% of pregnant women with TSH levels within range were positive for isolated hypothyroxinemia, 2.4% of pregnant hypothyroid women were diagnosed with overt hypothyroxinemia. This indicates that pregnant hypothyroxinemic and hypothyroid women may experience additional risks to themselves and their children.

In conclusion, we examined the laboratory test results of 502,036 pregnant women that represent the national population, unlike other studies (6, 8, 13). The 15% prevalence of hypothyroidism based on modern criteria is significantly higher than the 2 to 3% cited in older literature (19). Our nationally based study demonstrates that the pregnancy and postpartum testing rates for hypothyroidism are low, relative to the observed prevalence of subclinical hypothyroidism, based on the assay-specific, trimester-specific reference intervals. In addition, screening all pregnant women with either TSH or TPO Ab has been found to be more cost-effective than not screening at all (25), given that testing is widely available, easy (venipuncture), and relatively inexpensive. Treatment is also relatively inexpensive. Because national and international endocrine and obstetrical organizations may consider the implications of universal prenatal and antenatal screening (26), this study demonstrates that the proportion of women tested for gestational hypothyroidism is currently low; if outcomes are shown to improve with intervention, then this may have a significant impact on the health of a large number of women and their children.

Acknowledgments

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Disclosure Summary: A.J.B. is employed by Quest Diagnostics. J.M.N. and H.W.K. are employed by Quest Diagnostics and have equity interest in Quest Diagnostics.

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