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Gestational Hypothyroidism Is More Common Than Generally Acknowledged, But Testing for It Is Not Usually Performed

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SUMMARY

Background

Knowledge of current national thyroid testing rates and abnormal results during pregnancy is limited. Hypothyroidism, overt and subclinical, is associated with adverse outcomes for pregnant women and their offspring. The aim of this study was to provide an analysis of the status of testing for hypothyroidism during pregnancy in a large national sample.

Methods

Quest Diagnostics has over 145 million patient encounters yearly with individuals from all states and the District of Columbia. For the present study, the authors extracted testing data from 502,036 pregnant and postpartum women (18 to 40 years of age) during the 36-month study period of June 1, 2005, through May 30, 2008; these samples were sent to Quest Diagnostics for routine pregnancy screening blood tests at the beginning of pregnancy and between 30 and 45 weeks thereafter. 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 being pregnant. Gestational week was based on the reported gestational age based on information provided by the woman's maternal serum screen. An assay-specific, trimester-specific reference interval of "within range" TSH concentration was 0.10 to 2.50 mIU/L during the first trimester, 0.55 to 2.75 during the second trimester, and 0.43 to 2.91 during the third trimester. 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.

Results

Of the 502,036 women in the study, 117,892 (23%) were tested for gestational hypothyroidism by measuring TSH. Testing rates increased as the maternal age increased, Asian women had the highest testing rate (28%), whereas African American women had the lowest testing rate (19%). Women 35 to 40 years of age were 2.2 times as likely to be tested for gestational hypothyroidism as those who were 18 to 24. Women weighing over 275 lb (125 kg) were 1.3 times as likely to be tested for gestational hypothyroidism as those weighing between 100 and 124 lb (45.4 and 56.2 kg).

Of the pregnant women who were tested for gestational hypothyroidism, 15.5% of them had elevated serum TSH levels; 79% had TSH levels within the reference range for pregnancy. Multiple logistic-regression analysis was performed to examine the impact of age, race, and maternal weight on a woman's risk for gestational hypothyroidism. Women 35 to 40 years of age are 1.8 times as likely to have gestational hypothyroidism as those who are 18 to 24 years. In addition, women weighing over 275 lb are 2.5 times as likely to develop gestational hypothyroidism as those weighing between 100 and 124 lb. Asian women are almost five times as likely to have gestational hypothyroidism as African American women. A total of 24% (22,650 of 93,312) of women with TSH levels within normal range were also tested for gestational hypothyroxinemia; 0.2% had low FT_4 levels. In contrast, 33% (6072 of 18,291) of women with elevated TSH levels, were tested for FT_4; 2.4% of them (144 of 6072) had clinical hypothyroidism. Of the 18,291 pregnant women who had elevated TSH, 120 (0.7%) also received TPOAb testing; 78 (65%) women had a positive TPOAb result.

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Hispanic women had the highest TPOAb positivity rate, at 77.4%, whereas Asian women had the lowest rate at 45.5%. Only 1873 women with hypothyroidism returned for postpartum testing, and of those, 11.5% of them had postpartum hypothyroidism.

Conclusions

Gestational hypothyroidism is more common than generally acknowledged; testing is not common, and test selection is variable. There was a low rate of postpartum follow-up.

ANALYSIS AND COMMENTARY

The aim of the study was to analyze the status of testing for hypothyroidism during pregnancy in a large, national sample. During a 36-month study period (2005–2008), 502,036 samples were sent to the laboratory for routine pregnancy-screening blood tests at the beginning of pregnancy and between 30 and 45 weeks thereafter; serum TSH was also requested in 23% of them. A pregnant woman was found and included by having: (a) a rubella test, associated with the obstetric panel of tests typically ordered during the first prenatal visit; (b) a maternal serum screen result with both gestational age and race group recorded; and (c) any additional laboratory test performed at Quest Diagnostics between estimated weeks 30 and 45 of gestation. There are several problems with this study resulting, in my estimation, in erroneous conclusions.

The term gestational hypothyroidism is used without a definition, implying high serum TSH in pregnancy. I'm not aware of this term being used previously; my concern is that its use will create another literature controversy, similar to that for "gestational diabetes mellitus," which is defined as first recognition of glucose intolerance during pregnancy. Therefore, if the same criterion is used for "gestational hypothyroidism," women previously diagnosed with thyroid dysfunction should be excluded. It appears that the authors have assumed that women were euthyroid before conception, since they consistently used the phrase "to develop gestational hypothyroidism" (e.g., "Women ages 35 to 40 yr are 1.8 times as likely to develop gestational hypothyroidism as those ages 18 to 24 yr.").

In 23% (117,892) of women, the total serum samples were tested for gestational hypothyroidism by measuring TSH. The authors stated that "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." On the contrary, the authors do not provide information for the reasons or indications by the health care professional for ordering a serum TSH in their population. Routine thyroid testing was not mandated at the time of the study and is not at the present recommended by the American College of Obstetricians and Gynecologists (ACOG). The only available patient information to the authors was age, race, weight, and gestational age. Most of the requested serum TSH testing was included in the initial pregnancy-screening tests. The authors assumed, therefore, that serum TSH was ordered as a screening test, without considering the possibility that of those tested women, some were hypothyroid on replacement therapy before conception. It may be argued, therefore, that the majority of requested serum TSH tests were in women who were on thyroid-replacement therapy; the reported incidence of "high TSH values" early in pregnancy in hypothyroid women on thyroid-replacement therapy antedating pregnancy may be as high as 40% to 50% (1) as contrasted with the 2% to 4% in the general population after excluding women with known thyroid disease prepregnancy; the same conclusion could be reached for their high incidence of overt hypo-

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thyroidism (2.5%), as compared with 0.2% to 0.4 % in the literature (2).

The authors stated: "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." The reason for this recommendation is not given. The fact that very few TPOAb tests were requested in their population of women with gestational hypothyroidism suggests to me that the majority of their hypothyroid population indeed already had thyroid dysfunction and that there were no clinical indications for serum TPOAb testing. Furthermore, recently published clinical guidelines (3) do not recommend routine screening for TPOAb in pregnant women with elevated serum TSH.

Finally, the authors' conclusions that "gestational hypothyroidism is more common than generally acknowledged; testing is not common, and test selection is variable" are misleading, since no information about antepartum clinical status is given. The more plausible alternative hypothesis that could better explain their results is that serum TSH, with or without serum FT_4, was ordered by health care professionals in order to assess thyroid status early in pregnancy in women who were receiving thyroid-replacement therapy. No information is given about follow-up TSH results later in pregnancy.

— Jorge H. Mestman, MD

References

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