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Is There Sufficient Evidence That Thyroid Dysfunction and Autoimmunity Are Risk Factors for Gestational Diabetes?

Karakosta P, Alegakis D, Georgiou V, Roumeliotaki T, Fthenou E, Vassilaki M, Boumpas D, Castanas E, Kogevinas M, Chatzi L. Thyroid dysfunction and autoantibodies in early pregnancy are associated with increased risk of gestational diabetes and adverse birth outcomes. J Clin Endocrinol Metab. September 26, 2012 [Epub ahead of print].

SUMMARY

Background

Maternal thyroid dysfunction, especially in early pregnancy, may lead to pregnancy complications and adverse birth outcomes. The objective of the authors was to assess the prevalence of thyroid dysfunction and autoimmunity in pregnant women and to examine their relationship with adverse pregnancy and neonatal outcomes in a large-scale, population-based cohort of an iodine-sufficient area of the Mediterranean: Crete, Greece.

Methods

The study used data from the prospective mother–child cohort "Rhea" study in Crete, Greece. During a 12-month period, a total of 1170 women with singleton pregnancies participated in this analysis; maternal serum for the determination of TSH, FT_4, FT_3, TPOAb and TgAb was obtained at a mean (±SD) gestational age of 14.1±3.6 weeks. Multivariable log-Poisson regression models were used to adjust for confounders. Outcomes included gestational diabetes (GDM), gestational hypertension/preeclampsia, cesarean section, preterm delivery, low birth weight, and small-for-gestational-age neonates. The reference intervals of serum TSH levels were 0.05 to 2.53 mU/ml for the first trimester and 0.18 to 2.73 mU/ml for the second trimester.

Results

Mothers with serum TSH concentrations within the reference range were considered to have normal (n = 1062, 90.8%), high (n= 79, 6.8%), or low (n= 29, 2.5%) TSH status. High TPOAb titers were found in 153 (13%) and high TgAb in 83 (7%). Women were screened for GDM at 24 to 28 weeks and were classified as having GDM if two or more of the four plasma glucose values obtained during the 100-g, 3-hour oral glucose-tolerance test were abnormal. The combination of high TSH and thyroid autoimmunity in early pregnancy was associated with (1) a fourfold increased risk for gestational diabetes (relative risk [RR], 4.3; 95% CI, 2.1 to 8.9], affecting 6 of 32 women, only one of whom had a TSH level >4 mU/ml and (2) a threefold increased risk for low-birth-weight neonates, affecting 5 of 32 women (RR, 3.1; 95% CI, 1.2 to 8.0) after adjustment for several confounders. Euthyroid women positive for thyroid antibodies had a significant increase in spontaneous preterm delivery (22 of 148; RR, 1.7; 95% CI, 1.1 to 2.8). The obstetrical outcome was similar regardless of whether or not women were using thyroid medications.

Conclusions

High TSH levels and thyroid autoimmunity in early pregnancy may detrimentally affect pregnancy and birth outcomes.

ANALYSIS AND COMMENTARY

There is agreement in the literature that severe untreated or poorly controlled thyroid dysfunction in pregnancy is the cause of serious obstetrical and neonatal complications (1). However, there is no consistency in the overall obstetrical and neonatal outcomes of women with subclinical hypothyroidism or euthyroid chronic thyroiditis. It is accepted

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that women diagnosed with subclinical hyperthyroidism early in pregnancy do not have an increased incidence of complications, considering that in many of these situations a low serum TSH is a physiological finding early in pregnancy (2). Several publications in the past decade, including a meta-analysis (3), have reported a high incidence of miscarriages and prematurity in series of women suffering from subclinical hypothyroidism or euthyroid autoimmune disease, with some exceptions (4). In the vast majority of published articles, thyroid tests, including measurement of antibodies (mostly TPOAb), were done only in early pregnancy, without follow-up during the course of gestation, nor an indication of the prepregnancy thyroid status. Furthermore, the vast majority of the publications failed to mention whether hypothyroidism was properly corrected before delivery. The study by Karakosta et al. suffers from the same shortcomings: thyroid tests were performed only early in pregnancy (mean gestational age, 14.1 weeks); therefore, the authors were unable to assess miscarriage rate. They reported a significant incidence of GDM, but only in women with mild subclinical hypothyroidism (TSH <4 mU/ml) with positive antibodies, but not in euthyroid women with positive antibodies or those with high TSH and negative antibodies. The authors considered potential confounders, but hyperglycemia was not included. The incidence of other complications, such as prematurity, is limited to euthyroid women with positive antibodies and low-birth-weight neonates and to women with elevated serum TSH values, with or without antibodies. The authors did not comment or speculate about the disparity in outcomes in the different thyroid groups.

It is my personal opinion that in spite of the fourfold increased risk for GDM reported by the authors, larger studies with additional data obtained at different stages of gestation should be performed before accepting these findings. Interestingly, in their conclusions the authors did not mention their novel finding of thyroid dysfunction and autoimmunity as a risk factor for GDM.

— Jorge H. Mestman, MD

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