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Correlation of Maternal Thyroid Parameters During the First Half of Pregnancy and Cord Thyroid Parameters: Are They Associated with Adverse Pregnancy and Child Neuropsychological Outcomes?

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SUMMARY • • • • • • • •

Background

A number of studies have analyzed the effects of maternal thyroid status during pregnancy and mental and motor development of the child. However, limited data are available on the relation between maternal thyroid hormone (TH) levels during pregnancy and fetal TH levels. The authors' objective was to study maternal thyroid parameters during the first half of pregnancy as well as their relation to cord thyroid parameters.

Methods

This study was embedded in the Generation R Study, a population-based cohort from early fetal life onward in Rotterdam, The Netherlands. Mothers with a delivery date between April 2002 and January 2006 were enrolled in the study. Data on serum TSH, FT₄, and T₄ levels were complete for 5186 pregnant women after excluding those with thyroid disease who were on medication, those who had twin pregnancies, and those whose pregnancies were the result of fertility treatment. Maternal serum samples were obtained in early pregnancy (mean [±SD], 13.3±1.7 weeks), and cord serum samples (available in 3036 newborns) were obtained at birth (39.9±1.9 weeks), with the exclusion of those delivered at a gestational age less than 37 weeks.

Results

Reference ranges for maternal TSH, FT₄, T₄, and

cord TSH and FT₄ levels were defined as the range between the 2.5th and 97.5th percentiles. Ranges for the first and second trimesters were 0.01 to 4.00 and 0.05 to 4.05 mU/L for TSH, 10.86 to 24.00 and 10.28 to 21.50 pmol/L for FT₄, and 89.9 to 210.0 and 97.8 to 221.0 nmol/L for T₄. In the first trimester, 8.6% of the women with TSH levels in the normal range had a TSH level >2.5 mU/L. In the second trimester, 4.9%of the women with TSH levels in the normal range had a TSH level >3.0 mU/L.

Clinical

TPOAb positivity was associated with higher maternal TSH levels, lower FT₄ levels, an 8-fold higher risk of subclinical hypothyroidism, and a 26-fold higher risk of overt hypothyroidism.

Maternal and cord TSH levels were positively correlated, as were maternal and cord FT₄ levels. Associations remained similar after the exclusion of TPOAbpositive mothers and additional correction for smoking, socioeconomic status, and ethnicity.

Conclusions

The authors observed a positive correlation between maternal and cord thyroid parameters, a substantial number of women with TSH levels above 2.5 and 3.0 mU/L in the first and second trimesters, respectively, and a significantly increased risk of hypothyroidism in TPOAb-positive mothers.

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ANALYSIS AND COMMENTARY • • • • • •

The study had three observations of clinical interest. First, the authors mentioned the limited data available on the relations between maternal TH parameters during pregnancy and fetal TH levels. Few studies have analyzed these associations in mothers who had no known thyroid abnormalities but did not find any associations; however, sample sizes were either limited (1) or neonatal TH parameters were determined 2 days after birth, a time at which associations are likely to be influenced by the neonatal TSH surge (2). The authors found a positive correlation between maternal (early in pregnancy) and cord-blood serum TSH and FT₄ measured in 2563 mother-child pairs from euthyroid mothers. These associations could in part be explained by the placental transfer of T_4 as well as by shared factors between mother and child, which are known to influence thyroid parameters, such as genetics and nutrition (e.g., iodine intake). Further studies are needed to correlate maternal and cord-blood thyroid parameters and subsequent neuropsychological development in the child.

Second, serum TSH, FT_4 , and T_4 were measured in 5393 pregnant women in an iodine-sufficient population after the exclusion of women with TPOAb positivity, known thyroid disease, use of thyroid-interfering medication, twin pregnancies, and pregnancies after fertility treatment. A TSH level >2.5 mU/L was found in 8.6% of women in the first trimester and a level >3.0 mU/L in 4.9% of women in the second trimester. The authors underlined the importance of using population-specific reference ranges in the diagnosis of thyroid dysfunction in pregnancy, because following the recent recommendations of the ATA guidelines, these women would have been diagnosed as "hypothyroid" (3).

Third, the authors confirmed a previous study of a substantially increased risk of both subclinical and overt hypothyroidism in TPOAb-positive mothers (4). This finding is of significant clinical importance in relation to euthyroid women with Hashimoto's thyroiditis who are planning a pregnancy, in which case a preconception serum TSH level close to 1 mIU/L would be desirable to prevent the development of hypothyroidism early in pregnancy.

— Jorge H. Mestman, MD

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