The Incidence of Graves’ Hyperthyroidism Increases in Early Pregnancy and the Late Postpartum Period

Jorge H. Mestman


SUMMARY

Background
Hyperthyroidism in women of reproductive age is predominantly caused by Graves’ disease. Pregnancy-associated changes in the immune system may influence the onset of disease, but population-based incidence rates in and around pregnancy have not been reported. The objective of these authors was to estimate the incidence of maternal hyperthyroidism (defined by prescriptions for antithyroid drugs being filled) in and around pregnancy and to compare this with the incidence of other autoimmune diseases, such as rheumatoid arthritis (RA) and inflammatory bowel disease (IBD).

Methods
Danish nationwide registers provided for a population-based cohort study. In women giving birth to singleton liveborn children in Denmark from 1999 to 2008 (n = 403,958), the main outcome investigated was the incidence rates (IR) of maternal hyperthyroidism during a 4-year period beginning 2 years before and ending 2 years after the date when the mother gave birth for the first time during the study period.

Results
Altogether 3673 women (0.9%) were identified as having the onset of hyperthyroidism from 1997 to 2010. The IR of hyperthyroidism in and around pregnancy varied widely and was high in the first 3 months of pregnancy (incidence rate ratio [IRR] as compared with the remaining study period, 1.50), very low in the last 3 months of pregnancy (0.26), and at the highest level 7 to 9 months post partum (3.80). The incidence variation in and around pregnancy was different for RA and IBD.

Conclusions
The incidence of hyperthyroidism was high in early pregnancy and post partum, whereas this particular pattern was not observed for other diseases of autoimmune origin.

ANALYSIS AND COMMENTARY

In pregnant women, hyperthyroidism diagnosed in the first trimester of pregnancy includes those who had not been diagnosed with hyperthyroid symptoms before conception and women in remission from ATD with recurrent symptoms in the first few weeks after conception. Most of them have Graves’ disease; however, hyperemesis gravidarum, trophoblastic disease, and multiple pregnancies should be excluded. Tamaki et al. (1) observed an aggravation of hyperthyroidism in women in remission from the disease in the first trimester of pregnancy, a common finding in clinical practice; in such cases, a positive serum TRAb titer may detected. Four retrospective studies evaluated the onset of Graves’ disease in women in the first year after delivery; three of them concluded that the postpartum period poses a risk
factor for the onset of Graves’ disease (1-3), while another study concluded that the postpartum period was an overestimated risk factor (4). The postpartum time for diagnosis of Graves’ disease is between 7 and 12 months after delivery, although a few cases had occurred after the 4th month (3). In the first 3 months post partum, hyperthyroidism is usually due to postpartum thyroiditis. It has been postulated that maternal immune system adaptation during and throughout pregnancy to ensure tolerance of the fetus and sustained immune defense against infections account for the above observations (6).

In the present study, information obtained from the Danish nationwide data identified incident cases of maternal hyperthyroidism in a 13-year period in women 15 to 45 years of age. The diagnosis of hyperthyroidism was based on prescriptions to treat ATD in a 4-year period beginning 2 years before and ending 2 years after the birth of a liveborn child; no laboratory data were available to confirm the diagnosis or its cause. The time of onset of hyperthyroidism was defined by the date the first prescription of ATD was filled at a Danish pharmacy.

In women with several pregnancies, the first pregnancy was chosen because, the authors speculated, “if the postpartum period is a sufficient or strong factor for the development of disease in genetically disposed individuals, one may expect a tendency for disease onset to take place in the first postpartum period that the woman encounters.” The authors included in their study the incidence of RA and IBD as a potential general phenomenon for autoimmune diseases. An interesting observation from their study was the significant decrease in the incidence of hyperthyroidism, RA, and IBD in the period prior to pregnancy, suggesting low fertility or purposely not becoming pregnant.

Their results confirmed previous observations of a peak incidence of hyperthyroidism in the first trimester, with a drop in the second half of pregnancy and the highest peak in the postpartum period. The clinical course of Graves’ hyperthyroidism in the different trimesters of pregnancy coincides with the course of serum TRAb titers—an increase in the first trimester, a decrease in titers thereafter until delivery, and a rebound in the postpartum period (7). One other explanation for the first-trimester exacerbation of Graves’ hyperthyroidism was due to the hCG surge (8).

The authors were confident that the cause of hyperthyroidism in the vast majority of these women was Graves’ disease, since the incidence of nodular thyroid disease in Danish women 20 to 39 years of age is 5.7% in cases of hyperthyroidism. Hyperemesis gravidarum as a cause of hyperthyroidism was excluded because patients continued to fill prescriptions for ATD medications after the first trimester of pregnancy.

In comparison, the incidence of RA was low in pregnancy and increased in the postpartum period. As compared with hyperthyroidism, much less incidence variation of IBD in and around pregnancy was observed, and there was no statistically significant early pregnancy or postpartum surge. The authors suggest that further studies of autoimmune thyroid disease and other autoimmune disorders are needed to clarify the interaction between pregnancy and onset of disease and the possible different mechanisms involved.

References

The Incidence of Graves’ Hyperthyroidism Increases in Early Pregnancy and the Late Postpartum Period

Jorge H. Mestman


