

# Smoking in Pregnancy Increases Subsequent Maternal Hyperthyroidism Risk but Protects Against Subsequent Hypothyroidism

Elizabeth N. Pearce

Andersen SL, Olsen J, Wu CS, Laurberg P. Smoking reduces the risk of hypothyroidism and increases the risk of hyperthyroidism: evidence from 450,842 mothers giving birth in Denmark. Clin Endocrinol (Oxf). July 1, 2013 [Epub ahead of print].

## SUMMARY ●●●●●●●●●●●●●●●●●●

### Background

It has previously been shown that smoking increases the risk for Graves' disease and for Graves' ophthalmopathy (1,2). However, relationships between smoking and hypothyroidism have been inconsistent across studies. Smoking cessation was recently observed to be associated with a transiently increased risk for autoimmune hypothyroidism (3). The goal of this study was to determine associations between maternal smoking in pregnancy and the subsequent risk for thyroid dysfunction in a large population sample.

### Methods

This retrospective study was performed using data from linked Danish registries. All children born in Denmark between 1996 and 2008 were identified using a national birth registry. Maternal thyroid dysfunction and smoking status were ascertained using the Danish National Hospital Register, which includes inpatient and outpatient diagnosis codes. The Danish National Prescription register was used to obtain information about prescriptions for thyroid hormone and antithyroid drugs dispensed between 2005 and 2008. Hyperthyroidism was defined as a first-time hospital diagnosis of hyperthyroidism with prescription of an antithyroid medication or at least two dispensed prescriptions of antithyroid medication. Similarly, hypothyroidism was defined as a first-time hospital diagnosis of hypothyroidism with at least one thyroid hormone prescription or at least two prescriptions of thyroid hormone without any antithyroid medications.

Sociodemographic information was obtained from Statistic Denmark. Area of residence was used as a proxy for dietary iodine status. Cox proportional-hazards models were used to determine the risk of incident hyperthyroidism and hypothyroidism in smoking versus nonsmoking mothers, stratified by age, amount of smoking, and area of residence.

### Results

A total of 450,842 mothers (mean age, 29 years) were included in the analyses, of whom 19.7% smoked during the first pregnancy within the study period. Overall, 2.9% of women had thyroid dysfunction during the study period. Following pregnancy, hyperthyroidism developed in 1.03% of smokers and 0.68% of nonsmokers ( $P < 0.001$ ) over a mean follow-up of 4.2 years. After pregnancy, hypothyroidism developed in 1.27% of nonsmokers and 1.03% of smokers ( $P < 0.001$ ). The protective effects of smoking on hypothyroidism risk were most marked within the 2 years following delivery; (hypothyroidism developed in 0.35% of nonsmokers and 0.18% of smokers within 2 years;  $P < 0.001$ ) and in younger mothers (hazard ratio [HR], 0.54 [95% CI, 0.43 to 0.68] in women under age 30 and 0.78 in women older than 30 [95% CI, 0.70 to 0.86]). The risk of hyperthyroidism was increased in older mothers who smoked (HR, 1.26 [95% CI, 1.13 to 1.40] for women under age 30; and HR, 1.51 [95% CI, 1.35 to 1.69] for women 30 years or older). Smoking increased the risk for both Graves' disease (HR, 1.44; 95% CI, 1.28 to 1.62) and toxic nodular goiter (HR, 1.60; 95% CI, 1.16 to 2.21). Iodine status did not alter any of these associations.

*continued on next page*

# Smoking in Pregnancy Increases Subsequent Maternal Hyperthyroidism Risk but Protects Against Subsequent Hypothyroidism

## Conclusions

Smoking among pregnant women increases the risk for the subsequent development of hyperthyroid-

ism, but it appears to protect against the subsequent development of hypothyroidism.

## ANALYSIS AND COMMENTARY ● ● ● ● ●

A major strength of this study is the very large sample size. Future studies are needed to determine whether effects of smoking on the risk for thyroid dysfunction are durable over a longer follow-up period and how changes in smoking behavior affect thyroid risk. This study did not address any effects of maternal smoking on fetal or neonatal thyroid function.

These results are in accordance with previous data demonstrating that smoking is a risk factor for the exacerbation of Graves' hyperthyroidism. The mechanisms for this remain unknown. Thiocyanate, a metabolite of cigarette smoke, is an inhibitor of the sodium iodide symporter. Therefore, smoking might have been expected to increase the risk for hypothyroidism, especially in iodine-deficient women. Surprisingly, smoking appeared to protect against the development of hypothyroidism in this cohort.

Although antithyroid antibodies were not assessed in this study, smoking has previously been associated with a decreased risk for thyroid autoantibody positivity (4), which may be the reason for the protective effect against hypothyroidism.

How should these data alter clinical practice? Although the proportion of U.S. women who smoke during pregnancy has decreased substantially over the past two decades, in 2005, a total of 10.7% of U.S. pregnant women were still smokers (5). There are many reasons to counsel against smoking during pregnancy apart from the increased risk for hyperthyroidism, including increased risks for low-birth-weight infants, preterm delivery, and infant death (6). Providers should be particularly alert to signs and symptoms of hyperthyroidism among women who smoke during pregnancy, especially within the first 2 years after delivery.

## References

1. Asvold BO, Bjørø T, Nilsen TI, Vatten LJ. Tobacco smoking and thyroid function: a population-based study. *Arch Intern Med* 2007;167:1428-32.
2. Holm IA, Manson JE, Michels KB, Alexander EK, Willett WC, Utiger RD. Smoking and other lifestyle factors and the risk of Graves' hyperthyroidism. *Arch Intern Med* 2005;165:1606-11.
3. Carlé A, Bülow Pedersen I, Knudsen N, Perrild H, Ovesen L, Banke Rasmussen L, Jørgensen T, Laurberg P. Smoking cessation is followed by a sharp but transient rise in the incidence of overt autoimmune hypothyroidism—a population-based, case-control study. *Clin Endocrinol (Oxf)* 2012;77:764-72.
4. Belin RM, Astor BC, Powe NR, Ladenson PW. Smoke exposure is associated with a lower prevalence of serum thyroid autoantibodies and thyrotropin concentration elevation and a higher prevalence of mild thyrotropin concentration suppression in the third National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2004;89:6077-86.
5. Martin JA, Hamilton BE, Sutton PD, et al.; Centers for Disease Control and Prevention; National Center for Health Statistics. Births: final data for 2005. *Natl Vital Stat Rep* 2007;56:1-103.
6. Women and smoking: a report of the Surgeon General. Washington, DC: Department of Health and Human Services, 2001.