Maternal Thyroid Hormones in Early Pregnancy and Risk of Breech Presentation

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Abstract

Objective: To evaluate the relationship between breech presentation at term (≥ 37 weeks of gestation) and maternal thyroid hormone activity in early gestation.

Methods: We conducted a case–control study of thyroid hormone activity in 179 women who delivered a live term infant in breech presentation (cases) and 849 women who delivered a live term infant in cephalic presentation (control subjects). We used serum samples from prenatal screening at 15 to 16 weeks of gestation in 2006 and 2007 in Edmonton, Alberta. Maternal free thyroxin (fT4) and thyroid-stimulating hormone (TSH) were assayed. Logistic regression was used to estimate the odds of breech presentation in relation to the levels of thyroid hormones while controlling for potential confounders.

Results: There were no significant differences between the breech and cephalic groups when comparing fT4 levels (OR 0.94 per pmol/L; 95% CI 0.88 to 1.00) or TSH levels (OR 1.16 per mU/L; 95% CI 0.97 to 1.38) levels, after adjustment for all potential confounders. Segregating fT4 and TSH into quintiles showed the same pattern. Neither hypothyroidism nor hyperthyroidism was associated with risk of breech presentation.

Conclusion: Our results provide evidence that maternal thyroid hormone levels at 15 to 16 weeks of gestation are not related to risk of breech presentation at birth in term infants.

Résumé

Objectif : Évaluer la relation entre la présentation du siège à terme (≥ 37 semaines de gestation) et l'activité hormonale thyroïdienne maternelle aux débuts de la gestation.

Méthodes : Nous avons mené une étude cas-témoins portant sur l'activité hormonale thyroïdienne chez 179 femmes qui ont accouché d'un enfant vivant à terme en présentation du siège (cas) et chez 849 femmes qui ont accouché d'un enfant vivant à terme en présentation céphalique (témoins). Nous avons utilisé des prélèvements sériques issus du dépistage prénatal à 15–16 semaines de gestation en 2006 et en 2007 à Edmonton, en Alberta. Les taux maternels de thyroxine libre (fT4) et de thyréostimuline (TSH) ont été déterminés. Une régression logistique a été utilisée pour estimer les risques de présentation du siège en relation avec les taux d'hormones thyroïdiennes, tout en neutralisant les effets de variables confusionnelles potentielles.

Résultats : Nous n'avons constaté aucune différence significative entre les groupes « siège » et « céphalique » en matière de taux de fT4 (RC, 0,94 par pmol/l; IC à 95 %, 0,88 – 1,00) ou de TSH (RC, 1,16 par mU/l; IC à 95 %, 0,97 – 1,38), à la suite de la neutralisation des effets de toutes les variables confusionnelles potentielles. La ségrégation des taux de fT4 et de TSH en quintiles a donné lieu au même profil. Ni l'hypothyroïdisme ni l'hyperthyroïdisme n'ont été associés au risque de présentation du siège.

Conclusion : Nos résultats indiquent que les taux maternels d'hormones thyroïdiennes à 15-16 semaines de gestation ne sont pas liés au risque de présentation du siège à la naissance chez les enfants à terme.

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INTRODUCTION

Breech presentation occurs in approximately 3% to 4% of term deliveries[1,2] and is associated with high rates of fetal morbidity and mortality.[2] Even if rates of fetal morbidity and mortality may not increase in normal term breech deliveries,[3] they are still associated with increased maternal morbidity and mortality and higher health care costs because of the increased need for Caesarean section.[4,5]

Prematurity, multiple gestation, nulliparity, advanced parity, pelvic tumours and abnormalities, uterine anomalies, polyhydramnios, oligohydramnios, fundal implantation of the placenta, placenta previa, congenital fetal abnormalities, and previous breech delivery have all been reported to be predisposing factors for breech delivery.[1,6] Some other factors reported to be associated with breech delivery include short umbilical cord, low birth weight, intrauterine growth restriction, maternal smoking during pregnancy, advanced maternal age, and pre-existing maternal diabetes.[3,7] Despite identification of these risk factors, the etiology of most breech presentations has remained largely unknown[6] and therefore demands further investigation.

Pop et al.[8] first postulated that a deficit in thyroid hormone production in pregnancy could contribute to the risk of breech presentation. This idea was based on the observation that isolated maternal hypothyroxinemia (defined as an fT4 level below the 10th percentile, with a normal TSH level) in early gestation is a risk factor for motor and cognitive delay up to the age of two years.[9,10] Thyroid hormones are necessary for normal fetal brain development, and the fetal thyroid gland becomes fully functional only after 18 to 20 weeks of gestation.[11] Therefore, it has been hypothesized that fetal movement is necessary to establish a cephalic presentation and that early maternal shortage of thyroid hormone could affect fetal presentation at birth by an effect on intrauterine development and activity. [8] Pop et al. tested this hypothesis in a cohort study in the Netherlands by comparing women with a fT4 level below the 10th percentile (12.4 pmol/L) at 12 weeks of gestation with control subjects (matched for gravidity and parity) who had a fT4 level between the 50th and 90th percentiles at 12 weeks of gestation. Women found to be overtly hypothyroid or hyperthyroid at 12 weeks' gestation were excluded from their study. They observed that a maternal fT4 level lower than the 10th percentile at 12 weeks, but not at 24 or 32 weeks, was associated with a higher rate of breech delivery at term (OR 4.7; 95% CI 1.1 to 19); however, they did not observe any significant difference between the rates of breech and cephalic deliveries at term in women with subclinical hypothyroidism or hyperthyroidism at 12, 24, or 32 weeks of gestation.[8] Their results were based on a total of only 12 cases of breech presentation, leading to a highly imprecise estimate of risk. As argued by Poole,[12] this suggests that the initial findings were not robust. Further, exclusion of even subclinical hyperthyroid and hypothyroid women did not allow Pop et al.[8] to study the effect of either TSH levels or the full range of fT4 levels.

When Kuppens et al.[13] subsequently tested this hypothesis in a cohort study of 1058 term pregnancies in the same region of the Netherlands as the study of Pop et al.,[8] no association between fT4 levels and breech deliveries was found. However, it was observed that women who gave birth to term infants with a breech presentation had higher TSH levels than women with a cephalic presentation at 36 weeks' gestation, but not at 12 or 24 weeks' gestation (median TSH 1.60 vs. 1.30 mU/L, $P = 0.007$). In addition, a maternal TSH level above the 90th percentile (≥ 2.5 mU/L) at 36 weeks of gestation was found to be predictive of breech presentation at term (OR 1.55; 95% CI 1.14 to 2.10). The study of Kuppens et al.[13] was based on 58 cases of breech deliveries, 12 of which were in women with a TSH level above the 90th percentile. Again, the low number of breech deliveries in this study precludes a definitive conclusion about the hypothesis posited by Pop et al.[8]

Another recent cohort study of singleton pregnancies in Finland,[14] evaluating obstetrical outcomes, thyroid dysfunction, and antithyroid antibodies, found no association between maternal clinical and subclinical hypothyroidism and hyperthyroidism in early pregnancy (12 to 20 weeks of gestation) and non-cephalic presentation at birth.[14] Although this study had a relatively large number of non-cephalic deliveries (n = 193), this number included non-cephalic presentations other than breech, and both term and preterm deliveries. In addition, the statistical results were not adjusted for preterm deliveries. The other limitation of this study was the use of clinical definitions for thyroid disorders and clinical cut-off points of serum fT4 and TSH that were not specific for perinatal outcomes, which made it impossible to reach comprehensive conclusions about the possible effect of thyroid hormones on fetal presentation.

We set out to conduct an epidemiologically efficient study of breech presentation in relation to maternal thyroid hormone levels, using a case–control design nested in a prospective cohort to ensure that we had sufficiently large numbers of breech presentations to draw reliable conclusions. Specifically, we set out to investigate whether breech presentation in term singleton pregnancies is related to depressed fT4 and elevated TSH levels in mothers at 15 to 16 weeks of gestation, a time in gestation when the maternal thyroid produces the majority of these hormones, i.e., fetal thyroid hormones largely derive from maternal hormones crossing the placenta.

METHODS

We conducted a nested case–control study of term (≥ 37 weeks of gestation) singleton live births. Those with breech presentation at birth constituted the study group ("cases") and the control group consisted of those with a cephalic presentation. Cases of multiple gestation, stillbirth, infants with major congenital anomalies (as observed at delivery record), women with blood samples drawn outside the range 15 to 16 weeks of gestation, and cases of preterm birth (< 37 weeks of gestation) were excluded. Pregnant women who delivered infants with a cephalic presentation at term were chosen randomly as the control group using the same inclusion and exclusion criteria and the same time period of blood draw.

ABBREVIATIONS

APHP	Alberta Perinatal Health Program
fT4	free thyroxin
PHN	personal health number
TSH	thyroid-stimulating hormone