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Abnormal thyroid function parameters in the second trimester of pregnancy are associated with breech presentation at term: a nested cohort study

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ABSTRACT

Objective: Thyroid dysfunction has been described as a possible risk factor for having an abnormal fetal position at birth. In this study we aim to determine the association between thyroid function in early pregnancy and breech presentation at term.

Study design: We used data from the Amsterdam Born Children and their Development (ABCD) cohort. 3347 pregnant women were included between January 2003 and March 2004 in Amsterdam, the Netherlands. Thyroid function tests were performed between 5 and 37 weeks gestational age (median 12.9 weeks). The main outcome measure was the association between thyroid function in early pregnancy and breech presentation at term. Univariate and multivariate analysis were performed to determine the association between thyroid function and breech presentation.

Results: Increased TSH in pregnancy, defined as thyroid stimulating hormone (TSH) >97.5th percentile (>3.53 mIU/L), was associated with a higher risk for breech presentation at term (aOR 2.32, CI 1.1–4.8, $p = 0.02$) compared to euthyroidism (TSH between 2.5th and 97.5th percentile). After exclusion of overt hypothyroidism and hyperthyroidism the aOR was 2.34 (CI 1.1–5.0, $p = 0.03$). Trimester specific analysis showed a significant association of increased TSH levels (>3.68 mIU/L) in the second trimester with breech presentation (aOR 3.7, CI 1.7–7.8, $p = 0.001$). In the second trimester low free thyroxine (FT4) <2.5th percentile (<6.7 pmol/L) was also associated with breech presentation (aOR 2.5, CI 1.0–6.3, $p = 0.04$).

Conclusions: Increased TSH and decreased FT4 in the second trimester of pregnancy are associated with an increased risk for breech presentation at term. The association of abnormal thyroid parameters in the first of third trimester is still unclear.

Introduction

Breech presentation has a prevalence of 3–5% in term women and is associated with neonatal and maternal morbidity and mortality [1]. Many etiological factors and risk factors for breech presentation have been described, including prematurity, maternal age, BMI, ethnicity, primiparity, pelvic or uterine abnormalities and smoking during pregnancy [2–5]. However they only explain 15% of breech presentations [6]. Pregnant women who present with breech presentation at birth often undergo a caesarean section, which itself is associated with an increased risk for maternal morbidity and mortality and a greater risk for complications, like uterine rupture in subsequent pregnancies [7,8].

Thyroid dysfunction has been described as a possible risk factor for having an abnormal fetal position at birth [9–14]. There are two hypotheses on the potential causal relationship between thyroid stimulating hormone (TSH) levels and the increased risk for breech position. First, maternal thyroid dysfunction might have a negative effect on fetal movements and mobility as motor development of

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children born to hypothyroid mothers is delayed [12]. Fetal movements are necessary to establish a cephalic presentation [15]. The second hypothesis is that thyroid dysfunction has a negative effect on the uterine contractions which are important for final cephalic presentation at term [9]. Thyroid hormones may affect the myometrial contractility [16–18]. Hypothyroid rats have a lower amplitude and frequency of spontaneous rhythmic contractions of the myometrium. This altered contractility might be explained by a reduction of the uterine myometrial Ca^{2+} channel function [19–21]. It has also been reported that hypothyroidism negatively influences uterine morphology, endometrial volume and myometrial muscle layer [22].

To date five studies have reported on a potential association between thyroid disorders and breech presentation at birth. There were two studies that did not find an association between increased TSH and/or low free thyroxine (FT4) levels in the first trimester and breech presentation [11,13]. One case-control study found no differences in mean TSH levels in the first trimester when women presented in breech compared with women with fetuses in the cephalic position [9]. One prospective cohort study found an association between low FT4 levels in the first trimester and breech presentation [12]. Two studies reported an association between increased TSH levels in the third trimester and increased risk for breech presentation [9,10]. In some of the studies the low number of breech deliveries caused difficulties in a precise estimation of the risk because of insufficient statistical power. Moreover, different cut-off levels for plasma TSH and FT4 used in the previous studies hampers direct comparison of the studies. Detection of a possible risk factor for breech presentation is important as breech presentation is associated with maternal and neonatal morbidity and mortality. Alternatively, thyroid disorders are also associated with other pregnancy complications [23]. Therefore, targeted screening for thyroid disease is advised in pregnant women who are at risk for having a possible thyroid disease, e.g. a previous miscarriage or preterm birth [24,25]. If an association with breech presentation exists, targeted screening might be done in women with a previous breech presentation to detect possible thyroid disease and reduce the risk for associated complications in a subsequent pregnancy. Because thyroid disorders are prevalent in pregnancy (2–3%) [26] and the observations from earlier studies are inconsistent, we therefore aim to investigate the association of abnormal TSH and FT4 levels in early pregnancy and breech presentation. This was done in a large Dutch cohort study of more than 3000 pregnant women using population specific reference intervals as spin-off of a large epidemiological study.

Material and methods

Subjects

Our study was nested within a prospective cohort study of pregnant women from the Amsterdam Born Children and their Development (ABCD) study [27]. The main objective of the ABCD study is to determine the role of ethnic background, maternal lifestyle factors and psychosocial conditions on pregnancy outcome and health of the offspring. The ABCD study is a collaborative effort of the Municipal Health Services (GGD) and all hospitals and midwife practices in Amsterdam, the Netherlands. All pregnant women living in the city of Amsterdam were invited to participate at their first visit to an obstetric caregiver between January 2003 and March 2004. The study protocol was approved by the Institutional Review Boards of all Amsterdam hospitals and the Registration Committee of Amsterdam. All participants gave their written informed consent.

Physiological changes in TSH and FT4 occur during pregnancy. Trimester specific reference intervals have been shown to vary substantially between different cohorts [28]. Reference intervals are influenced by ethnicity, iodine status, TPO-Ab status and analytical method used for TSH quantification [29,30]. There is a clear need for population-based, trimester-specific reference intervals of thyroid hormone levels in pregnancy as this will improve diagnosis and treatment of thyroid disorders. Therefore we chose to define abnormal thyroid function based 2.5th and 97.5th percentiles in order to analyse the association with breech presentation in a large cohort with population specific reference intervals. Subjects with normal TSH levels (between 2.5th and 97.5th percentile of the study population) were compared to subjects with high TSH levels >97.5th percentile and low TSH <2.5th percentile. In addition, we compared subjects with normal FT4 levels (between 2.5th and 97.5th percentile of the study population) with subjects with low FT4 levels <2.5th percentile or high FT4 levels >97.5th percentile. Women that already used thyroid hormone therapy or thyreostatic drugs were excluded. Blood samples were analysed after delivery and therefore no intervention in case of an abnormal TSH or FT4 level was started during pregnancy.

Baseline characteristics

All pregnant women received a questionnaire at their home address within two weeks after their first antenatal visit. The questionnaire contained questions on demographics, health history, medication and lifestyle [31,32]. Ethnicity, smoking status during pregnancy, parity, female age, BMI (before pregnancy) and the use of thyroid medication were determined from the self-reported information and completed by information from the national obstetric registry (Perinatal Registration centre of the Netherlands). Information on birth weight, gestational age and fetal sex was based on data from the Youth Health Care Registration of Amsterdam's Municipal Health Services. Gestational age was based on ultrasound data or, and if ultrasound data were unavailable on the first day of last menstrual period. Information about the fetal position at birth was obtained from the national obstetric registry (Perinatal Registration centre of the Netherlands) after additional informed consent.

Assays

TSH (reference range, 0.34–5.60 mIU/L) and free thyroxine (FT4) concentration (reference range, 7.5–21.1 pmol/L) were measured in serum by means of Access immunoanalyzer of Beckman Coultier, Inc. The inter-assay variation for TSH was 5.0% and for free T4 3.1– 5.0%. Antibodies against Thyroid Peroxidase (TPO-Ab) were determined by Elisa ELIZEN TG Ab (E-CK-96), Zentech, Luik, Belgium. The inter-assay variation was 13.4%. A TPO-ab titre above 80 kIU/L was considered as positive.

Outcomes

The primary outcome was breech presentation at term.

Statistical analysis

The blood samples were not taken at the same gestational age for all women. Because thyroid function changes physiologically during pregnancy, we corrected TSH and FT4 levels for the gestational age at time of the blood sample (range 34–262 days of gestational age). The data showed a linear association between TSH and gestational age [29]. TSH levels were corrected with linear regression (Formula: $TSHcorrected = TSH - (timebloodsampling - 94) * 0.002$). FT4