Maternal Thyroid Hypofunction and Pregnancy Outcome

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OBJECTIVE: To estimate whether maternal thyroid hypofunction is associated with complications.

METHODS: A total of 10,990 patients had first- and second-trimester serum assayed for thyroid-stimulating hormone (TSH), free thyroxine (freeT4), and antithyroglobulin and antithyroid peroxidase antibodies. Thyroid hypofunction was defined as 1) subclinical hypothyroidism: TSH levels above the 97.5th percentile and free T4 between the 2.5th and 97.5th percentiles or 2) hypothyroxinemia: TSH between the 2.5th and 97.5th percentiles and free T4 below the 2.5th percentile. Adverse outcomes were evaluated. Patients with thyroid hypofunction were compared with euthyroid patients (TSH and free T4 between the 2.5th and 97.5th percentiles). Patients with and without antibodies were compared. Multivariable logistic regression analysis adjusted for confounders was used.

RESULTS: Subclinical hypothyroidism was documented in 2.2% (240 of 10,990) in the first and 2.2% (243 of 10,990) in the second trimester. Hypothyroxinemia was documented in 2.1% (232 of 10,990) in the first and 2.3% (247 of 10,990) in the second trimester. Subclinical hypothyroidism was not associated with adverse outcomes. In the first trimester, hypothyroxinemia was associated with preterm labor (adjusted odds ratio [aOR] 1.62; 95% confidence interval [CI] 1.00–2.62) and macrosomia (aOR 1.97; 95% CI 1.37–2.83). In the second trimester, it was associated with gestational diabetes (aOR 1.7; 95% CI 1.02–2.84). Fifteen percent (1,585 of 10,990) in the first and 14% (1,491 of 10,990) in the second trimester had antithyroid antibodies. When both antibodies were positive in either trimester, there was an increased risk for preterm premature rupture of membranes ($P=.002$ and $P<.001$, respectively).

CONCLUSION: Maternal thyroid hypofunction is not associated with a consistent pattern of adverse outcomes.

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LEVEL OF EVIDENCE: II

Although it is established that overt hypothyroidism in pregnancy is detrimental to the developing fetal brain, the effect of asymptomatic thyroid hypofunction on pediatric neurodevelopment is controversial.[1–4] Since 1999, several provocative studies have proposed that mild thyroid hypofunction during pregnancy affects brain development in utero and seems to be associated with abnormal pediatric neurologic outcome.[5–9] Antithyroid antibodies may also have an influence on the fetal brain and subsequent pediatric neurodevelopment.[10–12] Obstetric factors may be responsible for some of the differences in neurologic outcomes seen in the offspring of women with maternal thyroid hypofunction compared with their euthyroid counterparts.[4,13]

The purpose of this study was to estimate if maternal thyroid hypofunction, diagnosed during the first or second trimesters, affects obstetric outcomes in

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a subset of patients from the First And Second Trimester Evaluation of Risk (FASTER) Trial. The relationship between antithyroid antibodies in the first and second trimesters and obstetric outcomes was also explored.

MATERIALS AND METHODS

The FASTER Trial, a National Institute of Child Health and Human Development–sponsored study, was a prospective multicenter investigation of singleton pregnancies from an unselected obstetric population. From October 1, 1999, to December 31, 2002, this study evaluated first-trimester nuchal translucency measurements, along with first- and second-trimester serum markers for the purpose of assessing Down syndrome risk at 15 centers throughout the United States.[14] The FASTER Trial was approved by the institutional review board at each of the 15 participating study sites. After written informed consent was obtained, patients were enrolled between 10 3/7 and 13 6/7 weeks of gestation. All subjects had a live singleton intrauterine pregnancy without evidence of anencephaly or cystic hygroma, confirmed by ultrasonography at the time of trial enrollment.

A database was created containing detailed antenatal, birth, and pediatric outcomes on all enrolled patients. Postdelivery follow-up was performed by medical record review by the research coordinator at each site or by telephone interview of the patient. A single perinatologist and a pediatric geneticist reviewed detailed maternal and pediatric medical records for the following patient subsets: abnormal first- and/or second-trimester screening, adverse obstetric or pediatric outcomes, and 10% of normal subjects randomly selected at each site from the trial database. A purpose-designed computerized tracking system with up to 10 contacts per subject was used to ensure complete outcome collection. Pregnancy and pediatric outcomes were obtained in more than 98% of cases.

In five of 15 original FASTER sites, patients were given the option to consent to the use of residual serum for future research studies. Blood samples from assenting patients without fetal aneuploidy in which matched first- and second-trimester specimens of sufficient volume were available were included in this study. All samples and all data were made anonymous, and the results were not used in clinical practice. Institutional review board approval for this study was granted by the Columbia University Medical Center, New York and by Women and Infants Hospital, Brown University, Rhode Island.

First- and second-trimester maternal serum samples were assayed for levels of thyroid-stimulating hormone (TSH), free thyroxine (free T4), antithyroglobulin (anti-TG) antibodies, and antithyroid peroxidase (anti-TPO) antibodies, using chemiluminescent immunoassays on an automated platform (Immulite 2000 Analyzer; Siemens Medical Solutions Diagnostics., Los Angeles, CA) at the Division of Prenatal and Special Testing at Women and Infants Hospital. The TSH assay had a reported analytic sensitivity of 0.002 milliunits/L, and free T4 had an analytic sensitivity of 0.18 ng/dL. The anti-TG and anti-TPO assay sensitivities were 10 milliunits/L and 5.0 milliunits/L, respectively. Quality control samples were run daily, and the laboratory participated in an external proficiency survey for quality assurance. Results for each sample were recorded in a Microsoft Excel database.

Maternal thyroid hypofunction was defined as 1) subclinical hypothyroidism: TSH more than the 97.5th percentile and free T4 between the 2.5th and 97.5th percentiles or 2) hypothyroxinemia: TSH between the 2.5th and 97.5th percentiles and free T4 less than the 2.5th percentile.[15] Patients were considered antibody positive if the anti-TG antibody was greater than 40 international units/mL and/or if the anti-TPO antibody was greater than 35 international units/mL. Antibody negative was defined as anti-TG antibody less than 40 international units/mL and anti-TPO antibody less than 35 international units/mL.

The following adverse pregnancy outcomes were evaluated: miscarriage (fetal loss after enrollment but before 24 0/7 weeks), gestational hypertension (blood pressure more than 140/90 mmHg on at least two occasions greater than 6 hours apart without evidence of chronic hypertension or significant proteinuria), preeclampsia (criteria for gestational hypertension plus significant proteinuria), gestational diabetes (two abnormal values on a 3-hour glucose challenge test), placenta previa (placenta completely or partially covering the internal cervical os at the time of delivery), placental abruption (premature separation of a normally implanted placenta), preterm labor (persistent uterine contractions accompanied by cervical change on digital examination before 37 weeks of gestation), preterm premature rupture of membranes (PROM; membrane rupture before 37 weeks of gestation), preterm delivery (delivery before 37 weeks of gestation), low birth weight (birth weight of less than 2,500 g), macrosomia (birth weight of greater than 4,000 g), and perinatal mortality (intrauterine death after 23 6/7 weeks of completed gestation or neonatal death within 28 days of birth).

Potential confounding factors included maternal age, race, parity, body mass index, level of education, marital status, smoking, history of medical problems,

previous adverse pregnancy outcome, history of assisted conception such as ovulation induction or artificial reproductive technology (in vitro fertilization-transcervical embryo transfer, gamete and zygote intrafallopian transfer, frozen embryo transfer, or donor embryo transfer), and patient's study site.

Two independent samples *t* tests and χ^2 tests were used to assess the relationships between continuous and categorical confounding variables and maternal thyroid hypofunction. We used χ^2 tests to assess the unadjusted associations between maternal thyroid hypofunction and obstetric outcomes and between the presence of antithyroid antibodies and pregnancy outcomes. Multivariable logistic regression analysis was used to assess the associations between maternal thyroid hypofunction and obstetric outcomes adjusted for confounders. Because the numbers of outcome events were small, multivariable models were developed to adjust for a small number of confounders. Specifically, adjustments were made for maternal age, prior pregnancy, body mass index, and site.

RESULTS

A total of 38,033 patients enrolled in the FASTER Trial; 10,990 patients without fetal aneuploidy had consent to use stored serum and matched first- and second-trimester samples with adequate volume (Table 1). In the first trimester, 2.2% (240 of 10,990) were found to have subclinical hypothyroidism; 2.1% (232 of 10,990) were found to have hypothyroxinemia; less than 1% (33 of 10,990) were found to have overt hypothyroidism; 91% (10,021 of 10,990) were found to be euthyroid (TSH and free T4 between the 2.5th and 97.5th percentiles); and 4% (444 of 10,990) did not fit into any category. In the second trimester, 2.2% (243 of 10,990) were found to have subclinical hypothyroidism; 2.3% (247 of 10,990) were found to have hypothyroxinemia; less than 1% (22 of 10,990) were found to have overt hypothyroidism; 91% (9,981 of 10,990) were found to be euthyroid; and 4.4% (477 of 10,990) did not fit into any category. Table 2 demonstrates the range of values of TSH and free T4 making up the low (less than the 2.5th percentile), normal (between the 2.5th and 97.5th percentiles), and high (greater than the 97.5th percentile) categories.

Table 1. Comparison of the Demographic Characteristics of Patients Included and Not Included in This Study

Characteristic	Not Included (n=27,042)	Included (n=10,990)	*P*
Age (y)	30.3±5.9	29.6±5.6	<.01
Race			
White	59.0	86.6	<.01
African American	6.8	1.7	
Hispanic	28.9	7.2	
Prior pregnancy	68.6	68.5	.85
Parity	0.8±1.0	1.0±1.2	<.01
Body mass index	25.1±5.4	24.8±5.1	<.01
Education (y)	14.2±2.8	14.6±2.0	<.01
Married	72.5	91.4	<.01
Current smoker	5.6	3.0	<.01
History of chromosomal abnormality	1.5	0.9	<.01
ART in current pregnancy	5.2	4.4	<.01

ART, assisted reproductive technology.
Data are mean±standard deviation or %.

In both trimesters, there were statistically significant differences between the groups with regard to age, race, history of prior pregnancy, parity, body mass index, education, and marital status (Tables 3 and 4). Subclinical hypothyroidism in either the first or the second trimester was not associated with an increased risk for pregnancy complications. In the first trimester, hypothyroxinemia was associated with preterm labor and weight more than 4,000 g (adjusted odds ratio 1.62; 95% confidence interval [CI] 1.00–2.62 and 1.97; 95% CI 1.37–2.83, respectively). In the second trimester, it was associated with gestational diabetes (adjusted odds ratio 1.7; 95% CI 1.02–2.84) (Tables 5 and 6; Tables 7 and 8).

Approximately 15% of patients were antithyroid antibody positive in the first and in the second trimesters (Table 9). The presence of antithyroid antibodies in the first trimester was highly correlated with the presence of antithyroid antibodies in the second trimester and vice versa (Pearson correlation analysis; anti-TG: $r=0.929$; $r^2=0.863$; and anti-TPO: $r=0.948$; $r^2=0.899$). Patients with antithyroid antibodies had higher TSH levels ($P<.001$).

When both antibodies were positive together in the first trimester or in the second trimester, preterm PROM was noted to be significantly increased

Table 2. Actual Thyroid-Stimulating Hormone and Free Thyroxine Values (N=10,990)

	First Trimester	Second Trimester
TSH (milliunits/L)		
Less than 2.5th percentile	0.004–0.035	0.004–0.212
2.5th to 97.5th percentile	0.036–4.28	0.213–3.93
More than 97.5th percentile	4.29–67.0	3.94–67.5
Free thyroxine (ng/dL)		
Less than 2.5th percentile	0.3–0.71	0.3–0.71
2.5th to 97.5th percentile	0.72–1.46	0.72–1.32
More than 97.5th percentile	1.47–6.0	1.33–6.0

TSH, thyroid-stimulating hormone.

Table 3. First-Trimester: Comparison of the Demographic Characteristics of Patients With Thyroid Hypofunction Compared With Euthyroid Patients

Characteristic	Subclinical Hypothyroid (n=240)	Hypothyroxinemia (n=232)	Euthyroid (n=10,021)	*P*
Age (y)	29.8±5.7	31.6±5.6	29.5±5.6	<.001
Race				.019
White	90.8	83.2	87.0	
African American	–	3.9	1.6	
Hispanic	5.4	9.5	7.2	
Prior pregnancy (%)	67.8	79.3	68.0	.001
Parity	1.1 + 1.2	1.6±1.6	1.0±1.2	<.001
Body mass index	24.5±4.5	27.3±5.8	24.8±5.1	<.001
Education (y)	14.8±1.9	14.3±2.0	14.6±2.0	.010
Married	95.0	87.5	91.4	.015
Current smoker	2.1	6.1	2.9	.016
History of chromosomal abnormality	–	–	0.10	.790
ART in current pregnancy	5.4	2.2	4.4	.183

ART, assisted reproductive technology.
Data are mean ±standard deviation or %.

(*P*=.002 and *P*<.001, respectively) compared with patients without antithyroid antibodies. In the first trimester, preterm PROM was diagnosed in 3% of patients with both antibodies compared with 1% of patients without antibodies (odds ratio 2.4; 95% CI 1.4–4.1). In the second, preterm PROM was present in 4% of patients with both antibodies compared with 1% of patients without (odds ratio 3.1; 95% CI 1.8–5.2). No other differences were noted when adverse pregnancy outcomes were compared between the two groups in either trimester.

DISCUSSION

Women with thyroid hypofunction during pregnancy may have subtle hormone abnormalities that may be asymptomatic but suboptimal for the developing fetal brain. Early in pregnancy, maternal free T4 is imperative because the fetal thyroid gland does not produce this hormone until after 10 weeks.[16–19] At that point, the presence of fetal free T4 is necessary for optimal fetal neurodevelopment.[16,20]

In this study, adverse obstetric outcomes were not associated with subclinical hypothyroidism in either the first or the second trimester. Hypothyroxinemia was not associated with the majority of pregnancy complications, and with regard to an association with adverse outcomes, the findings were not consistent across trimesters. Hypothyroxinemia was associated with preterm labor and birth weight greater than 4,000 g in the first trimester and with the development of gestational diabetes in the second trimester.

Table 4. Second-Trimester: Comparison of the Demographic Characteristics of Patients With Thyroid Hypofunction Compared With Euthyroid Patients

Characteristic	Subclinical Hypothyroid (n=247)	Hypothyroxinemia (n=243)	Euthyroid (n=9,981)	*P*
Age (y)	29.6±5.5	31.5±5.1	29.5±5.6	<.001
Race				<.001
White	88.5	76.9	87.1	
African American	–	4.5	1.6	
Hispanic	7.8	15.4	7.0	
Prior pregnancy	70.3	79.0	68.1	.001
Parity	1.1 + 1.1	1.2±1.4	1.0±1.2	.014
Body mass index	23.9±4.2	27.6±5.7	24.7±5.1	<.001
Education (y)	14.8±1.9	14.3±2.1	14.6±2.0	.003
Married (%)	94.7	85.0	91.5	<.001
Current smoker	2.1	4.5	3.0	.286
History of chromosomal abnormality	0.4	–	0.1	.245
ART in current pregnancy	2.5	5.3	4.4	.276

ART, assisted reproductive technology.
Data are mean±standard deviation or %.

Table 5. First-Trimester Thyroid Hypofunction and Pregnancy Outcome

Outcome	Subclinical Hypothyroid (%)	Euthyroid (%)	Unadjusted Odds Ratio	Unadjusted 95% CI	Adjusted* Odds Ratio	Adjusted* 95% CI
Miscarriage	0.4	0.6	0.68	0.09–4.89	0.69	0.10–5.00
Gestational hypertension	3.8	5.5	0.68	0.34–1.33	0.72	0.37–1.42
Preeclampsia	0.9	1.0	0.88	0.22–3.60	0.99	0.24–4.07
Gestational diabetes	2.6	3.0	0.84	0.37–1.91	0.86	0.37–1.96
Placenta previa	0.4	0.4	0.98	0.13–7.11	0.98	0.13–7.12
Placental abruption	0.9	0.9	1.00	0.25–4.09	0.98	0.24–4.02
Preterm labor	6.0	6.1	0.98	0.57–1.70	0.99	0.57–1.72
Preterm PROM	2.1	1.3	1.58	0.64–3.89	1.63	0.66–4.03
Delivery less than 37 wk	5.6	7.2	0.76	0.43–1.34	0.78	0.44–1.37
Birth weight less than 2,500 g	2.6	4.2	0.61	0.27–1.37	0.62	0.28–1.41
Birth weight more than 4,000 g	4.3	8.9	0.46	0.24–0.86	0.47	0.25–0.89
Perinatal mortality	0.0	0.3	–	–	–	–

PROM, premature rupture of membranes.
*Adjusted for maternal age, prior pregnancy, body mass index, and study site.

Although this study had more than 10,000 patients, the number of patients with maternal thyroid hypofunction was small. Many adverse pregnancy outcomes are uncommon (0 to 10% incidence), and differences between groups may not have been possible to detect with this small number of patients with maternal thyroid hypofunction.

It was interesting to note that the presence of both antithyroid antibodies in either trimester is associated with an increased risk for preterm PROM. These antibodies may be a marker for an inflammatory process making women susceptible to this complication.

The literature pertaining specifically to maternal thyroid hypofunction and pregnancy outcome is sparse. In a study published in 2005 of 17,298 patients who enrolled in prenatal care at or before 20 weeks gestation, Casey et al[4] compared pregnancy outcomes from women with subclinical hypothyroidism (TSH greater than the 97.5th percentile with free T4 greater than 2.5th percentile) with patients with normal TSH levels (TSH levels between the fifth and the 95th percentiles). In this prospective study, there were 404 patients (2.3%) with subclinical hypothyroidism and 15,689 patients with normal TSH levels. Placental abruption and preterm delivery (birth at or before 34 weeks) were increased in the women with subclinical hypothyroidism (relative risk 3.0 and 1.8, respectively). The authors speculate that prematurity may be the link between decreased neurodevelopment in

Table 6. First-Trimester Thyroid Hypofunction and Pregnancy Outcome

Outcome	Hypothyroxinemia (%)	Euthyroid (%)	Unadjusted Odds Ratio	Unadjusted 95% Confidence Interval	Adjusted* Odds Ratio	Adjusted* 95% Confidence Interval
Miscarriage	0.0	0.6	–	–	–	–
Gestational hypertension	4.4	5.5	0.79	0.42–1.51	0.74	0.38–1.41
Preeclampsia	1.3	1.0	1.39	0.44–4.42	1.21	0.37–3.94
Gestational diabetes	6.2	3.0	2.13	1.23–3.70	1.45	0.82–2.56
Placenta previa	0.4	0.4	1.02	0.14–7.43	0.98	0.13–7.26
Placental abruption	1.8	0.9	2.11	0.77–5.80	1.91	0.69–5.33
Preterm labor	8.4	6.1	1.43	0.89–2.31	1.62	1.00–2.62
Preterm PROM	1.3	1.4	0.98	0.31–3.10	1.00	0.31–3.18
Delivery less than 37 wk	9.3	7.2	1.33	0.84–2.09	1.15	0.72–1.84
Birth weight less than 2,500 g	2.7	4.2	0.63	0.28–1.43	0.58	0.26–1.32
Birth weight more than 4,000 g	16.9	8.9	2.08	1.46–2.96	1.97	1.37–2.83
Perinatal mortality	0.4	0.3	1.45	0.20–10.67	1.02	0.14–7.61

PROM, premature rupture of membranes.
*Adjusted for maternal age, prior pregnancy, body mass index, and study site.

Table 7. Second-Trimester Thyroid Hypofunction and Pregnancy Outcomes

Outcome	Subclinical Hypothyroid (%)	Euthyroid (%)	Unadjusted Odds Ratio	Unadjusted 95% Confidence Interval	Adjusted* Odds Ratio	Adjusted* 95% Confidence Interval
Miscarriage	0.9	0.6	1.34	0.33–5.49	1.29	0.31–5.36
Gestational hypertension	4.6	5.4	0.86	0.47–1.59	0.99	0.53–1.84
Preeclampsia	0.8	1.0	0.87	0.21–3.55	1.08	0.26–4.43
Gestational diabetes	1.7	3.0	0.56	0.21–1.53	0.63	0.23–1.73
Placenta previa	0.8	0.4	2.03	0.49–8.44	1.96	0.47–8.18
Placental abruption	0.8	0.9	0.93	0.23–3.80	0.93	0.23–3.81
Preterm labor	3.8	6.2	0.60	0.31–1.17	0.61	0.31–1.20
Preterm PROM	1.7	1.4	1.22	0.45–3.33	1.33	0.49–3.64
Delivery less than 37 wk	5.1	7.3	0.69	0.38–1.24	0.71	0.40–1.28
Birth weight less than 2,500 g	2.5	4.2	0.59	0.26–1.34	0.61	0.27–1.40
Birth weight more than 4,000 g	7.6	8.9	0.85	0.52–1.38	0.93	0.57–1.51
Perinatal mortality	0.0	0.3	–	–	–	–

PROM, premature rupture of membranes.
*Adjusted for maternal age, prior pregnancy, body mass index, and study site.

women with subclinical hypothyroidism during pregnancy.

In 2007, Casey et al[15] published a study on maternal hypothyroxinemia (TSH between the 2.5th and 97.5th percentile and free T4 less than the 2.5th percentile) and pregnancy outcomes. This study used samples from the 17,298 patients from the 2005 study. Anti-TPO antibody status was also evaluated. Isolated maternal hypothyroxinemia was found in 233 patients (1.3%), and these women were not at increased risk for adverse pregnancy outcomes. Thirty-one percent of women with subclinical hypothyroidism were found to have anti-TPO antibodies, whereas only 4% of normal women and 5% of women with isolated hypothyroxinemia had them. The authors question the biologic significance of isolated maternal hypothyroxinemia.

It is possible that the increased risk for adverse outcomes in the patients with subclinical hypothyroidism in the 2005 study by Casey et al[4] was secondary to a patient population at risk for poor obstetric outcomes. The patients in Casey's study were medically indigent and delivered at a single university hospital. The patients in the current study were from an unselected obstetric population from several sites from a large research trial on screening for aneuploidy, all of whom entered prenatal care during the first trimester. This population was pre-

Table 8. Second-Trimester Thyroid Hypofunction and Pregnancy Outcome

Outcome	Hypothyroxinemia (%)	Euthyroid (%)	Unadjusted Odds Ratio	Unadjusted 95% Confidence Interval	Adjusted* Odds Ratio	Adjusted* 95% Confidence Interval
Miscarriage	0.0	0.6	–	–	–	–
Gestational hypertension	9.5	5.4	1.85	1.19–2.87	1.55	0.99–2.43
Preeclampsia	1.7	1.0	1.71	0.62–4.69	1.29	0.46–3.59
Gestational diabetes	7.4	3.0	2.62	1.60–4.29	1.70	1.02–2.84
Placenta previa	0.0	0.4	–	–	–	–
Placental abruption	0.4	0.9	0.45	0.60–3.26	0.42	0.06–3.08
Preterm labor	7.0	6.2	1.14	0.69–1.88	1.17	0.71–1.94
Preterm PROM	1.7	1.4	1.19	0.44–3.25	1.05	0.38–2.87
Delivery less than 37 wk	9.1	7.3	1.28	0.82–2.00	1.20	0.77–1.88
Birth weight less than 2,500 g	4.6	4.2	1.08	0.59–2.00	1.09	0.59–2.02
Birth weight more than 4,000 g	13.6	8.9	1.63	1.12–2.36	1.31	0.90–1.92
Perinatal mortality	0.0	0.3	–	–	–	–

PROM, premature rupture of membranes.
*Adjusted for maternal age, prior pregnancy, body mass index, and study site.

Table 9. Presence of Antithyroid Antibodies in the First or Second Trimester (N=10,990)

	First Trimester		Second Trimester	
	n	%	n	%
Antithyroglobulin antibody positive	393	4	350	3
Antithyroid peroxidase antibody positive	674	6	715	7
Both antibodies positive	518	5	426	4
Antibody negative	9,382	85	9,476	86

dominantly white (87%), from the private sector, and included many women who had achieved pregnancy through fertility treatments.

The 1999 study by Pop et al,[5] which indicated that free T4 levels below the fifth and 10th percentiles in the first trimester but not at 32 weeks were associated with lower Bayley Psychomotor Developmental Index scores in offspring at 10 months of age when compared with offspring whose mothers had higher free T4 levels, excluded patients with complicated pregnancies such as preterm delivery and low birth weight. Likewise, in the study by Haddow et al,[6] which suggested that the offspring of women with elevated TSH during pregnancy had lower intelligent quotient scores between the ages of 7 and 9 years than the offspring of women with normal TSH, the mean gestational age at delivery and birth weight were similar for the patients with and without thyroid hypofunction. Thus, it is less likely that prematurity is the main cause of impaired neurodevelopment in the offspring of women with mild thyroid hypofunction during pregnancy.

Long-term pediatric neurodevelopmental outcome was not evaluated in this study. This type of testing is best performed at approximately 7 to 8 years of age. The FASTER Trial offspring are just reaching this age, and the FASTER Consortium is planning a follow-up study to better evaluate the effect of maternal thyroid hypofunction on pediatric neurodevelopment.

In summary, we did not find a link between subclinical hypothyroidism and adverse pregnancy outcomes. Hypothyroxinemia in either the first or second trimesters was not associated with the majority of pregnancy complications. Those that were associated were not consistent across trimesters. A national study is currently ongoing to elucidate the effect of maternal subclinical hypothyroidism and hypothyroxinemia on pediatric neurodevelopment and to determine whether thyroid supplementation improves pediatric outcomes. If thyroid hypofunction is confirmed to contribute to decreased pediatric neurodevelopment, the public health implications will be immense. Until these studies are completed, routine screening for maternal thyroid hypofunction and empiric treatment of this condition in pregnancy is not indicated.[21–23]

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