Maternal Thyroid Antibodies Associates With Cardiometabolic Risk Factors in Children at the Age of 16

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Context and Objective: The objective of this study was to determine the effects of maternal thyroid dysfunction or antibodies during pregnancy on the cardiometabolic risk factors in children.

Design, Setting, and Participants: This prospective population-based cohort study, Northern Finland Birth Cohort 1986, included all pregnancies within a year in the area. Maternal serum samples were collected before the 20th week of gestation and analyzed for thyrotropin, free T4, thyroid-peroxidase antibodies (TPO-Abs), and thyroglobulin antibodies (Tg-Abs). Cardiometabolic risk factors in children at the age of 16 years were evaluated via blood sampling and clinical examination. Data were available for 3229 to 4176 mother–child pairs.

Main Outcome Measures: Waist circumference, blood pressure, lipids and lipoproteins, and insulin resistance were measured. Odds ratios (ORs) with 95% confidence intervals (CIs) of cardiometabolic risk factors in children with and without mothers with thyroid dysfunction or antibodies were calculated with logistic regression and adjusted for covariates.

Results: Children of TPO-Ab–positive mothers had higher odds of metabolic syndrome (OR, 2.57; 95%, CI 1.26 to 5.25) and waist circumference indicative of metabolic syndrome (OR, 1.69; 95% CI, 1.14 to 2.50). They were also more likely to be overweight or obese (OR, 1.56; 95% CI, 1.04 to 2.34). Maternal thyroid dysfunction or Tg-Ab positivity did not associate with cardiometabolic risk factors in children.

Conclusion: Metabolic syndrome, greater waist circumference, and higher body mass index were more prevalent in children of TPO-Ab–positive mothers, indicating an adverse cardiovascular health profile. (***J Clin Endocrinol Metab*** **102: 4184–4190, 2017)**

The intrauterine milieu affects a child's later cardiovascular health (1). The possible factors leading to these effects can be maternal, such as chronic diseases, or environmental, such as smoking and nutrition. Normal thyroid function is essential in maintaining a normal pregnancy (2). Maternal thyroid dysfunction is prevalent in up to 5% of pregnancies, and 5% to 15% of all pregnant women are thyroid autoantibody positive (3, 4). Maternal thyroid hormones and antibodies cross the placenta, and thyroid hormones have an important role in fetal development (5). Therefore, maternal thyroid dysfunction can have serious consequences for the fetus (2, 4–7).

Maternal thyroid dysfunction has been associated with several perinatal complications, poor motor development,

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in USA

Received 17 May 2017. Accepted 5 September 2017.
First Published Online 11 September 2017

Abbreviations: BMI, body mass index; CI, confidence interval; fT4, free thyroxine; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OR, odds ratio; Tg-Ab, thyroglobulin antibody; TPO-Ab, thyroid-peroxidase antibody; TSH, thyrotropin.

and adverse neuropsychological development of the child (4, 8–10). There are very few data on the effects of maternal thyroid dysfunction on the cardiometabolic risk factors of the child. Low maternal thyrotropin (TSH) concentrations have been associated with lower body mass index (BMI), total fat mass, and diastolic blood pressure of the child at the age of 6 years (11). That same study also showed that high maternal free thyroxine (fT4) concentrations are associated with lower childhood BMI (11). Studies on older children or adolescents are, to our knowledge, lacking. Among adults, hypothyroidism has been associated with cardiovascular diseases, but studies concerning cardiovascular disease or its risk factors and thyroid-peroxidase antibody (TPO-Ab) positivity are inconsistent (12–14).

The aim of this study was to investigate the relationship between maternal thyroid dysfunction and antibodies during pregnancy and components of metabolic syndrome in the child at the age of 16 years.

Materials and Methods

The study was based on data of the Northern Finland Birth Cohort 1986, which included all expected deliveries from 1 July 1985 to 30 June 1986 from the two northernmost provinces of Finland. A total of 9362 mothers and 9479 children participated, which covers 99% of all the deliveries in the area during the study period. The cohort has been followed since the first maternity welfare clinic visit from the 8th to the 12th week of gestation, and mothers were recruited to the study by 24th week of gestation (15, 16).

Data on maternal and familial demographics, maternal health, pregnancy, delivery, and neonatal outcomes were collected from the participants during routine visits at communal, free-of-charge maternity welfare clinics (overall participation rate, 99.8% in Finland) and via questionnaires during the index pregnancies.

Since birth, data on the health of the children and familial demographic data have been obtained via visits to free-of-charge community child welfare clinics and via questionnaires, supplemented with data from various national registers. Informed consent was obtained from all subjects. The Ethics Committees of the Northern Ostrobothnia Hospital District and the National Institute for Health and Welfare approved this study.

Study population

After excluding twins (n = 222), those with maternal serum samples drawn after the 20th week of pregnancy (n = 187), those with insufficient or missing maternal samples (n = 3014), and those refusing the use of their data (n = 251), the final population consisted of 3229 to 4176 mother–child pairs (Fig. 1; the numbers vary due to missing data for some of the outcome measures).

Laboratory methods

According to national practice, all mothers underwent infectious disease screening in early pregnancy (mean gestational age at sampling, 10.7 weeks; standard deviation, 2.8). The leftover serum samples were stored thereafter at the premises of the Finnish Maternity Cohort, where they were frozen

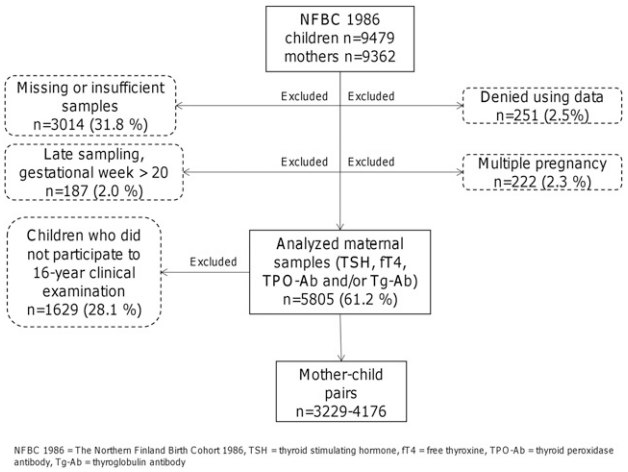

Figure 1. Flowchart of the study population in the Northern Finland Birth Cohort 1986.

at −25°C. These samples (n = 5805; 61.2% of the Northern Finland Birth Cohort 1986 cohort) were analyzed for TSH, fT4, TPO-Abs, and thyroglobulin antibodies (Tg-Abs) using the Abbott Architect i2000 method (Abbott Diagnostics, Abbott Park, IL) in 2006. Laboratory data collection, analysis, and the effect of long-term storage on these laboratory parameters have been reported previously (17, 18). The reference intervals for the population have been established previously (8). Reference intervals for TSH were 0.07 to 3.1 mU/L in the first trimester and 0.10 to 3.5 mU/L in the second trimester. Respective fT4 reference intervals were 11.40 to 22.40 pmol/L and 11.09 to 18.90 pmol/L. Mothers were TPO-Ab or Tg-Ab positive if their antibody concentration was over the 95th percentile of the study population (≥167.7 IU/mL for TPO-Ab and ≥47.7 IU/mL for Tg-Ab). Based on maternal TSH, fT4, TPO-Ab, and Tg-Ab concentrations, the following groups were formed: euthyroidism, hypothyroidism, hyperthyroidism, hypothyroxinemia, TPO-Ab negative, TPO-Ab positive, Tg-Ab negative, and Tg-Ab positive (8, 19).

Outcome data

Clinical follow-up examination of the children at the age of 16 years included measurements of weight, height, waist circumference, and blood pressure. Blood pressure was measured twice 2 minutes apart in a sitting position after 15 minutes rest, and the average of those readings was used (20). BMI was calculated by dividing the body weight in kilograms by the squared height in meters. Waist circumference was measured at the level midway between the lowest rib margin and the iliac crest (21). Adolescents completed questionnaires that included questions about puberty, nutrition, smoking habits, and use of alcohol.

Blood samples were drawn after an overnight fast and were analyzed for glucose, insulin, lipids [total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides] and apolipoprotein A and B (21). Plasma glucose, total cholesterol, HDL, LDL, and triglycerides were determined by enzymatic assay methods, and apolipoprotein A and apolipoprotein B were determined by the turbidimetric immunological method (Cobas Integra 700; Roche Diagnostics, Basel, Switzerland). Serum insulin was analyzed by radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden). Finnish or International Diabetes Federation's recommendations

were used in determining cardiometabolic risk factors (Table 1) (22, 23). However, we used the lowest 10th percentile to determine abnormal insulin sensitivity (measured by homeostatis model assessment) and apolipoprotein A and the highest 90th percentile as a cut-off to determine abnormal β-cell function and apolipoprotein B (Table 1). The metabolic syndrome was defined by International Diabetes Federation criteria for 10- to 16-year-old adolescents, and it was diagnosed when children had abdominal obesity (Table 1) and two or more of the following clinical features: elevated triglycerides, low HDL-cholesterol, high blood pressure, and increased plasma glucose (22).

Statistical analyses

Crosstabs and Fisher's exact test were used to investigate the characteristics of the mothers and the distribution of cardiometabolic risk factors among the children. Odds ratios (ORs) with 95% confidence intervals (CIs) of cardiometabolic risk factors for children with and without mothers with thyroid dysfunction or antibodies were calculated with logistic regression. All results were adjusted for maternal age, smoking, parity, and overweight/obesity. As a sensitivity analysis, we excluded mothers who were diagnosed with diabetes before pregnancy. The data were also stratified by sex of the children. Statistical analyses were performed using SPSS version 22.0 software (SPSS Inc., Chicago, IL).

Results

Data on TSH and fT4 were available for 5779 and 5726 mothers, respectively. TPO-Abs were measured from 5763 mothers and Tg-Abs from 5705 mothers. Complete data on maternal thyroid function, maternal antibody status, and the metabolic parameters of the children were available for 3229 to 4176 mother–child pairs (Fig. 1). Of these children, 51.3% were boys and 48.7% were girls.

Demographic characteristics of the mothers are presented in Table 2. Hyperthyroid ($P < 0.001$), hypothyroxinemic ($P = 0.012$), and Tg-Ab–positive ($P = 0.003$) mothers were older than euthyroid and Tg-Ab–negative mothers. Hypothyroid and Tg-Ab–positive mothers smoked less than euthyroid and Tg-Ab–negative mothers ($P = 0.002$ and $P < 0.001$, respectively). Hyperthyroid ($P < 0.001$), TPO-Ab–positive ($P = 0.048$), and Tg-Ab–positive ($P = 0.005$) mothers had greater parity than euthyroid and TPO-Ab/Tg-Ab–negative mothers. In addition, hypothyroxinemic and Tg-Ab–positive mothers more often had a BMI >25 kg/m^2 than euthyroid and Tg-Ab–negative mothers ($P = 0.028$ and $P = 0.010$, respectively).

Maternal thyroid dysfunction or Tg-Ab positivity was not associated with any cardiometabolic risk factors in children at the age 16 years to a statistically significant degree (Tables 3 and 4). However, children of hypothyroxinemic mothers seemed to have a nonsignificant trend for adverse metabolic outcomes compared with children of euthyroid mothers (Table 3). In addition, maternal hyperthyroidism was associated with better insulin sensitivity in children compared with children of euthyroid mothers (OR, 0.24; 95% CI, 0.06 to 0.99) (Table 3).

Children of TPO-Ab–positive mothers had higher odds of having a metabolic syndrome than children of TPO-Ab–negative mothers (OR, 2.57; 95% CI, 1.26 to 5.25) (Table 4; Fig. 2). Of the components of the metabolic syndrome, an association with maternal TPO-Ab positivity was seen only with waist circumference (OR, 1.69; 95% CI, 1.14 to 2.50) but not with other components (Table 4). Additionally, children of TPO-Ab–positive mothers were more often overweight or obese (BMI ≥25 kg/m^2) (OR, 1.56; 95% CI, 1.04 to 2.34).

In our nonadjusted analysis, children of TPO-Ab–positive mothers had higher fasting glucose concentrations, and children of Tg-Ab–positive mothers had higher LDL concentrations than children of TPO-Ab– and Tg-Ab–negative mothers, respectively, but these associations

Table 1. Metabolic Parameters for Children, Their Cut-Off Values, and Number of Samples

Metabolic Parameter	Cut-Off Values	Sample Size (n)
Fasting glucose	≥5.6 mmol/L	3811
Waist circumference	Girls: ≥80 cm; boys: ≥87.5 cm	4178
Triglyceride	≥1.7 mmol/L	3935
Total cholesterol	≥5.0 mmol/L	3936
HDL	≤1.03 mmol/L	3936
LDL	≥3.0 mmol/L	3936
Blood pressure	Systolic ≥130 mm Hg or diastolic ≥85 mm Hg	4209
Lipoprotein A	≤Lowest 10% = 1.12 g/L	4030
Lipoprotein B	≥Highest 10% = 0.87 g/L	4030
HOMA-B	≥Highest 10% = 152.00	3747
HOMA-S	≤Lowest 10% = 47.68	3747
BMI	≥25	4200
Metabolic syndrome	Waist circumference plus two of the following: blood pressure, HDL, triglyceride, fasting glucose	4141

Abbreviations: HOMA-B, homeostatis model assessment to determine abnormal β-cell function; HOMA-S, homeostatis model assessment to determine abnormal insulin sensitivity.

Table 2. Demographic Characteristics of the Pregnant Women Grouped According to Maternal Thyroid Hormone and Thyroid Antibody Status

	Euthyroid (n = 4842–4957)	Hypothyroid (n = 371–375)	Hyperthyroid (n = 126–127)	Hypothyroxinemia (n = 67–73)	TPO-Ab Negative (n = 5343–5469)	TPO-Ab Positive (n = 287–294)	Tg-Ab Negative (n = 5298–5420)	Tg-Ab Positive (n = 277–285)
Mean age in years (SD)	28.1 (5.3)	28.4 (5.5)	30.0 (5.4)[a]	30.0 (6.3)[a]	28.2 (5.4)	28.6 (5.0)	28.1 (5.4)	29.1 (5.4)[a]
Smoking, n (%)	1064 (21.6)	55 (14.8)[b]	19 (15.1)	18 (25.0)	1153 (21.2)	57 (19.6)	1162 (21.5)	34 (12.1)[b]
Parity >0, n (%)	3259 (65.9)	245 (65.7)	105 (82.7)[b]	49 (68.1)	3612 (66.2)	210 (71.9)[b]	3576 (66.2)	210 (74.2)[b]
BMI ≥25 kg/m^2, n (%)	774 (16.0)	73 (19.7)	23 (18.3)	18 (26.9)[b]	863 (16.2)	58 (20.2)	846 (16.0)	61 (22.0)[b]
Mean BMI, kg/m^2 (SD)	22.2 (3.4)	22.6 (3.6)[a]	22.4 (3.3)	23.9 (4.9)[a]	22.2 (3.4)	22.8 (4.1)[a]	22.2 (3.4)	22.7 (4.0)[a]

In the euthyroid group, TSH and fT4 are between the trimester-specific reference intervals. In the hypothyroid group, TSH is above its upper reference limit and fT4 is low or normal. In the hyperthyroid group, TSH is below its lower reference limit and fT4 is high or normal. In the hypothyroxinemia group, TSH is between its reference intervals and fT4 is below its lower limit. In TPO-Ab-Negative group maternal TPO-Ab concentration is under 95th percentile of the study population. In TPO-Ab-Positive group maternal TPO-Ab concentration is over 95th percentile of the study population. In Tg-Ab-Negative group maternal Tg-Ab concentration is under 95th percentile of the study population. In Tg-Ab-Positive group maternal Tg-Ab concentration is over 95th percentile of the study population.

Abbreviation: SD, standard deviation.

[a] $P < 0.05$ when comparing groups of hypothyroid, hyperthyroid or hypothyroxinemia with group of euthyroid or comparing the antibody-positive group with the antibody-negative group with t tests.

[b] $P < 0.05$ when comparing groups of hypothyroid, hyperthyroid or hypothyroxinemia with group of euthyroid or comparing the antibody-positive group with the antibody-negative group with χ^2 test.

were nonsignificant after adjusting for covariates (data not shown).

Sensitivity analysis

The exclusion of mothers with prepregnancy diabetes had little effect on the results (data not shown). The result of the analysis stratified by the children's sex was similar to the main analysis, but the smaller sample size rendered the analysis less robust. Like the main analysis, maternal antibody positivity seemed to have a greater effect on the cardiometabolic profile of the child than maternal thyroid dysfunction. Boys of TPO-Ab–positive mothers had a higher prevalence of greater waist circumference, metabolic syndrome, and decreased insulin sensitivity, and girls of TPO-Ab–positive mothers had increased plasma glucose concentration compared with boys and girls of TPO-Ab–negative mothers. In the children of mothers with thyroid dysfunction, girls of hypothyroid mothers had higher blood pressure, and girls of hypothyroxinemic mothers had decreased insulin sensitivity compared with girls of euthyroid mothers.

Discussion

In this large, population-based, prospective cohort study, the odds of metabolic syndrome were more than twofold among 16-year-old children of TPO-Ab–positive mothers compared with children of TPO-Ab–negative mothers. In addition, these children had greater waist circumference, and they were more often overweight or obese. Maternal thyroid dysfunction or Tg-Ab positivity was not associated with cardiometabolic risk factors in children. This study evaluated the association between maternal thyroid antibody status during pregnancy and cardiometabolic risk factors in children. The data are scarce evaluating the effect of maternal thyroid dysfunction on the cardiovascular health of children. In one previous study, the children of mothers with low maternal TSH or high fT4 concentrations were reported to have lower BMI at the age of 6 years (11). We cannot explain the difference in the results, but we do note that the children were younger and the cut-off of low TSH concentration was lower in the study by Godoy *et al.* (11) than in our study. The effect of maternal thyroid dysfunction on the growth of children warrants more research.

We have previously shown that mothers with hypothyroidism during pregnancy more often have diabetes and hypertension later in life, but maternal TPO-Ab positivity during pregnancy does not associate with a subsequent risk of maternal diabetes or hypertension (17). These previous results suggest an adverse cardiometabolic profile among pregnant women with hypothyroidism but not among those with TPO-Ab positivity. An adverse metabolic profile of the mother could result in the same phenomenon in her children. Therefore, the association between maternal TPO-Ab positivity and metabolic syndrome in children was somewhat unexpected. It seems that maternal thyroid antibodies may have a bigger role than maternal thyroid hormones when considering the association with cardiometabolic risk factors in children. More than half (55%) of the mothers with TPO-Ab positivity during pregnancy were euthyroid, suggesting that the effect was not driven by maternal TSH or thyroid hormone concentrations.

Interestingly, maternal Tg-Ab positivity did not associate as strongly with cardiometabolic risk factors in children as did maternal TPO-Ab positivity. We observed a weak association between maternal Tg-Ab positivity and high LDL in children, but this association was nonsignificant after adjusting for covariates. Only 38% of TPO-Ab–positive mothers were also Tg-Ab positive. Clinically, TPO-Abs are

Table 3. Comparison of Metabolic Parameters in Children According to Maternal Thyroid Hormone Status

Metabolic Parameters	Euthyroid, n/N (%)	Hypothyroid, n/N (%)	Hypothyroid, OR (95% CI)	Hyperthyroid, n/N (%)	Hyperthyroid, OR (95% CI)	Hypothyroxinemia, n/N (%)	Hypothyroxinemia, OR (95% CI)
Fasting glucose	530/3284 (16.1)	27/215 (12.6)	0.73 (0.48–1.11)	11/81 (13.6)	0.85 (0.44–1.61)	10/44 (22.7)	1.67 (0.81–3.45)
Waist circumference	430/3593 (12.0)	26/237 (11.0)	0.90 (0.58–1.39)	7/91 (7.7)	0.66 (0.30–1.44)	8/52 (15.4)	1.33 (0.61–2.93)
Triglyceride	128/3386 (3.8)	9/222 (4.1)	1.00 (0.48–2.08)	0/85 (0)	NA	3/47 (6.4)	1.88 (0.57–6.21)
Cholesterol	576/3387 (17.0)	35/222 (15.8)	0.85 (0.58–1.26)	20/85 (23.5)	1.58 (0.94–2.63)	7/47 (14.9)	0.78 (0.33–1.86)
HDL	292/3386 (8.6%)	26/223 (11.7)	1.30 (0.83–2.02)	6/85 (7.1)	0.81 (0.35–1.88)	3/47 (6.4)	0.77 (0.24–2.50)
LDL	367/3387 (10.8)	24/222 (10.8)	0.94 (0.59–1.48)	12/85 (14.1)	1.39 (0.74–2.59)	7/47 (14.9)	1.57 (0.69–3.57)
Blood pressure	501/3620 (13.8)	37/241 (15.4)	1.08 (0.75–1.57)	12/91 (13.2)	0.91 (0.48–1.72)	5/52 (9.6)	0.74 (0.29–1.88)
Metabolic syndrome	75/3555 (2.1)	6/238 (2.5)	1.06 (0.42–2.66)	0/91 (0)	NA	2/52 (3.8)	1.89 (0.44–8.01)
Lipoprotein A	340/3468 (9.8)	32/229 (14.0)	1.45 (0.97–2.15)	6/88 (6.8)	0.70 (0.30–1.63)	5/49 (10.2)	1.12 (0.44–2.87)
Lipoprotein B	366/3468 (10.6)	19/229 (8.3)	0.70 (0.42–1.16)	8/88 (9.1)	0.85 (0.41–1.78)	7/49 (14.3)	1.52 (0.67–3.43)
HOMA-B	325/3229 (10.1)	29/211 (13.7)	1.47 (0.97–2.21)	3/81 (3.7)	0.36 (0.11–1.16)	5/43 (11.6)	1.25 (0.48–3.23)
HOMA-S	329/3229 (10.2)	18/211 (8.5)	0.86 (0.52–1.41)	2/81 (2.5)	0.24 (0.06–0.99)	8/43 (18.6)	2.08 (0.94–4.61)
BMI	407/3612 (11.3)	25/241 (10.4)	0.91 (0.58–1.41)	9/90 (10.0)	0.99 (0.49–2.01)	9/52 (17.3)	1.75 (0.82–3.72)

In the euthyroid group, TSH and fT4 are between the trimester-specific reference intervals. In the hypothyroid group, TSH is above its upper reference limit and fT4 is low or normal. In the hyperthyroid group, TSH is below its lower reference limit and fT4 is high or normal. In the hypothyroxinemia group, TSH is between its reference intervals and fT4 is below its lower limit. ORs adjusted with maternal age, smoking, parity and overweight/obesity.

Abbreviations: HOMA-B, homeostatis model assessment to determine abnormal β-cell function; HOMA-S, homeostatis model assessment to determine abnormal insulin sensitivity; NA, not applicable.

more meaningful indicators of cytotoxic effects, which may explain the difference (24). In our sensitivity analysis stratified by the children's sex, we found some differences between girls and boys. However, the overall effect was similar to the main analysis, suggesting that maternal antibody positivity was more often associated with an adverse cardiometabolic profile in children than was maternal thyroid dysfunction.

Maternal thyroid antibody positivity is associated with a risk of pregnancy loss and may have adverse effects on a child's development (8, 25). The effect between thyroid autoimmunity and obesity or cardiovascular diseases in children is more controversial or lacking evidence from research (26, 27). In addition, our previous study has shown that TPO-Ab–positive mothers have TPO-Ab–positive children more often than TPO-Ab–negative mothers (19). Thyroid antibodies seem to be related to higher levels of interleukins, which may be a marker of systemic inflammation (28, 29). Inflammation is often found along with metabolic syndrome (30). Thus, TPO-Ab could be linked to metabolic syndrome via inflammation. However, we cannot clearly determine whether our findings in this study are due to the intrauterine environment and programming or due to a genetic predisposition to autoimmune and cardiometabolic risk factors.

One strength of this study was the large sample size and prospective data collection beginning from early pregnancy. More than 70% of the children participated

Table 4. Comparison of Metabolic Parameters in Children According to Maternal Thyroid Antibody Status

Metabolic Parameters	TPO-Ab Negative, n/N (%)	TPO-Ab Positive, n/N (%)	TPO-Ab Positive, OR (95% CI)	Tg-Ab Negative, n/N (%)	Tg-Ab Positive, n/N (%)	Tg-Ab Positive, OR (95% CI)
Fasting glucose	561/3609 (15.5)	37/173 (21.4)	1.43 (0.98–2.09)	566/3554 (15.9)	28/188 (14.9)	0.92 (0.61–1.40)
Waist circumference	456/3954 (11.5)	35/191 (18.3)	1.69 (1.14–2.50)	453/3899 (11.6)	27/204 (13.2)	1.03 (0.66–1.61)
Triglyceride	143/3730 (3.8)	5/175 (2.9)	0.76 (0.30–1.85)	132/3673 (3.6)	11/191 (5.8)	1.58 (0.81–3.07)
Cholesterol	635/3731 (17.0)	32/175 (18.3)	1.03 (0.69–1.54)	626/3674 (17.0)	35/191 (18.3)	1.02 (0.69–1.51)
HDL	325/3730 (8.7)	15/176 (8.5)	0.99 (0.57–1.70)	317/3674 (8.6)	21/191 (11.0)	1.33 (0.83–2.14)
LDL	411/3731 (11.0)	21/175 (12.0)	1.00 (0.61–1.62)	396/3674 (10.8)	30/191 (15.7)	1.47 (0.97–2.23)
Blood pressure	543/3983 (13.6)	33/193 (17.1)	1.33 (0.91–1.96)	548/3929 (13.9)	27/205 (13.2)	0.93 (0.61–1.42)
Metabolic syndrome	77/3921 (2.0)	9/188 (4.8)	2.57 (1.26–5.25)	80/3862 (2.1)	5/204 (2.5)	1.29 (0.51–3.25)
Lipoprotein A	381/3816 (10.0)	19/182 (10.4)	1.06 (0.65–1.73)	372/3758 (9.9)	26/199 (13.1)	1.39 (0.91–2.14)
Lipoprotein B	401/3816 (10.5)	20/182 (11.0)	0.94 (0.57–1.55)	398/3758 (10.6)	22/199 (11.1)	0.96 (0.60–1.54)
HOMA-B	349/3546 (9.8%)	24/172 (14.0)	1.47 (0.94–2.30)	349/3495 (10.0)	18/185 (9.7)	0.96 (0.57–1.60)
HOMA-S	346/3546 (9.8)	23/172 (13.4)	1.45 (0.92–2.28)	345/3495 (9.9)	17/185 (9.2)	0.93 (0.55–1.57)
BMI	438/3974 (11.0)	31/193 (16.1)	1.56 (1.04–2.34)	439/3922 (11.2)	21/203 (10.3)	0.85 (0.52–1.39)

TPO-Ab negative indicates maternal TPO-Ab concentration under 95th percentile, and TPO-Ab positive indicates maternal TPO-Ab concentration over 95th percentile of the study population. Tg-Ab negative indicates maternal Tg-Ab concentration under 95th percentile, and Tg-Ab positive indicates maternal Tg-Ab concentration over 95th percentile of the study population. ORs were adjusted for maternal age, smoking, parity, and overweight/obesity.

Abbreviations: HOMA-B, homeostatis model assessment to determine abnormal β-cell function; HOMA-S, homeostatis model assessment to determine abnormal insulin sensitivity.

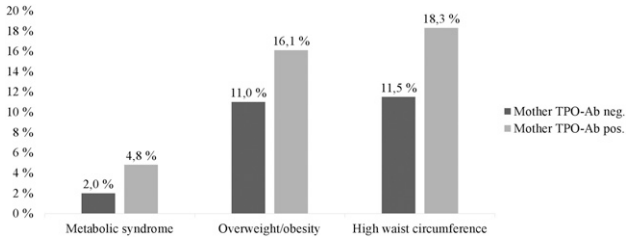

Figure 2. Prevalence of metabolic syndrome, overweight/obesity, and high waist circumference in children grouped by maternal antibody status.

in the follow-up examination at the age of 16. We were able to adjust the results for many different covariates, including maternal cardiometabolic risk factors, such as smoking and overweight or obesity during pregnancy. In addition, during the 1980s, Finland was iodine sufficient, so iodine deficiency did not confound our results (31–33).

As a limitation, our data were limited to those mothers with available serum samples (~62% of the original cohort) and to children who attended a clinical examination at the age 16 (~74%). However, the mothers with and without laboratory analyses did not have significant differences in maternal demographic characteristics and birth outcomes (8). Also, we did not have data on the fathers or on genetics. We performed several statistical tests that may produce type 1 error. The significant findings that we report in this article (BMI, waist circumference, and metabolic syndrome) are related, and therefore we believe that the findings in our study are not by chance.

Metabolic syndrome and overweight in childhood often extend to adulthood and increase the risk of type 2 diabetes and cardiovascular diseases (34–36). Over most of the world, the rate of childhood obesity has increased. In Finland, the prevalence of overweight and obesity in adolescents has increased threefold in last three decades (37–39). Approximately one out of two overweight adolescents remains overweight as an adult. The association between maternal thyroid autoimmunity and childhood metabolic syndrome and overweight at the age of 16 might suggest a previously undetected pathway. This warrants further studies.

Our findings do not support universal screening of pregnant women for TPO-Ab positivity. However, interventional studies undergoing like the TABLET trial may bring new information on this area (40).In summary, maternal TPO-Ab positivity was associated with greater waist circumference, higher BMI, and metabolic syndrome in children at age 16. Thus, children with a family history of diabetes, metabolic syndrome, or thyroid diseases would most probably benefit from health education, follow-up, and counseling. In addition to being an important risk factor during pregnancy, maternal TPO-Ab positivity appears to affect the lifetime health of the child.

Acknowledgments

We thank Dr. Heljä-Marja Surcel and the personnel from the Finnish Maternity Cohort for their valuable assistance with the early pregnancy laboratory analyses; the personnel from the Northern Finland Birth Cohort 1986, particularly Professor Marjo-Riitta Järvelin, Tuula Ylitalo, and Sarianna Vaara; and Dr. Aimo Ruokonen and Katri Puukka for their expertise.

Financial Support: This work was supported in part by grants from the Jalmari and Rauha Ahokas Foundation (Finland), the Northern Ostrobothnia Hospital District (Finland), and the Finnish Medical Association of Clinical Chemistry.

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Disclosure Summary: The authors have nothing to disclose.

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