Adequate Animal Protein Intake Maintains Normal Thyroid Antibody Levels in Pregnant Women With Mild Iodine Deficiency

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Research

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Abstract

Background: Both of the iodine and animal protein may affect thyroid function. We explored the association between animal protein intake and thyroid antibody status in pregnant women after universal salt iodization.

Method: Pregnant women were enrolled by using a multistage, stratified random sampling method. 4,646 eligible participants were interviewed in person with questionnaires physical examination and thyroid antibody test.

Results: Only thyrotropin receptor antibodies (TR-Ab) positive rates were different among different animal protein intake groups. The median of urinary iodine concentration (UIC) in thyroid peroxidase antibodies (TPO-Ab) positive groups was higher than the negative group. The median of total protein intake, animal protein intake and UIC in TR-Ab positive group was higher than the negative group. The medians of total protein intake and UIC in TPO-Ab/TG-Ab/TR-Ab positive group were higher than the negative group. The above differences were statistically significant ($P < 0.05$). The multivariable logistic regression results showed that insufficient iodine had a negative correlation with TPO-Ab positive and TR-Ab positive ($P < 0.05$). The middle third and top third animal protein intakes served as protective factors for TR-Ab (coefficient = 0.559, 95% CI = 0.415–0.752; coefficient = 0.0406, 95% CI = 0.266–0.621) and positive TPO-Ab/TR-Ab/TG-Ab (coefficient = 0.817, 95% CI = 0.687–0.971; coefficient = 0.805, 95% CI = 0.672–0.964).

Conclusions: Adequate animal protein intake protects against elevated anti-thyroid antibody levels in pregnant women with mild iodine deficiency.

Introduction

The autoimmune thyroid disease (AITD) represents the main cause of hypothyroidism during pregnancy, prevalence between 5 and 20% with an average of 7.8% [1, 2]. The AITD, which is 10 times more common in women than in men[3], is characterized by the rising of thyroid peroxidase antibodies (TPO-Ab), thyroglobulin antibodies (TG-Ab), and thyrotropin receptor antibodies (TR-Ab). According to a review, the environmental factors accounted for about 20–30% to the pathogenesis of AITD, nutritional status is one of the most important environmental factors [4].

Hormonal changes and metabolic stimulation affect the endocrine system and thyroid function during different stages of pregnancy[5, 6]. During the first trimester, maternal thyroxine is essential for proper fetal development. Pregnant women who are positive for thyroid antibodies are at significant risk for abortions and hypothyroidism during pregnancy[7]. Shanghai, which is the largest coastal city in China, has implemented the compulsory universal salt iodization since 1996. Even though the iodine nutritional status of the population is adequate, pregnant women are at risk for mild iodine deficiency[8, 9]. A study in endemic zone of a sub-Himalayan region reported that a negative correlation was observed between urinary iodine concentration (UIC) and anti-TPO Ab[10]. And also, a cross-sectional study in 10 cities in China after mandatory universal salt iodization for 16 years showed that the prevalence of AITD has increased[11]. But data from a representative sample of pregnant women in Shanghai have not been published.

Dietary protein is closely related to thyroid function. Thyroxine is composed of amino acid derivatives[12], and protein depletion decreases the responsiveness of animals to the catabolic functions of the thyroid[13]. Besides, animal protein contains casein protein, which also has a close relationship with the thyroid to capture and use iodine[14]. Animal studies have shown that low iodine intake with high protein intake maintains thyroid hormone synthesis that protein deficiency may affect the function of immune cells and collectively cause autoimmune diseases[15, 16]. Based on nutritional surveys from 1982 to 2012, the mean protein intake in Shanghai was always above 70.0 g/d which was more than 65 g/d of the recommended protein intake, and the proportion of protein from animal sources including milk increased from 15.5–46.8% [17, 18].

All of these indicated that high protein intake may be related to maintaining the thyroid health in Shanghai pregnant women. In this study, we intended to investigate the role of the different sources of protein intake on thyroid antibodies in pregnant women.

Materials And Methods

Study Sample

Our data was collected from the iodine status in pregnancy and offspring health cohort (ISPOHC), conducted in April–October 2017. The formula for calculating complex sampling sample size was used to calculate the sample size required for analysis. At least 3,510 pregnant women were needed in the study. A multistage, stratified random sampling method was used to obtain a representative sample. In light of the sample size and the number of pregnant women in each administrative district in 2016, we determined the survey number in each administrative district. Each district was divided into five sections, a street was randomly selected from each section, and an equal number of pregnant women were selected from each section. Different gestational weeks were evenly represented in this study.

Data Collection and diet evaluation

Eligible subjects were interviewed face-to-face on demographics, pregnancy history, dietary habits, household condiments, physical activity and other information. Dietary habits were reported through a validated food frequency questionnaire (FFQ) [19] that consisted of 68 items that assessed the frequency and amount of foods consumed including dietary supplements over the past three months. The frequency of food intake was measured in four categories: “times per day”, “times per week”, “times per month”, “times per 3 months”. Similar foods were counted together. To estimate daily protein and iodine intake, we used food composition tables published for China [20].

A household condiment weighing method was used to collect data on cooking oil, salt, and soy sauce by documenting changes in the condiment inventory over one week. Additionally, the number of people who consumed the household condiments at each meal was recorded, and a household salt sample was

collected for iodine concentration analysis. All data was reviewed by the local district project team and at least 5% of the data was reviewed by our project team.

According to the dietary recommendations intakes for Chinese 2013 edition, the estimated energy requirement and recommended nutrient intake (RNI) of protein were 1,800 kcal/d and 55 g/d (early pregnancy), 2,100 kcal/d and 70 g/d (middle pregnancy), and 2,250 kcal/d and 85 g/d (late pregnancy), respectively. The RNI of iodine was 230 µg/L. [18]

Urine sample collection, testing, and evaluation

Subjects collected 5 mL urine in the morning, prior to food consumption. All samples were immediately stored at 4°C, transported to the laboratory within 6 h, where they were stored at under 80°C. The laboratory complied with international standards ISO/IEC17025 and ISO/IEC 17020. Each urine sample was acid-digested (As3+-Ce4+ catalytic spectrophotometry) at designated test laboratory. Internal quality control samples for UIC were supplied by the Chinese National Iodine Deficiency Disorders Reference Laboratory.

Iodine status was estimated using World Health Organization (WHO)/ United Nations Children's Fund (UNICEF)/ International Council for Control of Iodine Deficiency Disorders (ICCIDD) criteria from 2007 and other published criteria as follows, severely insufficient (median UIC < 50 µg/L), moderately insufficient (median UIC > 50 µg/L and < 100 µg/L), mildly insufficient (median UIC > 100 µg/L and < 150 µg/L), adequate (median UIC > 150 µg/L and < 249 µg/L), and excessive (median UIC > 250 µg/L)[21].

As the high within-person variability of a single spot urine, the WHO has limited the use and interpretation based on single spot urine per participant to the population median of a sufficiently large group (in general, > 30) [8]. In our study, the sampling error (95% confidence interval (CI) of the MUIC) was considered and calculated using bootstrapping. Pregnant women are divided into 80 units according to the district. When the upper cut-off level of MUIC's 95% CI in one unit was higher than 250 µg/L, all pregnant women were assigned to the excessive iodine group in this unit. When the upper cut-off level was lower than 150 µg/L, all pregnant women were assigned to the insufficient iodine group. The rest were assigned to the adequate iodine group.

Thyroid antibody testing and evaluation

Thyroid antibody data was obtained from tertiary hospitals or women's health centers. Due to the inconsistency of detection methods and reagents at different hospitals, only qualitative analyses were performed. Subjects with positive TPO-Ab/TG-Ab/TR-Ab had at least one positive thyroid antibody indicator. Otherwise, the subjects were TPO-Ab/TG-Ab/TR-Ab negative.

Statistical Analysis

All analyses were carried out using Excel (2010 Edition, Microsoft, Redmond, Washington, USA) and SPSS (version 21.0, IBM Corp., Armonk, NY, USA). Continuous and categorical variables were expressed as median (interquartile range) and percentage, respectively. Continuous variables were analyzed using one-way analysis of variance. We used the nonparametric Mann-Whitney and Kruskal-Wallis tests for data that were not normally distributed. The multivariable logistic regression (forward stepwise) was used for univariate analyses. The criterion for inclusion in the regression model was $p < 0.05$, and the criterion for exclusion was $p > 0.1$. Statistical significance was set at $P < 0.05$. Coefficient and 95% confidence intervals were calculated.

Results

Energy, protein, and iodine intakes

A total of 4646 qualified subjects were investigated and included in the analysis except those who were loss to follow-up, did not have complete recordings or had previous thyroid diseases. The median of energy, protein and iodine intake was 1985.6 kcal, 80.1g and 119.1µg, respectively. Among the subjects, 62.3% exceeded protein RNI and 19.0% exceeded iodine RNI (Table 1).

Characteristics and thyroid antibodies stratified by animal protein

The positive rate of TPO-Ab, TG-Ab, TR-Ab and TPO-Ab / TG-Ab b / TR-Ab was 10.40%, 9.43%, 8.47% and 20.56% in all subjects, respectively.

According to the animal protein intake, the subjects were divided into three tertiles: bottom third intake (< 30.9 g/d), middle third intake (30.9–50.3 g/d), and top third intake (> 50.3 g/d). In the pooled sample, there were significant differences in the constituent ratio of educational level and family income last year among the three animal protein intake groups ($P < 0.05$). Just looking at the data, the proportions of better educational background and higher family income last year were higher in the middle third intake group. The median UIC in pregnant women was 139.3 µg/L. There were no significant differences in age, median UIC, occupational status, and alcohol consumption among the three animal protein intake groups. The results of the different gestational stages are shown in Table 2.

The TR-Ab positive rate was significantly different in the pooled sample ($P < 0.05$). Pairwise comparisons were performed among the three groups. The findings showed that the TR-Ab positive rate was higher in the bottom third intake group than in the other two groups ($P < 0.05$). TPO-Ab positive rate was higher in the middle pregnancy in top third intake group than in the other groups ($P < 0.05$).

Energy, protein, and iodine intakes and UIC in thyroid antibody positive and negative groups

UIC and intakes of energy, total protein, animal protein (including milk protein), and iodine were compared between thyroid antibody positive and negative groups (table 3). The results showed that there was no significant difference in energy intake between both groups. In the pooled sample, the difference in UIC between TPO-Ab positive and negative groups was statistically significant ($P < 0.05$), and there was a statistically significant difference in total protein intake,

animal protein intake, and UIC between TR-Ab positive and negative groups and in total protein intake and UIC between TPO-Ab/TG-Ab/TR-Ab positive and negative groups ($P < 0.05$).

Factors associated with positive thyroid antibodies

Multivariable logistic regression analyses were conducted using general characteristics, animal protein intake (including milk protein), UIC, and other related factors as independent variables and thyroid antibodies as dependent variables (Table 4).

Compared to the bottom third animal protein intake, the middle third and the top third animal protein intake served as protective factors for positive TR-Ab (coefficient = 0.559, 95% CI = 0.415–0.752, $P = <0.001$; coefficient = 0.406, 95% CI = 0.266–0.621, $P = <0.001$) and positive TPO-Ab/TR-Ab/TG-Ab (coefficient = 0.817, 95% CI = 0.687–0.971, $P = 0.022$; coefficient = 0.805, 95% CI = 0.672–0.964, $P = 0.018$), respectively. There was no significant association between animal protein intake and positive TPO-Ab or positive TG-Ab.

Compared to the low educational level, the senior high school and college level and Bachelor degree and above level served as protective factors for positive TR-Ab and TPO-Ab/TR-Ab/TG-Ab. Mental work compared with physical work served as risk factors for positive TPO-Ab, TG-Ab and TPO-Ab/TR-Ab/TG-Ab. The insufficient iodine group compared with adequate iodine group served as risk factors for positive TPO-Ab, TR-Ab and TPO-Ab/TR-Ab/TG-Ab. $> 30\%$ energy from fat compared with $\leq 30\%$ served as risk factors for positive TPO-Ab and TR-Ab. The above differences were statistically significant, $P < 0.05$.

Discussion

Dietary protein plays an essential role in thyroid function. The median total protein and animal protein intake of the subjects were 80.1 g/d and 38.9 g/d. The protein intake exceeded protein RNI in 62.3% of the subjects, consistent with recent other population data from the Shanghai survey[22]. The positive rate of TPO-Ab, TG-Ab, and TR-Ab was 10.40%, 9.43%, and 8.47%, respectively. Studies have shown that TPO-Ab positivity is common in women of childbearing age with a prevalence ranging between 5.1% and 12.4%[7], consistent with the result of this study. Surveillance in iodine adequate areas of China showed an isolated TG-Ab positive rate of about 7% in pregnant women[23].

Pregnant women had a median UIC of 139.3 $\mu\text{g/L}$, which was slightly below the recommended median UIC range (150–249 $\mu\text{g/L}$) established by WHO/UNICEF/ICCIDD for pregnant women. The insufficient iodine group had high rates of positive TPO-Ab, TR-Ab, and TPO-Ab/TG-Ab/TR-Ab, which is in accordance with the findings of Laurberg who reported that mild iodine deficiency might increase thyroid antibody levels[24]. Even though the iodine intake among Shanghai pregnant women is insufficient, their animal protein intake is adequate. The Qinghai Preventive Institute of Endemic Diseases in China conducted an animal experiment that assessed thyroid function in mice when they had a low daily intake of iodine and a relatively high intake of protein. The findings revealed that thyroid glands of mice were able to maintain basic function and produce thyroid hormones[15]. Even though adequate iodine intake is important, intake of high-quality protein might effectively prevent the occurrence and development of thyroid disorders[15].

Our findings have shown that adequate animal protein intake is a protective factor for TR-Ab and TPO-Ab/TR-Ab/TG-Ab positivity. Unfortunately, we did not observe statistical association between animal protein intake and TPO-Ab or TG-Ab positivity, probably due to the relative sensitivity of TPO-Ab and TG-Ab to dietary fat. In our study, the percentage of energy from fat $> 30\%$ is a risk factor for TPO-Ab and TG-Ab positivity. Researchers, who investigated the relationship between diet and thyroid function in 97,000 people from the USA and Canada, reported that vegan diets are associated with a lower risk[25, 26]. A study that evaluated the relationship between dietary patterns and thyroid antibodies revealed that the frequent consumption of animal fat is associated with positive TPO-Ab and/or positive Tg-Ab[27]. There is a positive association between saturated fatty acids from animal fat and high-sensitivity C-reactive protein levels, which may stimulate inflammatory responses[28] and induce AITD.

The different results among TPO-Ab, TG-Ab, and TR-Ab may be attributed to gestational stage and diverse antigen location. Pregnant women have lower levels of thyroid antibodies than non-pregnant women, due to the synthesis of maternal regulatory T-cells that maintain a state of tolerance to fetal alloantigen to prevent rejection of the fetus[29]. This pattern of antibody behavior can show a noticeable fall in levels of antibody against TR-Ab[30]. Additionally, antigen location is different among the three antibodies. TR-Ab is extracellular, and cells have access to antigens without tissue destruction, which suggests that it tends to be earlier affected. However, it is also more likely to be influenced by more confounders like other inflammatory parameters in serum. TPO-Ab is intracellular and TG-Ab is intrafollicular, only after thyrocyte destruction can antigen be accessed; as a result, TPO-Ab may relatively more steadily be affected by animal protein[31].

High educational level had a protective effect against thyroid antibody positivity, while mental work increased the risk. Pregnant women with high educational level are likely to have higher health literacy and healthier dietary habits[32]. Additionally, job engagement might empower pregnant women to make better decisions on their dietary habits and healthcare[33], which positively affects their well-being. Mental workload contributes to fatigue condition and stressful emotion[34], which could be a risk factor for AITD[35].

To the best of our knowledge, this is the first study with a representative sample in pregnant women that examined the association between animal protein intake and thyroid antibodies. Our study had some limitations. First, even though the thyroid antibody data was acquired from hospitals and women's health centers, the detection methods and instruments were inconsistent. Therefore, we could not perform a quantitative analysis of thyroid antibodies. Second, due to complex food composition data, there are probably some unknown confounders that may have affected the results.

Conclusion

In conclusion, adequate animal protein intake is a protective factor for thyroid antibody positivity, especially in pregnant women with iodine deficiency. Increased energy intake from fat increases the risk for positive thyroid antibodies. Therefore, pregnant women should limit their fat intake while consuming

adequate amounts of animal protein. Iodine supplements are recommended for pregnant women with iodine deficiency.

Abbreviations

AITD

Autoimmune thyroid disease; FFQ:Food frequency questionnaire; ICCIDD:International Council for Control of Iodine Deficiency Disorders; ISPOHC:Iodine status in pregnancy and offspring health cohort; RNI:recommended nutrient intake; TG-Ab:Thyroglobulin antibodies; TPO-Ab:Thyroid peroxidase antibodies; TR-Ab:Thyrotropin receptor antibodies; UIC:Urinary iodine concentration; UNICEF:United Nations Children's Fund; WHO:World Health Organization.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Shanghai Municipal Centre for Disease Control and Prevention (CDC) (NO.2016-5). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

Please contact author for data requests.

Competing interests

All authors declare that we have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

Data curation, ZW and JZ; Funding acquisition, ZW and JZ; Investigation, ZW, XC, QS, ZS and JZ; Project administration, ZW, CG, JS and JZ; Supervision, CG and JS; Writing – original draft, ZW and JS; Writing – review & editing, ZW, JS, CG, JS and JZ. All authors read and approved the final manuscript.

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Tables

Table 1. Distributions of energy, different food sources of protein and iodine in pregnant women stratified by pregnancy stage

Pregnancy stage	N	Quantile	Energy (kcal)	Total protein (g)	Animal protein (including milk protein, g)	Animal protein (no milk protein) (g)	Milk protein (g)	Iodine (µg)
Pooled	4646	P20	1430.1	55.7	24.5	20.3	1.4	47.4
		P33.3	1683.6	66.6	30.9	26.3	2.8	78.7
		P40	1809.3	71.8	33.9	28.9	3.9	94.2
		P50	1985.6	80.1	38.9	33.8	5.5	119.1
		P60	2194.7	89.9	44.8	39.5	5.5	146.0
		P66.7	2371.2	99.0	50.3	44.6	5.5	162.9
		P80	2846.7	124.1	64.6	59.5	6.9	226.0
Early pregnancy	1686	P20	1376.3	52.9	22.6	18.6	1.2	46.0
		P33.3	1620.7	63.0	28.8	24.5	2.8	74.3
		P40	1735.0	68.3	31.4	27.3	3.1	88.6
		P50	1897.8	75.2	36.1	31.8	4.9	114.7
		P60	2093.6	83.7	41.4	36.6	5.5	141.3
		P66.7	2230.0	92.5	45.5	40.7	5.5	160.2
		P80	2729.9	116.1	60.8	55.7	6.9	222.4
Middle pregnancy	1671	P20	1451.5	57.7	24.5	20.5	1.2	47.5
		P33.3	1719.8	67.2	30.6	26.2	2.8	80.3
		P40	1850.5	72.8	34.0	28.5	3.7	97.1
		P50	2037.5	81.6	38.9	33.8	5.5	124.0
		P60	2260.5	91.1	45.4	39.4	5.5	149.9
		P66.7	2442.9	100.3	51.3	44.8	5.5	165.9
		P80	2863.5	124.9	64.6	59.6	6.9	229.9
Late pregnancy	1389	P20	1469.1	58.5	27.2	22.2	1.6	50.0
		P33.3	1716.3	70.0	33.7	28.3	3.4	84.6
		P40	1851.3	75.6	37.0	31.7	4.1	97.7
		P50	2049.7	84.8	42.2	37.0	5.5	119.1
		P60	2272.0	95.6	48.7	43.2	5.5	146.5
		P66.7	2450.6	105.0	55.7	48.3	6.4	163.7
		P80	2960.3	130.7	68.0	62.8	6.9	222.6

*The estimated energy requirement and recommended nutrient intake (RNI) of protein were 1,800 kcal/d and 55 g/d (early pregnancy), 2,100 kcal/d and 70 g/d (middle pregnancy), and 2,250 kcal/d and 85 g/d (late pregnancy), respectively. The RNI of iodine was 230 µg/L.

Due to technical limitations, table 2 is only available as a download in the Supplemental Files section.

Table 3. Energy, protein, iodine, and UIC in thyroid antibody positive vs. negative groups (median p25, p75)

	Pool			Early pregnancy			Middle pregnancy			Late pregnancy		
	+	-	<i>P</i>	+	-	<i>P</i>	+	-	<i>P</i>	+	-	<i>P</i>
TPO-Ab												
Energy intake (kcal)	1978.7 (1549.5-2663.5)	1988.8 (1257.0-2641.4)	0.751	1972.0 (1569.0-2458.2)	1887.2 (1451.4-2524.8)	0.555	1964.6 (1558.5-2764.9)	2054.5 (1566.5-2699.6)	0.986	2016.7 (1425.0-2732.9)	2069.6 (1590.4-2775.4)	0.284
Total protein intake (g)	83.1 (62.5-114.0)	80.0 (59.9-112.9)	0.206	79.6 (58.4-109.4)	74.6 (56.5-104.6)	0.189	84.7 (63.0-119.0)	81.3 (61.1-113.6)	0.151	82.7 (64.4-109.2)	85.6 (63.8-120.8)	0.502
Animal protein intake (including milk protein; g)	40.8 (28.9-61.7)	38.8 (27-58.8)	0.059	39.6 (27.4-58.1)	35.8 (24.9-52.8)	0.163	43.5 (31.3-64.6)	38.7 (27-59)	0.021	40.8 (30.5-61.5)	42.9 (29.8-63.1)	0.584
Iodine intake (µg)	115.0 (52.7-192.2)	119.0 (61.1-197.1)	0.503	106.0 (45.6-173.7)	116.0 (58.9-192.3)	0.241	133.0 (53.4-208.7)	123.0 (60.3-199.3)	0.888	120.0 (59.6-190.8)	118.0 (64.2-199.2)	0.942
UIC (µg/L)	123.8 (69.2-202.0)	140.6 (83.9-221.3)	0.002	127.4 (72.2-204.7)	150.5 (89.4-239.3)	0.002	129.6 (74.4-196.5)	140.5 (87.0-219.7)	0.240	103.3 (52.7-202.4)	124.8 (71.1-200.2)	0.127
TG-Ab												
Energy intake (kcal)	1925.2 (1513.8-2591.1)	1994.7 (1531.8-11092.3)	0.194	1888.4 (1507.7-2353.1)	1897.0 (1460.7-2531.8)	0.466	1961.5 (1575.7-2698.8)	2054.5 (1565.2-2706.0)	0.688	2103.5 (1492.1-2803.0)	2055.7 (1582.1-2759.3)	0.641
Total protein intake (g)	77.5 (58.5-109.2)	80.4 (60.4-113.2)	0.142	73.6 (55.8-100.6)	75.2 (56.9-105.6)	0.359	76.6 (59.6-114.8)	82.1 (61.7-114.1)	0.495	88.8 (62.5-117.2)	85.1 (64.0-120.4)	0.861
Animal protein intake (including milk protein; g)	37.6 (27.0-57.0)	39.0 (27.2-59.0)	0.316	35.3 (24.6-52.4)	36.1 (25.1-53.3)	0.401	38.4 (28.7-57.0)	39.1 (27.1-59.4)	0.828	41.1 (28.5-63.9)	42.7 (29.9-62.9)	0.783
Iodine intake (µg)	118.0 (56.9-189.5)	119.0 (60.5-197.3)	0.542	106.0 (45.3-170.4)	115.0 (59.1-193.6)	0.076	138.0 (77.0-206.2)	123.0 (58.3-199.8)	0.261	128.0 (64.7-191.2)	118.0 (64.0-197.5)	0.934
UIC (µg/L)	132.4 (73.4-204.7)	139.9 (82.6-221.0)	0.205	132.8 (73.4-198.4)	150.0 (88.9-240.5)	0.009	146.2 (84.7-219.8)	138.8 (85.0-217.3)	0.630	115.4 (55.1-213.0)	123.7 (70.3-199.5)	0.684
TR-Ab												
Energy intake (kcal)	1910.9 (1443.6-2588.2)	1994.7 (1537.9-2651.7)	0.169	1945.4 (1501.9-2493.6)	1889.3 (1459.9-2523.4)	0.470	1847.0 (1360.7-2560.1)	2058.8 (1586.7-2713-3)	0.095	1937.6 (1447.9-2691.3)	2072.7 (1591.3-2783.6)	0.347
Total protein intake (g)	71.9 (52.8-100.3)	81.1 (60.9-113.6)	<0.001	75.7 (56.4-97.7)	75.0 (56.8-106.3)	0.966	66.0 (51.7-99.8)	82.4 (62.3-114.3)	0.004	64.7 (48.6-105.7)	86.6 (65.4-120.6)	<0.001
Animal protein intake (including milk protein; g)	31.4 (24.5-49.4)	39.5(27.5-59.4)	<0.001	32.7 (26.2-49.3)	36.5 (24.9-53.8)	0.545	30.2 (24.2-52.4)	39.8(27.5-59.1)	0.028	31(22.7-48.5)	43.8 (30.7-63.2)	<0.001
Iodine intake (µg)	130.0 (59.1-211.5)	118.0 (60.1-194.7)	0.114	115.0 (52.1-183.2)	114.0 (58.1-193.5)	0.829	138.0 (45.6-211.6)	123.0 (60.4-199.2)	0.716	148.0 (93.0-280.1)	117.0 (62.8-192.5)	0.001
UIC (µg/L)	117.6 (68.0-205.1)	141.0 (82.8-221.0)	0.001	120.0 (68.1-215.4)	150.3 (89.1-239.1)	0.001	110.7 (63.5-172.3)	141.1 (87.1-219.8)	0.003	117.9 (69.1-213.4)	124.0 (69.5-198.5)	0.756

TPO-Ab/TG-Ab/TR-Ab												
Energy intake (kcal)	1945.5 (1493.7–2638.6)	2001.7 (1538.3–2647.3)	0.166	1924.7 (1516.4–2466.3)	2072.7 (1451.4–2534.6)	0.578	1916.1 (1496.9–2656.7)	2073.9 (1587.1–2712.7)	0.177	1989.2 (1457.7–2803.6)	1885.0 (1606.1–2758.6)	0.264
Total protein intake (g)	76.8 (57.6–108.7)	80.9 (60.8–113.5)	0.024	76.8 (57.1–102.3)	86.6 (56.7–106.4)	0.716	76.3 (58.1–114.8)	82.6 (62.4–114)	0.147	77.2 (58.5–114.2)	74.6 (65.4–121.1)	0.018
Animal protein intake (including milk protein) (g)	36.6 (26.1–57.1)	39.5 (27.5–59.1)	0.061	35.2 (26.0–54.5)	43.9 (24.9–52.8)	0.892	36.6 (26.6–58.5)	39.6 (27.4–59.3)	0.666	37.9 (25.8–61.7)	36.2 (30.7–63.2)	0.012
Iodine intake (µg)	119.0 (57.3–198.7)	119.0 (60.8–195.7)	0.578	109.0 (50–173.7)	118.0 (59.1–195.7)	0.254	138.0 (63.6–209.1)	121.0 (59.4–198.1)	0.217	126.0 (65.7–213.9)	117.0 (63.6–194.4)	0.172
UIC (µg/L)	123.0 (70.6–204.4)	142.2 (85.2–222.5)	<0.001	126.6 (71.6–208.7)	154.1 (91.8–246.1)	<0.001	126.4 (75.8–198.0)	142.0 (88.0–220.6)	0.043	113.7 (63.0–206.5)	126.0 (71.4–198.4)	0.392

Table 4. Factors associated with positive thyroid antibody

	TPO-Ab				TG-Ab				TR-Ab				TPO-Ab/TG-Ab/TR-Ab		
	β	Coeff.	95% CI	<i>P</i>	β	Coeff.	95% CI	<i>P</i>	β	Coeff.	95% CI	<i>P</i>	β	Coeff.	95% CI
Age															
< 35 y	reference				reference				reference				reference		
≥ 35 y	0.106	/	/	0.442	0.149	/	/	0.294	-0.115	/	/	0.480	0.019	/	/
Educational level															
≤ 9 y	reference				reference				reference				reference		
Senior high school and college	0.117	/	/	0.474	-0.012	/	/	0.937	-0.588	0.555	0.418-0.737	<0.001	-0.234	0.792	0.64 0.98
Bachelor degree and above	0.256	/	/	0.137	0.024	/	/	0.888	-1.044	0.352	0.253-0.49	<0.001	-0.343	0.710	0.56 0.89
Occupational status															
Physical work	reference				reference				reference				reference		
Mental work	0.225	1.253	1.029-1.526	0.025	0.213	1.237	1.009-1.517	0.041	0.099	/	/	0.385	0.178	1.195	1.02 1.39
Family income last year, YUAN															
< 100,000	reference				reference				reference				reference		
100,000-200,000	-0.004	/	/	0.980	-0.096	/	/	0.512	-0.041	/	/	0.776	-0.122	/	/
$\geq 200,000$	0.001	/	/	0.995	-0.303	/	/	0.058	-0.289	/	/	0.085	-0.209	/	/
Pregnancy stage															
Early pregnancy	reference				reference				reference				reference		
Middle pregnancy	-0.089	/	/	0.448	-0.382	0.682	0.538-0.865	0.002	-0.799	0.450	0.344-0.587	<0.001	-0.348	0.706	0.59 0.84
Late pregnancy	-0.198	/	/	0.112	-0.509	0.601	0.465-0.778	<0.001	-0.580	0.560	0.429-0.731	<0.001	-0.299	0.742	0.62 0.88
Energy intake															
Bottom third (< 1,683.6 kcal/d)	reference				reference				reference				reference		
Middle third (1,683.6–2,371.2 kcal/d)	-0.169	/	/	0.234	-0.078	/	/	0.596	0.200	/	/	0.199	-0.061	/	/
Top third (> 2,371.2 kcal/d)	-0.259	/	/	0.102	-0.011	/	/	0.947	0.300	/	/	0.091	-0.045	/	/
Animal protein (including milk protein)															
Bottom third (< 30.9 g/d)	reference				reference				reference				reference		
Middle third (30.9–50.3 g/d)	0.204	/	/	0.155	-0.120	/	/	0.406	-0.582	0.559	0.415-0.752	<0.001	-0.202	0.817	0.68 0.97
The top third (> 50.3 g/d)	0.179	/	/	0.219	-0.105	/	/	0.600	-0.901	0.406	0.266-0.621	<0.001	-0.217	0.805	0.67 0.96
Percentage of animal protein from total protein															
Bottom third (< 45%)	reference				reference				reference				reference		
Middle third	-0.122	/	/	0.389	-0.160	/	/	0.274	0.205	/	/	0.180	-0.044	/	/

(45%–54%)															
Top third (> 54%)	-0.090	/	/	0.580	0.037	/	/	0.824	0.231	/	/	0.201	-0.007	/	/
Iodine intake															
Bottom third (< 78.7 µg/d)	reference				reference				reference				reference		
Middle third (78.7–162.9 µg/d)	-0.073	/	/	0.619	-0.075	/	/	0.623	0.318	/	/	0.075	0.084	/	/
Top third (> 162.9 µg/d)	0.007	/	/	0.971	0.032	/	/	0.867	0.385	/	/	0.073	0.165	/	/
Median of UIC															
Adequate iodine group	Reference				reference				reference				reference		
Insufficient iodine group	0.246	1.279	1.009-1.621	0.042	0.110	/	/	0.374	0.377	1.457	1.119-1.899	0.005	0.286	1.331	1.11 1.58
Excessive iodine group	0.037	1.038	0.764-1.409	0.813	-0.021	/	/	0.892	-0.066	0.936	0.657-1.333	0.714	0.009	1.009	0.80 1.26
Percentage of energy from fat															
≤ 30%	reference				reference				reference				reference		
> 30%	0.236	1.301	1.013-1.671	0.039	0.221	1.285	1.004-1.581	0.046	0.117	/	/	0.403	0.159	/	/

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