Letter to the Editor

Effect of Iodine Supplementation on Iodine Nutrition and Thyroid Function in Pregnant Women: A Cross-Sectional Study*

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This study aimed to describe the situation of iodine supplementation in pregnant women, and to explore the effects of such supplementation measures on iodine nutrition and thyroid function. Pregnant women in seven provinces were selected by multi-stage sampling. Basic information was collected and a food frequency questionnaire was administered. Salt iodine, urinary iodine, and thyroid function were determined. Subjects were divided into five groups based on iodine supplementation. For pregnant women, the median urinary iodine concentration (MUIC) in seven provinces was 164.3 μg/L, and thyroid nodules (15.75%) were a common thyroid disease. Gestation, iodine supplementation, etc. impacted iodine nutrition and thyroid function. Compared with other groups, simultaneous iodine supplementation with iodized salt, iodine-rich foods, and iodine preparations (the ISFP group) was the most effective approach for improving iodine nutrition; supplementation *via* iodine-rich foods only showed the lowest prevalence of TPOAb-positive (5.48%) and TgAb-positive (1.37%) diseases. In addition, pregnant women with MUIC in the 150–249 μg/L range showed higher rates of TPOAb-positive (13.78%) disease and sub-hypothyroidism (5.38%) compared to those with MUIC in the 100–149 μg/L range; however, goiter showed the opposite trend. Our results indicate that iodine supplementation needs vary from person to person.

Iodine is one of the essential trace elements in the human body and can only be obtained from the diet. Iodine can influence metabolism and growth by affecting the synthesis of thyroid hormone. Pregnant women are a special population, in which iodine intake is not only needed to meet the woman's own health needs, but is also required to supply the growing fetus[1]; therefore, it is very important for pregnant women to supplement with iodine. In recent years, there has been controversy about the appropriate standard for median urinary iodine concentration (MUIC) in pregnant women. A study by Wu M, et al.[2,3] found that the appropriate MUIC in pregnant women was far below that recommended by the World Health Organization (WHO) and subjects with MUIC in of 100–150 μg/L had normal thyroid function. As a result, in this study we compared thyroid function in pregnant women with MUIC ranges of 100–149 μg/L and 150–249 μg/L.

Universal salt iodization (USI) had alleviated the risk of iodine deficiency disorders (IDD). However, some thyroid diseases have been increasing in prevalence in recent years, leading to a heated discussion about iodine supplementation measures and consumption amounts[4]. Ling W et al. argued that daily intake of iodized salt and iodine-rich food should complement one another to increase iodine nutrition.

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Drinking iodine-containing water can also help to supplement iodine, but can also induce iodine excess[5]. Moreover, iodine supplement preparations (e.g., multi-vitamin pills) have been more frequently recommended to pregnant women by clinical doctors. In this study, we provide a summary of various iodine supplementation measures and their respective effects on iodine nutrition, thyroid function, and thyroid-related diseases.

In our study, a multi-stage sampling method was adopted. First, seven provinces were selected according to their location in China. Four counties in each province were selected according to their economic level (high or low) and geographical characteristics (coastal or inland for Fujian and Liaoning; plateau or plain for Shanxi, Xinjiang, Anhui, Hubei, and Sichuan). Next, each participating county was divided into five sampling areas (east, west, south, north, and middle). According to the reliability of the iodine nutrition surveys, 100 individuals in each county were surveyed in our investigation, which was consistent with a 90% confidence interval within a precision range of ± 10%. Finally, 2,850 pregnant women were included in the study according to the inclusion and exclusion criteria, as follows: 1) age 20 to 40 years old without a history of smoking or alcohol abuse; 2) no use of iodine preparations in the past three days; 3) no special dietary habits, such as vegetarian food, etc; 4) healthy with no history of thyroid or family genetic diseases, etc; 5) no occupational iodine exposure (such as medical personnel who use iodine disinfectant or iodine contrast agent); and 6) recently had an angiography examination. This study was conducted according to the guidelines established in the Declaration of Helsinki, and all procedures involving human volunteers were approved by the Ethics Committee of Harbin Medical University. Written informed consent was obtained from each pregnant woman (20190502).

Questionnaires were used to collect basic information, consumption of iodized salt, foods intake (iodine content more than 10 μg/100 g, and choosing the contribution rate of various iodine-containing foods more than 1% for pregnant women through literatures), and iodine supplement preparations. A total of 2,643 household salt samples, 2,557 urine samples, and 2,525 blood samples were collected at the local health center for determination of iodine content and thyroid function. The household salt iodine was measured by direct titration. Urinary iodine concentration was measured using As^{3+}–Ce^{4+}catalytic spectrophotometry. Thyroid volume and function were respectively detected by B-ultrasound and electrochemiluminescence at the provincial Center for Disease Control (CDC). The following reference ranges for thyroid stimulating hormone (TSH) and free thyroxine (FT_4) were determined using the "Guidelines for the management of thyroid diseases during pregnancy and postpartum (Second Edition)"[6]: first trimester, TSH, 0.09–4.52 mU/L and FT_4, 13.15–20.78 pmol/L; second trimester, TSH, 0.45–4.32 mU/L and FT_4, 9.77–18.89 pmol/L; third trimester, TSH, 0.30–4.98 mU/L and FT_4, 9.04–15.22 pmol/L, The reference for antibodies and free triiodothyronine (FT_3) were thyroid peroxidase antibody (TPOAb), 0–34 IU/mL, thyroglobulin antibody (TgAb), 0–115 IU/mL, FT_3, 3.1–6.8 pmol/L. Furthermore, the reference of thyroid volume was less than 18 mL. In this study, urinary iodine concentration (UIC) in the 150–249 μg/L group was defined as iodine sufficient, and the thyroid-related diseases that were defined included hypothyroidism, sub-hypothyroidism, hyperthyroidism, sub-hyperthyroidism, TPOAb-positive, TgAb-positive, and double antibody positive.

Iodine intake for different sources was calculated according to consumption. To study the effects of different measures on iodine nutrition and thyroid function, pregnant women were divided into five groups : 1) an IF group (refers to eating 50 grams or more in wet weight of kelp, seaweed etc., more than once per month; participants); 2) an iodized salt group (IS, participants); 3) an iodized salt + iodine-rich food group (ISF, 1,164 participants); 4) an iodized salt + iodine supplement preparations group (ISP, in which there was a self-reported iodine supplementation habit for the last year prior to the investigation; 42 participants); and 5) iodized salt + iodine-rich food + iodine supplement preparations group (ISFP, participants). To explore the potential influence of each factor on urinary iodine and thyroid function, subjects were grouped by gestation, habitation (urban/rural), annual income, vomiting reaction (none; slight: occasional vomiting reaction; moderate: less than four times per day without weight loss; and serious: frequent reaction with weight loss), and dietary habits (times of meals each day). Other indicators calculated included the iodine supplementation rate of pregnant women (refers to the proportion of pregnant women receiving iodine supplements through either iodized salt and iodine supplement preparations or iodine rich food in all surveyed pregnant women), iodine supplement contribution (refers to the proportion of dietary iodine intake from drinking water, food, iodine preparations, or iodized salt), consumption rate of qualified iodized salt (refers to the rate of iodized salt with iodine content between 18–33 mg/kg).

SPSS 22.0 (International Business Machines Corp) was used for statistical analysis. For data with normal distribution, the mean and standard deviation were calculated (e.g., the iodine intake of iodized salt, food, and preparations); for skewed distribution data, median and interquartile range were analyzed (such as MUICs and the iodine intake of drinking water). Non-parametric rank test, Chi-square test, and Fisher's exact probability were used to study the effect of different iodine supplement on urinary iodine. Binary logistic regression was adopted to analyze factors of iodine nutrition and thyroid function. All tests were two-side and $P < 0.05$ was defined as significant.

As for basic information (Supplementary Table S1, available in www.besjournal.com), rural pregnant women accounted for 63.3% of study participants. Furthermore, there were 428 first trimester participants (17.6%), 1,102 in the second trimester (45.2%), and 907 in the third trimester (37.2%). In view of dietary habits, most pregnant women (64.1%) followed a habit of eating three meals per day, but others had meals more frequently.

The MUIC of all study participants was 164.3 μg/L (first trimester: 160.16 μg/L; second trimester: 156.90 μg/L; third trimester: 148.20 μg/L; Table 1), which is close to the lower limit of adequate iodine status (150 μg/L). The MUICs in Fujian (132.9 μg/L) and Liaoning (127.1 μg/L) were low, and more iodine intake was required. Concerning iodine supplementation measures, iodized salt (contribution rate of 42.93%) was the most common measures for supplementing iodine in pregnant women. Food supplementation was the other most common measure, with a contribution rate of 35.44%. However, the most important measure in Xinjiang was iodine supplement preparations (59.34%), followed by iodized salt (22.93%) and food supplementation (17.10%). It was also found that the iodine supplementation rate in pregnant women was above 90% in all provinces. With the exception of Sichuan, consumption rates of qualified iodized salt were all also above 90%.

We next compared thyroid-related diseases in different MUIC (100–149 μg/L and 150–249 μg/L, Supplementary Table S2, available in www.besjournal.com). Counties with MUIC in the 150–249 μg/L range showed a higher prevalence of sub-hypothyroidism, TPOAb-positive and double antibody positive disease types than those with MUIC in the 100–149 μg/L range. However, the prevalence of goiter showed the opposite trend.

Diseases related to thyroid function had the highest prevalence (19.76%, Supplementary Table S3, available in www.besjournal.com), which is consistent with a prior investigation from 2010–2012[7]. The next most prevalent condition was thyroid nodules (15.75%). Among diseases related to thyroid function, TPOAb-positive was the most prevalent (12.36%), and Sichuan had the highest

Table 1. Iodine nutrition and iodine supplementation measures in pregnant women

Province	Number	MUIC* (μg /L)	Sources of iodine intake (μg/d) (contribution rate, %)[3]				Iodine supplement (%)	
			Iodized salt, Mean	Food, mean	Preparations, mean	Drinking water, median	Iodine supplement rate[1]	Consumption rate of qualified iodized salt[2]
Fujian	329	132.9	121.3 (51.49)	98.6 (39.74)	17.5 (7.41)	2.4 (2.40)	99.0	93.6
Liaoning	369	127.1	98.9 (48.41)	84.9 (44.41)	6.1 (2.96)	6.5 (4.22)	99.0	90.7
Shanxi	401	155.6	100.7 (49.15)	84.5 (47.39)	1.3 (0.47)	5.0 (2.99)	99.8	97.1
Sichuan	360	192.7	117.0 (50.56)	98.4 (38.23)	18.9 (8.33)	1.7 (2.88)	99.8	88.5
Xinjiang	367	229.8	117.9 (22.93)	102.8 (17.10)	312.5 (59.34)	3.1 (1.17)	100.0	90.1
Anhui	386	156.8	135.8 (57.59)	114.5 (41.28)	1.8 (0.75)	1.5 (0.38)	100.0	97.5
Hubei	321	175.0	100.2 (48.68)	104.9 (46.77)	6.8 (3.31)	2.0 (1.24)	99.5	96.3
Total	2,533	164.3	113.1 (42.93)	98.3 (35.44)	47.7 (19.78)	3.1 (1.85)	99.0	89.7

Note. *MUIC, population median urinary iodine concentration. [1]Iodine supplement rate, the proportion of pregnant women who took iodized salt, iodine supplement preparations and iodine-rich foods. [2]Consumption rate of qualified iodized salt, salt samples with iodine of 18–33 mg/kg / total number of samples. [3]Contribution rate, iodine intake in drinking water, food, iodine preparations, or salt / all amounts of iodine intake.

rates of TPOAb-positive and sub-hypothyroidism, at 25.63% and 7.24%, respectively. In addition, both the prevalence of sub-hyperthyroidism in Fujian, Anhui and Shanxi (3.46%, 3.24%, and 2.54%, respectively), and TgAb-positive rates in Shanxi (9.14%), Liaoning (8.99%), and Sichuan (7.24%) were higher than the overall level. As for thyroid nodules, the prevalence in Shanxi and Liaoning was higher (22.74% and 20.8%, respectively). Goiter is a thyroid-related disease and the lowest prevalence (i.e., 3.25%) was in Liaoning.

Multivariate binary logistic regression analysis was adjusted for age. Pregnant women living in urban areas were less likely to have low iodine nutrition (UI < 150 μg/L, Supplementary Table S4, available in www.besjournal.com), which may be because they were likely to pay attention to the overall and balance of iodine nutrition. With respect to factors influencing thyroid function (Supplementary Table S5, available in www.besjournal.com), gestation, family annual income and vomiting reaction all had impacts on FT_4. Compared with the second or third trimesters, pregnant women in their first trimester were at greater risk for having low FT_4 levels, which may be due to changing hormone levels and increased need for iodine early in pregnancy. Moreover, concerning family annual income, pregnant women with high annual income had higher FT_4 levels, likely due to the diversity and quality of their diets. For TSH, the third trimester had risks of both high and low TSH levels; in addition, dietary habits also had an effect on TSH. For factors influencing thyroid antibody (Supplementary Table S6, available in www.besjournal.com), it was found that higher annual income had a positive effect on the value of TPOAb, which may be consistent with the cause of high FT_4 in these participants.

By comparing different iodine supplementation measures, iodine supplementation in ISFP group (MUIC of 205.1 μg/L) resulted in significantly improved iodine nutrition in pregnant women (Figure 1A).

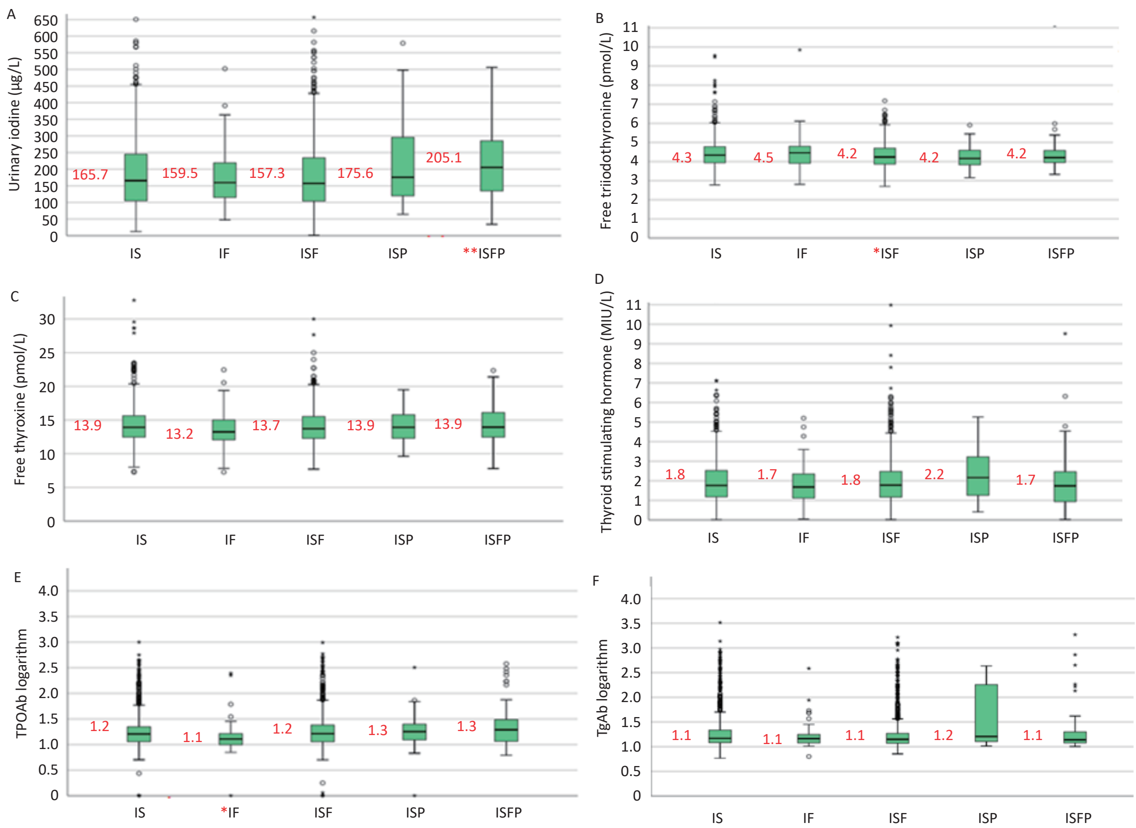

Figure 1. Urinary iodine and thyroid function of pregnant women with different iodine supplementation measures. All data are presented as median and interquartile range. (A) urinary iodine; (B) FT_3 levels; (C) FT_4 levels; (D) TSH levels; (E) TPOAb levels; (F) TgAb levels. IS, iodized salt; IF, iodine rich food; ISF, iodized salt + iodine rich food; ISP, iodized salt + iodine supplement pills; ISFP, iodized salt + iodine rich food + iodine supplement pills. *Represents that the indicator in this group was the lowest level in all groups; **represents that the indicator in this group was the highest level in all groups.

Compared with other iodine supplementation measures, the IF group had significantly reduced TPOAb values (P < 0.01, Figure 1E), While, the ISP group had the highest TgAb levels (Figure 1F). For thyroid-related diseases, different measures affected the prevalence of sub-hyperthyroidism and antibody status (Table 2). Among these, the IF group had the lowest prevalence of TPOAb-positive (5.48%) and TgAb-positive (1.37%). However, the ISP group had the highest prevalence of TgAb-positive (23.81%), followed by the ISFP group; furthermore, and the positive rate of TPOAb was highest in the ISFP group (24.14%). In addition, the prevalence of sub-hyperthyroidism in the ISF group was the highest (8.59%).

Accessing appropriate iodine supplementation measures promotes the health of pregnant women. Gao CH et al.[8] found that iodine-rich herbs such as kelp and seaweed had positive effects on the recovery of iodine deficiency goiter, and in this study, pregnant women supplementing iodine in the IF group had a lower prevalence of thyroid antibody-

Table 2. Effect of iodine supplementation measures on thyroid diseases

Indication	Classification	Iodine supplement measures					Value (χ^2/Fisher)	P[6]
		IS[1] n = 1,066	IF[2] n = 73	ISF[3] n = 1,164	ISP[4] n = 42	ISFP[5] n = 58		
Hypothyroidism	Yes	9	0	5	0	0	1.602	0.750
	No	1,057	73	1,159	42	58		
	Rate (%)	0.84	0	0.43	0	0		
Sub-hypothyroidism	Yes	42	3	45	1	1	0.457	0.975
	No	1,024	70	1,119	41	57		
	Rate (%)	3.94	4.11	3.87	2.38	1.72		
Hyperthyroidism	Yes	18	2	16	1	1	2.458	0.532
	No	1,048	71	1,148	41	57		
	Rate (%)	1.69	2.74	1.37	2.44	1.72		
Sub-hyperthyroidism	Yes	23	2	10	1	1	8.647	0.047
	No	1,043	71	1,154	41	57		
	Rate (%)	2.16	2.74	8.59	2.44	1.72		
TPOAb-positive	Yes	129	4	137	4	14	104.261	0.000
	No	937	69	1,027	38	44		
	Rate (%)	12.10	5.48	11.77	9.52	24.14		
TgAb-positive	Yes	76	1	62	10	6	28.806	0.000
	No	990	72	1,102	32	52		
	Rate (%)	7.13	1.37	5.33	23.81	10.34		
Double antibodypositive	Yes	54	1	43	0	4	6.293	0.152
	No	1,012	72	1,121	42	54		
	Rate (%)	5.07	1.37	3.69	0	6.90		
Goiter	Yes	8	0	81	0	0	0.142	1.000
	No	1,034	73	1,143	35	58		
	Rate (%)	0.77	0	0.70	0	0		
Nodules	Yes	152	18	196	8	6	8.621	0.071
	No	903	55	960	33	52		
	Rate (%)	14.41	24.66	16.96	19.51	10.34		

Note. [1]IS, iodine salt. [2]IF, iodine rich food. [3]ISF, iodine salt + iodine rich food. [4]ISP, iodine salt + Iodine preparations. [5]ISFP, iodine salt + iodine rich food + iodine preparations. [6]Chi-square test and Fisher's exact test.

positive conditions. Bai JJ et al. confirmed that the intake of meat, milk, seafood, and other food also had an impact on the iodine nutrition of pregnant women[9], which is consistent with the findings of the study. Iodine supplementation in the ISFP group was the best approach for pregnant women to improve iodine nutrition, but attention should be paid to excessive iodine intake; furthermore, ISF and ISFP approaches to iodine supplementation may increase the prevalence of antibody-positive thyroid disease. In addition, our study found that higher MUIC (150–249 μg/L) increased the risk of autoimmune and sub-hypothyroidism, which may result from excess iodine consumption leading to autoimmune activity that further causes hypothyroidism[10]. However, it is misunderstood that pregnant women should decrease iodine intake; pregnant women with MUIC in the range of 100–150 μg/L have increased risk of goiter. Through this study, we found that different iodine supplements had different effects on thyroid function and iodine nutrition, and the effects varied from person to person. Therefore, iodine should be supplemented using scientific approaches.

In this study, the food weighing method was not used, and the food frequency questionnaire may have resulted in some bias, although every investigator was trained to ensure the accuracy of survey results. Due to time limitations, our investigation ignored some information, which may have resulted in an incomplete assessment of influencing factors and interactions. As China has a high coverage of USI, the numbers of iodine supplementation with IF, ISP, and ISFP approaches were relatively few, which would make some stratified analysis difficult and limit the analysis of results. Therefore, future studies should aim to expand the sample size. Moreover, the changes of various indicators of the same subject during the whole pregnancy period were not observed, and a cohort study will be conducted if future opportunities allow.

Many factors can affect iodine nutrition status and thyroid function in pregnant women, such as habitation (urban/rural), gestation, family annual income, pregnancy vomiting reaction, dietary habits, and iodine supplementation measures. Iodine should be supplemented scientifically, and our findings suggest that iodine supplementation with ISFP is the most effective measure to improve iodine nutrition in pregnant women if the iodine is not excess. In the case of adequate iodine nutrition, iodine supplementation only with iodine-rich food can significantly reduce the positive rate of antibodies and reduce the incidence of autoimmune disease. Accessing appropriate iodine supplementation measures promotes the healthy development of pregnant women.

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Authorship PL designed the study; LZ, WDL, QZJ, JHW, JSL, ZHC, and BYZ carried out the research; RS, TTQ, LCL, MZ, and WJC analyzed the data; and RS wrote the paper. RS and TTQ held primary responsibility for the final content. All authors read and approved the final manuscript.

Data Availability Data described in the manuscript, code book, and analytic code will not be made available.

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Supplementary Table S1. Basic information of pregnant women in seven provinces

Indication	Classification	Number	Proportion (%)
Habitation	Village	1,518	63.3
	Urban	879	36.7
Gestation	First trimester	428	17.6
	Middle trimester	1,102	45.2
	Last trimester	907	37.2
Level of education	Primary school	114	4.8
	Junior high school	850	35.5
	Senior high school	534	22.3
	Junior college	564	23.5
	Bachelor degree	314	13.1
	Master degree or above	21	0.8
Householdannual income, yuan a year	< 20,000	349	14.6
	20,000–29,999	403	16.8
	30,000–59,999	685	28.6
	60,000–100,000	651	27.2
	> 100,000	309	12.8
Pregnancy vomiting reaction	No	600	25.0
	Slight	1,171	48.9
	Moderate	420	17.5
	Serious	206	8.6
Dietary habit	Three meals a day	1,537	64.1
	Four meals a day	300	12.5
	Five or six meals a day	395	16.5
	Rule-less	165	6.9
Total		2,397	100.0

Supplementary Table S2. Comparison of thyroid diseases prevalence grouped by counties and individual with different MUIC[1] or UI[2]

Kind of disease	Rate (%) grouped by median urinary iodine (counties, μg/L)		P^3	Rate (%) grouped by urinary iodine (individual, μg/L)			P^3
	100–149	150–249		< 150	150–249	250–499	
Hypothyroidism	0.46	0.50	0.888	0.27	0.87	0.78	0.174
Sub-hypothyroidism	2.46	5.38	0.000	2.67	5.24	3.72	0.014
Hyperthyroidism	1.55	1.65	0.842	1.42	1.50	2.94	0.078
Sub-hyperthyroidism	1.55	1.82	0.616	1.96	1.62	2.94	0.351
TPOAb positive	8.95	13.78	0.004	11.39	11.66	16.38	0.011
TgAb positive	6.19	6.69	0.623	6.35	6.13	7.71	0.489
Double antibody positive	3.78	5.48	0.034	4.41	3.44	5.39	0.188
Goiter	1.02	0.41	0.027	1.10	0.50	4.90	0.000
Nodules	16.44	17.15	0.646	17.10	15.30	14.40	0.321

Note. [1]MUIC, population median urinary iodine concentration. [2]UI, personal urinary iodine concentration. [3]Chi-square test and Fisher's exact test.

Supplementary Table S3. Prevalence of thyroid diseases for pregnant women in different provinces

Provinces	Number	Prevalence of thyroid function related diseases (%)								Goiter[1] rate (%)	Thyroid nodule[2] rate (%)
		Hypo-thyroidism[3]	Subclinical hypo-thyroidism[4]	Hyper-thyroidism[5]	Subclinical hyper-thyroidism[6]	TPOAb positive[7]	TgAb positive[8]	Double antibody positive[9]	Total		
Xinjiang	365	1.65	3.56	0.82	0.82	10.96	5.21	1.10	22.47	0.00	8.22
Sichuan	359	0.56	7.24	1.95	1.39	25.63	7.24	5.57	33.98	0.25	10.07
Shanxi	394	0.76	4.31	0.51	2.54	10.15	9.14	6.09	17.01	0.46	22.74
Liaoning	367	0.27	3.27	4.36	0.27	10.35	8.99	4.63	17.71	3.25	20.80
Fujian	318	0.31	1.26	2.52	3.46	7.55	3.14	2.20	15.09	0.52	14.25
Anhui	401	0.50	2.74	0.75	3.24	11.22	6.23	4.49	15.96	0.00	16.67
Hubei	321	0.31	3.74	0.62	1.25	10.28	4.98	4.98	15.89	0.50	16.54
Total	2,525	0.67	3.76	1.62	1.86	12.36	6.53	4.20	19.76	0.72	15.75

Note. [1]Goiter, thyroid volume is beyond the upper limit of the normal range. [2]Thyroid nodule, pathological changes caused by local abnormal growth of thyroid cells. [3]Hypothyroidism, TSH is greater than the upper limit of the normal range, and FT_4 is less than the lower limit of the normal range. [4]Subclinical hypothyroidism, TSH is greater than the upper limit of the normal range, and FT_4 is within the normal range. [5] Hyperthyroidism, TSH is less than the lower limit of the normal range, and FT_4 is greater than the upper limit of the normal range. [6]Subclinical hyperthyroidism, TSH is less than the lower limit of the normal range, and FT_4 is within the normal range. [7]TPOAb positive, TPOAb is greater than the upper limit of the normal range. [8]TgAb positive, TgAb is greater than the upper limit of the normal range. [9]Double Antibody positive, both TPOAb and TgAb are greater than the upper limit of the normal rang.

Supplementary Table S4. Factors affecting pregnant women's urinary iodine

Classification	Normal group[1] and low group[2]						Normal group and high group[3]					
	β	SE	Wald χ^2	*OR*	95% *CI*	P^4	β	SE	Wald χ^2	*OR*	95% *CI*	P^4
Age												
30−40 years old	0.006	0.091	0.004	1.006	0.842, 1.201	0.952	0.020	0.111	0.032	1.020	0.821, 1.268	0.858
Gestation												
Middle trimester	0.095	0.137	0.482	0.905	0.705, 1.162	0.434	0.043	0.159	0.073	1.000	0.743, 1.347	0.999
Last trimester	0.095	0.148	0.412	0.893	0.680, 1.171	0.412	−0.113	0.170	0.439	0.862	0.621, 1.195	0.372
Habitation												
Urban	0.494	0.106	21.679	0.704	0.575, 0.862	0.001	−0.041	0.129	0.104	1.186	0.915, 1.536	0.198
Annual income, Yuan												
20,000−29,999	0.218	0.191	1.302	1.145	0.793, 1.653	0.469	−0.356	0.230	2.394	0.997	0.639, 1.555	0.988
30,000−59,999	−0.089	0.280	0.100	1.749	1.016, 3.013	0.044	−0.173	0.343	0.255	0.859	0.441, 1.671	0.654
60,000−100,000	0.267	0.303	0.778	1.342	0.748, 2.407	0.325	0.048	0.377	0.016	1.268	0.614, 2.620	0.521
> 100,000	0.509	0.424	1.441	1.449	0.646, 3.248	0.368	−0.452	0.577	0.614	1.515	0.501, 4.584	0.462
Pregnancy vomiting reaction												
Slight	0.055	0.234	0.055	0.678	0.427, 1.076	0.099	0.086	0.298	0.083	1.137	0.637, 2.030	0.663
Moderate	0.006	0.456	0.000	0.534	0.224, 1.277	0.159	0.242	0.610	0.158	0.984	0.311, 3.117	0.978
Serious	−0.578	0.728	0.630	0.695	0.180, 2.692	0.599	0.505	0.988	0.262	0.652	0.101, 4.193	0.653
Dietary habit												
Four meals a day	−0.470	0.189	6.207	2.207	1.514, 3.217	0.000	−0.659	0.236	7.832	0.565	0.352, 0.908	0.018
Five or six meals a day	−0.322	0.406	0.629	1.807	0.844, 3.869	0.128	−0.400	0.545	0.538	0.870	0.315, 2.403	0.788
Rule-less	0.341	0.560	0.369	0.884	0.310, 2.522	0.818	−0.150	0.187	0.637	0.750	0.191, 2.942	0.680

Note. [1]Normal group, urinary iodine concentration is within the range of 150−249 μg/L. [2]Low group, urinary iodine concentration is less than the 150 μg/L. [3]High group, urinary iodine concentration is greater than the 249 μg/L. [4]Multivariate Binary logistic regression.

Supplementary Table S5. Factors affecting pregnant women's thyroid function

Indicator	Classification	Normal group and low group[1]						Normal group and high group[1]					
		β	SE	Waldχ^2	*OR*	95% *CI*	P^2	*β*	SE	Waldχ^2	*OR*	95% *CI*	P^2
FT_4	Age												
	30–40 years old	−0.137	0.210	0.427	0.872	0.577, 1.316	0.513	0.053	0.138	0.148	1.055	0.804, 1.383	0.700
	Gestation												
	Middle trimester	−2.219	0.278	63.644	0.120	0.075, 0.193	0.000	−0.102	0.330	0.096	1.154	0.622, 2.143	0.649
	Last trimester	−2.056	0.330	38.854	0.151	0.081, 0.281	0.000	2.470	0.307	64.679	14.683	8.201, 26.288	0.000
	Habitation												
	Urban	0.174	0.236	2.542	1.715	1.101, 2.670	0.017	0.322	0.156	4.260	1.049	0.766, 1.436	0.766
	Annual income, Yuan												
	20,000–29,999	−0.338	0.408	0.683	0.810	0.395, 1.662	0.566	−0.032	0.295	0.012	1.046	0.563, 1.943	0.888
	30,000–59,999	0.514	0.866	0.352	2.948	0.590, 14.724	0.188	0.703	0.495	2.015	3.361	1.258, 8.981	0.016
	60,000–100,000	−0.100	0.891	0.012	2.485	0.461, 13.388	0.289	1.825	0.537	11.547	8.097	2.820, 23.248	0.000
	> 100,000	−2.070	1.281	2.611	0.334	0.024, 4.699	0.417	2.310	0.663	12.132	7.212	1.997, 26.045	0.003
	Pregnancy vomiting reaction												
	Slight	−1.041	0.819	1.616	0.191	0.042, 0.875	0.033	−1.300	0.425	9.367	0.270	0.118, 0.621	0.002
	Moderate	1.865	1.158	2.591	1.994	0.199, 19.949	0.557	−2.707	0.863	9.835	0.087	0.016, 0.464	0.004
	Serious	−7.750	1.017	0.986	41.291	0.752, 66.017	0.069	−5.462	1.442	14.339	0.012	0.001, 0.132	0.000
	Dietary habit												
	Four meals a day	−1.022	0.479	4.554	0.759	0.329, 1.747	0.516	0.388	0.314	1.530	1.642	0.884, 3.051	0.117
	Five or six meals a day	−2.074	0.967	4.601	0.187	0.028, 1.248	0.083	0.542	0.759	0.510	1.563	0.359, 6.809	0.552
	Rule-less	−9.373	1.227	0.823	36.800	0.109, 52.238	0.995	3.526	1.285	7.528	17.754	2.197, 143.491	0.007
TSH	Age												
	30–40 years old	0.030	0.202	0.022	1.031	0.694, 1.531	0.881	0.203	0.247	0.676	1.225	0.755, 1.986	0.411
	Gestation												
	Middle trimester	0.100	0.347	0.083	1.485	0.785, 2.810	0.224	0.283	0.523	0.292	1.059	0.429, 2.611	0.901
	Last trimester	1.352	0.346	15.245	5.216	2.739, 9.933	0.000	1.487	0.502	8.788	4.673	1.988, 10.988	0.000
	Habitation												
	Urban	0.445	0.232	3.669	1.267	0.809, 1.986	0.301	0.256	0.281	0.828	1.898	1.139, 3.163	0.014
	Annual income, Yuan												
	20,000–29,999	−0.193	0.467	0.171	0.608	0.254, 1.456	0.264	0.120	0.551	0.047	1.521	0.551, 4.195	0.418
	30,000–59,999	0.999	0.876	1.299	3.867	0.708, 21.124	0.118	0.365	0.748	0.238	2.837	0.689, 11.672	0.149
	60,000–100,000	2.102	0.896	5.500	9.375	1.650, 53.285	0.012	0.323	0.858	0.142	2.664	0.513, 13.823	0.244
	> 100,000	2.310	1.147	4.054	11.675	1.196, 113.932	0.035	−2.184	1.937	1.271	0.853	0.015, 47.781	0.938
	Pregnancy vomiting reaction												
	Slight	−1.148	0.793	2.094	0.247	0.051, 1.186	0.081	0.002	0.605	0.000	0.440	0.135, 1.431	0.172
	Moderate	−1.333	1.158	1.325	0.167	0.017, 1.615	0.122	−15.466	47.167	0.000	0.000	0.000, 1.978	0.997
	Serious	−1.778	1.856	0.918	0.232	0.008, 6.846	0.397	−12.652	57.168	0.000	0.000	0.000, 1.325	0.998
	Dietary habit												
	Four meals a day	−0.043	0.372	0.013	1.036	0.500, 2.147	0.925	−0.619	0.677	0.837	1.886	0.582, 6.116	0.290
	Five or six meals a day	−1.709	0.864	3.906	0.167	0.031, 0.904	0.038	15.136	44.163	0.000	0.000	0.000, 5.348	0.997
	Rule-less	−1.214	1.403	0.749	0.278	0.027, 2.909	0.285	13.819	37.167	0.000	0.000	0.000, 7.616	0.998

Note. [1]Normal, low and high group, FT_4 or TSH is within, below and above the normal range, respectively. [2]Multivariate Binary logistic regression.

Supplementary Table S6. Factors affecting pregnant women's thyroid related antibodies

Indication	Classification	Normal group[1] and high group[1]					
		β	SE	Wald χ^2	*OR*	95% *CI*	P^2
TPOAb	Age						
	30–40 years old	−0.068	0.123	0.308	0.934	0.734, 1.188	0.579
	Gestation						
	Middle trimester	−0.323	0.176	3.359	0.645	0.466, 0.892	0.008
	Last trimester	0.014	0.185	0.006	1.010	0.720, 1.417	0.955
	Habitation						
	Urban	−0.069	0.140	0.244	0.937	0.716, 1.227	0.638
	Annual income, yuan						
	20,000–29,999	−0.445	0.254	3.058	0.629	0.383, 1.033	0.067
	30,000–59,999	−1.189	0.343	12.027	0.409	0.209, 0.802	0.009
	60,000–100,000	−1.116	0.373	8.946	0.400	0.193, 0.830	0.014
	> 100,000	−1.640	0.580	8.008	0.228	0.075, 0.701	0.010
	Pregnancy vomiting reaction						
	Slight	0.856	0.285	9.037	1.666	0.946, 2.935	0.077
	Moderate	1.026	0.632	2.640	1.572	0.461, 5.357	0.470
	Serious	−0.410	1.375	0.089	0.271	0.019, 3.855	0.335
	Dietary habit						
	Four meals a day	0.025	0.256	0.010	1.534	0.929, 2.533	0.095
	Five or six meals a day	−0.053	0.588	0.008	1.463	0.475, 4.508	0.508
	Rule-less	1.656	1.200	1.905	9.583	0.923, 99.493	0.058
TgAb	Age						
	30–40 years old	−0.055	0.158	0.122	0.946	0.695, 1.289	0.727
	Gestation						
	Middle trimester	−0.251	0.226	1.226	0.674	0.453, 1.005	0.053
	Last trimester	−0.208	0.245	0.718	0.763	0.493, 1.181	0.225
	Habitation						
	Urban	−0.112	0.185	0.364	0.820	0.578, 1.165	0.269
	Annual income, Yuan						
	20,000–29,999	0.027	0.296	0.008	0.798	0.452, 1.407	0.435
	30,000–59,999	0.078	0.481	0.026	1.103	0.444, 2.739	0.833
	60,000–100,000	−0.078	0.524	0.022	0.917	0.341, 2.466	0.864
	> 100,000	0.059	0.774	0.006	0.721	0.173, 3.010	0.653
	Pregnancy vomiting reaction						
	Slight	−0.421	0.411	1.047	0.613	0.279, 1.351	0.225
	Moderate	−1.462	0.997	2.152	0.231	0.036, 1.502	0.125
	Serious	−20.132	47.560	0.000	0.000	0.000, 3.997	0.997
	Dietary habit						
	Four meals a day	0.210	0.324	0.421	1.682	0.914, 3.097	0.095
	Five or six meals a day	1.203	0.914	1.734	3.471	0.627, 19.225	0.154
	Rule-less	19.462	59.660	0.000	0.000	0.000, 5.991	0.997

Note. [1]Normal and high group, TPOAb or TgAb is within and greater than the normal range, respectively. [2]Multivariate Binary logistic regression.