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Thyroid Function: Comparison of Women in Late Pregnancy With Control Women of Reproductive Age in Regions of Dietary Iodine Excess

Quxiao Du, MMedSc[1], Hong Zhu, BSMed[2], Li Yao, BSMed[1]

Abstract

Three hundred pregnant women and 300 women of reproductive age (controls) were selected from regions with a dietary iodine excess to evaluate thyroid and autoimmune thyroid functions. Fasting morning urine and venous blood samples were collected. Urinary iodine concentration, serum free tri-iodothyronine (FT_3), free thyroxine (FT_4), sensitive thyroid stimulating hormone (sTSH), serum thyroid peroxidase antibody (TPOAb), and thyroglobulin antibody (TGAb) levels were determined. Iodine levels were excessive in 83.7% of pregnant women and 80.7% of the control women. The former showed lower rates of total thyroid disease and subclinical hypothyroidism than the latter (21.7% vs 29.7%, $P < 0.05$; 19.7% vs 27.3%, $P < 0.05$). The FT_3 level, FT_4 level, and TGAb positive rate of pregnant women were lower than that in the controls ($P < 0.05$). Thus, both excessive iodine intake and pregnancy can influence the thyroid and autoimmune thyroid functions of women.

Keywords

autoimmune thyroid function, excessive iodine, pregnant women, reproductive-age women, thyroid function

Introduction

Iodine is a trace element necessary for human body growth that cannot be synthesized. It is an important molecule for the synthesis of the thyroid hormone, but excessive iodine intake causes disorders such as goiter and hypothyroidism.[1-3] Universal table salt iodization can improve the dietary iodine status of populations, and urinary iodine level is an important index of this. Because of changes in the physiology of pregnant and lactating women, they can exhibit iodine malnutrition even when ingesting it from daily food. Pregnancy causes great changes to thyroid and autoimmune thyroid functions, which can easily lead to autoimmune thyroid disease.[4-6]

By comparing pregnant women and normal women of reproductive age, this research explored the influence of pregnancy and excessive iodine intake on the thyroid and autoimmune thyroid

[1]Department of Gynecology, People's Hospital of Zhengzhou, China
[2]Health Center of Henan Military Area Training Unit, Zhengzhou, China

Corresponding Author:
Li Yao, Department of Gynecology, People's Hospital of Zhengzhou, Zhengzhou 450002, China.
Email: yaoli1104@126.com

functions of women. This provided a theoretical basis for the decreased thyroid function and autoimmune thyroid function disorders among pregnant women, caused by excessive iodine intake, and should help in improving public health.

Methods

Experimental Group

Dietary iodine excess areas were selected with a range of iodine content in drinking water of 185.3 to 2840.4 μg/L. Three hundred women late in pregnancy (27 weeks after pregnancy) aged 26.7 ± 5.1 years were selected as the experimental group and 300 controls aged 29.2 ± 6.0 years were selected as the control group during March to September 2011. Eligible subjects needed to meet the following inclusion criteria: absence of thyroid diseases or other autoimmune diseases; absence of endocrine, heart, chronic, or genetic diseases; and no abnormal anatomy of the reproductive system. The subjects needed to be healthy and without unusual dietary habits. Women who took extra iodine preparations during pregnancy were excluded. Subjects were informed about the research methods and content, and provided signed informed consent. This project was approved by the ethics committee of People's Hospital of Zhengzhou.

Urine Collection and Iodine Level Determination

Fasting 5 mL urine samples from the survey subjects collected in the morning were sealed in clean vinyl tubes and stored at −20°C. Urinary iodine levels were determined by arsenic-cerium catalytic spectrophotometry. The measuring instruments were an ND-N-type constant temperature digest instrument (Beijing Lanxingguang Display Equipment Technology Co. Ltd) and a type 722 spectrophotometer (Shanghai Tianxiang Optical Instrument Co. Ltd).

Blood Collection and Determination of Hormone Levels

Fasting 5ml venous blood samples of the subjects were collected. After two hours of standing time, the sample was centrifuged at 1200*g* for five minutes and then stored frozen at −80°C. Serum free tri-iodothyronine (FT_3), free thyroxine (FT_4), and sensitive thyroid stimulating hormone (sTSH) were determined using an ADVIA Centaur automatic chemiluminescence immunoassay (Siemens AG, Munich, Germany). Thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TGAb) levels were determined using radioimmunoassay kits (Shanghai Jianglai Biotech Co. Ltd) according to the manufacturer's instructions. The result was deemed positive if TPOAb >15% and TGAb >30%. The coefficients of variability for TPOAb and TGAb measurements in the same product batch were 4.1% and 3.7%, respectively. The coefficients of variability for TPOAb and TGAb measurements in different product batches were 4.4% and 4.7%, respectively. The 95% confidence intervals (95% CI) for TPOAb and TGAb measurements were 9.6% - 11.2% and 7.9% - 9.3%, respectively.

Diagnostic Criteria

The normal range of thyroid hormone levels among the pregnant women was determined by chemiluminescence, as described.[5] Diagnostic criteria for the pregnant women were as follows. (1) Hyperthyroidism: having clinical manifestations of hyperthyroidism, with serum sTSH <0.47 mIU/L and FT_4 >16.70 pmol/L (or FT_3 > 5.20 pmol/L). (2) Subclinical hyperthyroidism: without clinical manifestation of hyperthyroidism, with serum sTSH <0.47 mIU/L, FT_4 9.20 ≤ 16.70 pmol/L, and FT_3 3.52 ≤ 5.20 pmol/L. (3) Hypothyroidism: serum sTSH >4.54

Table 1. Distribution of Pregnant Women's Urinary Iodine Levels.

Iodine Intake	MUI (μg/L)	Number of Participants (%)
Deficiency (0-149 μg/L)	139.1	5 (1.7%)
Sufficiency (150-249 μg/L)	244.6	2 (0.6%)
Super sufficiency (250-499 μg/L)	430.0	42 (14.0%)
Excess (>500 μg/L)	1512.1	251 (83.7%)

Abbreviation: MUI, median urinary iodine.

Table 2. Frequency Distribution of Control Women's Urinary Iodine Levels.

Iodine Intake	MUI (μg/L)	Number of Participants (%)
Deficiency (0-99 μg/L)	59.9	7 (2.3%)
Sufficiency (100-199 μg/L)	149.9	28 (9.3%)
Super sufficiency (200-299 μg/L)	235.2	23 (7.7%)
Excess (>300 μg/L)	1098.3	242 (80.7%)

Abbreviation: MUI, median urinary iodine.

mIU/L and FT_4 <9.20 pmol/L. (4) Subclinical hypothyroidism: serum sTSH >4.54 mIU/L and FT_4 9.20 ≤ 16.70 pmol/L.

Diagnostic criteria for the controls were as follows. (1) Hyperthyroidism: having clinical manifestations of hyperthyroidism, with serum sTSH <0.3 mIU/L and FT_4 >23.5 pmol/L (or FT_3 > 6.5 pmol/L). (2) Subclinical hyperthyroidism: without clinical manifestation of hyperthyroidism, with serum sTSH <0.3 mIU/L, serum FT_4 <23.5 pmol/L, and FT_3 <6.5 pmol/L. (3) Hypothyroidism: serum sTSH >5.0 mIU/L and serum FT4 <11.5 pmol/L. (4) Subclinical hypothyroidism: serum sTSH >5.0 mIU/L and serum FT_4 >11.5 pmol/L.

Statistical Analysis

All the data were subjected to statistical analysis using SPSS software (version 17.0; SPSS Inc, Chicago, IL). The variables in normally distributed data are expressed as the mean ± standard deviation. Student's *t* test or analyses of variance were used for group comparisons. Comparisons of numerical data used the χ^2 test, and $P < 0.05$ was assumed to be statistically significant. Other data are expressed as the median and 95% CI or odds ratio (OR).

Results

Urinary Iodine Levels

The median urinary iodine (MUI) levels of the pregnant women and control women were 1227.9 μg/L (95% CI = 681.1-1973.3) and 951.2 μg/L (95% CI = 428.8-1294.8) μg/L, respectively. The subjects were classified as having iodine deficiency, iodine sufficiency, iodine super sufficiency, or iodine excess according to WHO recommendations.[6] Most pregnant women and controls had an iodine excess condition; there were a few with iodine sufficiency and super sufficiency conditions, and few subjects had iodine deficiency (Tables 1 and 2).

Table 3. Serum FT_3, FT_4, and sTSH Levels of the Pregnant Women and Control Groups.

Group	Number of Participants	FT_3 (pmol/L)	FT_4 (pmol/L)	sTSH (mIU/L)
Pregnant women	300	4.0 ± 0.6	13.5 ± 1.6	2.9 ± 1.2
Controls	300	4.7 ± 1.1[a]	14.3 ± 3.3[a]	3.1 ± 1.2

Abbreviations: FT_3, free tri-iodothyronine; FT_4, free thyroxine, sTSH, sensitive thyroid stimulating hormone.
[a]Group comparison, $P < .01$.

Table 4. The Prevalence of Thyroid Diseases Among the Pregnant Women and Control Groups.

Group	Number of Participants	Hyperthyroidism	Subclinical Hyperthyroidism	Hypothyroidism	Subclinical Hypothyroidism
Pregnant women	300	1 (0.3%)	59 (19.7%)	2 (0.7%)	6 (2.0%)
Controls	300	9 (3.0%)	82 (27.3%)	1 (0.3%)	1 (0.3%)

Thyroid Function

The FT_3, FT_4, and sTSH levels of the pregnant women and controls are summarized in Table 3. The FT_3 and FT_4 levels of pregnant women were significantly lower than that of controls (both $P < 0.01$). The total prevalence rates of thyroid disease among the pregnant women and controls were 22.7% and 31.0%, respectively; that of the pregnant women was lower than that of the controls ($\chi^2 = 5.3$; $P = 0.021$ to < 0.05; OR: 1.5; 95% CI: 1.1-2.2). Among all the cases of thyroid disease, the prevalence rate of subclinical hyperthyroidism was the highest at 19.7% in pregnant women and 27.3% in controls; that of the controls was lower than in the pregnant women ($\chi^2 = 4.9$; $P = 0.027$ to < 0.05; OR: 1.5; 95% CI: 1.0-2.2). The prevalence rates of hyperthyroidism, hypothyroidism, and subclinical hypothyroidism in pregnant women were 0.4%, 0.7%, and 2.0%, respectively. The prevalence rates of hyperthyroidism, hypothyroidism, and subclinical hypothyroidism in the controls were 3.0%, 0.3%, and 0.3% respectively. These differences between the two groups were all statistically significant ($P < 0.05$, Table 4).

Autoimmune Thyroid Function

The TPOAb positive rate of pregnant women was 15.4%, whereas their TGAb positive rate was 7.7%. The TPOAb positive rate of controls was 19.1%, while their TGAb positive rate was 13.5%. The TGAb positive rate of pregnant women was significantly lower than that of the controls ($\chi^2 = 5.667$; $P < 0.05$), whereas there was no significant difference in the TPOAb positive rate ($\chi^2 = 1.418$; $P > 0.05$).

When we compared pregnant women having autoimmune thyroid disease with those without, neither the TPOAb positive rate difference (22.3% and 13.7%, respectively) nor the TGAb positive rate difference (10.7% and 6.3%) was statistically significant ($P > 0.05$). When we compared controls having thyroid disease with those without, neither the TPOAb positive rate difference (19.6% and 17.6%, respectively) nor the TGAb positive rate difference (13.3% and 14.3%) was statistically significant($P > 0.05$). Thus, the thyroid function measures were not associated with the autoimmune thyroid function of pregnant women and controls.

We compared the autoimmune thyroid function of pregnant women and controls with or without thyroid disease. For the pregnant women and controls with thyroid disease, neither the TPOAb positive rate difference (22.3% and 19.6%, respectively) nor the TGAb positive rate difference (10.7% and 13.3%) was statistically significant ($P > 0.05$). For the pregnant women and controls

without thyroid disease, the TPOAb positive rate difference (13.7% and 17.6%, respectively) was not statistically significant ($P > 0.05$); however, the TGAb positive rate difference (6.3% vs 14.3%) was statistically significant ($P = 0.015$ to < 0.05). Thus, in women with normal thyroid function, pregnancy might influence their autoimmune thyroid function in iodine excess areas.

Discussion

The human infant's brain completes its growth by 2 years of age. The iodine nutrition level of pregnant women directly influences brain development and the physical growth of fetuses and infants. The newborn infant birth defect (dysgnosia) induced by iodine deficiency is one disease that can be prevented.[7] According to the iodine nutrition level assessment criteria proposed by ICCIDD/UNICEF/WHO in 2007,[8] in the present investigation, 83.7% of the pregnant women and 80.7% of the controls in this study were in an iodine excess condition, which might be associated with the high iodine content in water in the local environment. Moreover, pregnancy can increase the glomerular filtration rate, increase the renal clearance rate of iodine, and damage glomerular reabsorption, resulting in an increase in urinary iodine excretion.[9-11]

Long-term high iodine intake can harm the human body and increase the prevalence of hyperthyroidism; moreover, iodine excess in the early trimester of pregnancy can increase the prevalence rate of subclinical hyperthyroidism among pregnant women.[12] The total prevalence of thyroid disease among pregnant women in regions of normal iodine supply was 7.8%, but the prevalence of hyperthyroidism including subclinical hyperthyroidism (1.1%), was obviously lower than that of hypothyroidism, including subclinical hypothyroidism (6.8%). However, no difference in prevalence between the two diseases could be observed in normal women.[13,14] Compared with regions with normal iodine levels, the prevalence of thyroid disease among pregnant women and controls—especially subclinical hyperthyroidism—in iodine excess areas of our study was obviously higher. The results indicate that dietary iodine excess can increase the risk of subclinical hyperthyroidism among both pregnant women and controls.

During pregnancy, the thyroid is under the double regulation of the hypothalamus-pituitary-thyroid axis and placenta-thyroid axis, which will affect the secretion of thyroid hormones. We found here that both the FT_3 and FT_4 levels of pregnant women were lower than that of controls. The reasons appear to be as follows: increased thyroid hormone consumption is caused by the increased basic metabolic rate in late pregnancy; moreover, there is an increase in urine iodine excretion caused by an increase in the renal excretion rate and an increased iodine demand associated with the rapid growth of the fetus. These and other reasons cause a decrease in thyroid hormone synthesis. On the other hand, because estrogen levels increase during pregnancy, the circulating level of thyroglobulin-binding protein also increases.[15,16] At the same time, chorionic gonadotropin can increase the total thyroxine and decrease the FT_4 and FT_3 secretion rates during pregnancy, as it functions similarly to TSH in reinforcing thyroid function.[17]

Apart from influencing thyroid function, pregnancy also affects the autoimmune function of the thyroid. Muller et al.[18] suggested that the maternal body can develop an immune rejection to fetuses carrying the major histocompatibility complex antigens of the parents; therefore, to protect the fetus, the maternal system undergoes immunosuppression. We found here that the TGAb positive rate of pregnant women with normal thyroid function was lower than that of the controls, showing that pregnancy might reduce the levels of thyroid autoantibodies.

Li et al[19] found that continuous excessive iodine intake increased the positive rate of thyroid autoantibodies. The TPOAb positive rate of pregnant women and controls in iodine excess areas was higher than that of the normal pregnant women in late pregnancy (3.3%) and controls (9.4%) in iodine-sufficient areas.[20] The TGAb positive rate of controls (11.17%) was higher than that of normal women.[13] Whether or not the thyroid function of women in late pregnancy and controls is normal, iodine excess can induce thyroid autoimmune disorders. Long-term production of

TPOAb is harmful in pregnancy, as it increases the risk of premature delivery, abortion, and mental defects in fetuses.[21,22] We found that excessive iodine intake could aggravate autoimmune disorders of the thyroid. Therefore, more attention should be paid to screening for thyroid autoantibodies in pregnant women and women of reproductive age.

In iodine-sufficient areas, the TPOAb positive rate of pregnant women in late pregnancy was lower than that of controls of similar age in the same area.[13] In our research, compared with the controls, the TPOAb positive rate of these women in late pregnancy had a tendency to decline, but the difference was not statistically significant. We conjecture that this change might reflect the combined effect of iodine excess and the influence of pregnancy on thyroid autoimmunity. Excessive iodine intake increases the TPOAb positive rate, whereas pregnancy reduces it; the combined effect manifests as a decrease in the TPOAb positive rate of pregnant women. Excessive iodine saturates the immunogenicity of the thyroid gland, which leads to little influence of excessive iodine on the increase in TGAb. This makes the inhibiting effect of pregnancy on the TGAb level more serious, so that the TGAb positive rate of women in late pregnancy is lower than that in controls.[23-25]

In summary, excessive dietary iodine increased the prevalence rate of thyroid disease and the positive rate of thyroid autoantibodies. For pregnant women in these dietary iodine excess areas, both the thyroid hormone levels and TGAb positive rate were lower than in controls. Thus, we should take the influence of excessive iodine and pregnancy on thyroid function into consideration and take measures to rectify any excessive iodine intake. We also propose that both women of reproductive age and pregnant women should undertake regular progestational and antenatal checks and monitor their thyroid function and thyroid autoantibody levels. Preventing thyroid disease is of vital significance for protecting women's health.

Declaration of Conflicting Interests

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