Original Article

Iodine intake level and incidence of thyroid disease in adults in Shaanxi province: a cross-sectional study

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Background: Exploring the relationship between adult iodine intake level and thyroid disease in Shaanxi area is of great significance for adult scientific iodine supplement and individual iodine supplement strategy. At present, the relationship between iodine and incidence of thyroid disease has not been determined.

Methods: This study was based on the clinical data of 1,159 patients from the Shaanxi Province aged over 18 years and diagnosed with thyroid-related diseases who were admitted to the Xijing Hospital from 2016 to 2020, and 182 provincial healthy volunteers aged over 18 years who agreed and signed informed consent for physical examination in 2020. The chi-square test and nonparametric test were used to investigate the relationship between iodine intake level and thyroid disease.

Results: (I) A total of 1,341 patients were enrolled and observed in this study. The median urinary iodine (MUI) was 233.20 ug/L. Compared with the control, group participants the urine iodine (UI) of those with hyperthyroidism, Hashimoto's thyroiditis (HT), papillary thyroid cancer (PTC), and benign nodules was significantly different ($P<0.05$). (II) The incidence of PTC was higher in women with excessive iodine intake and people aged ≥45 years ($P<0.05$). (III) There was no significant difference in urinary iodine (UI), age, gender, and other factors between benign nodules and PTC ($P>0.05$).

Conclusions: The iodine intake level of adults in Shaanxi is high, which is related to hyperthyroidism, HT, benign nodules, thyroid cancer, and other diseases. There were 3 factors, including excessive iodine intake, age ≥45 years, and female gender, found to be associated with the development of PTC.

Keywords: Iodine intake level; urinary iodine (UI); thyroid disease; papillary thyroid cancer (PTC)

Submitted Aug 26, 2021. Accepted for publication Oct 13, 2021.
doi: 10.21037/atm-21-4928
View this article at: https://dx.doi.org/10.21037/atm-21-4928

Introduction

Iodine is closely related to human health, with insufficient or excessive iodine intake leading to thyroid diseases. Iodine is an important synthetic raw material for the synthesis of thyroxine in the human body, which is closely related to human health. Both iodine deficiency and excess lead to thyroid diseases. The thyroid has a certain capacity for adjustment, within a certain range of iodine deficiency or iodine excess normal thyroid function can be maintained; when iodine intake exceeds the adaptive capacity of the thyroid, some people will manifest disease, with hypothyroidism may occur due to the thyroid losing its inhibitive ability. In the middle of the last century, as it became apparent that inadequate iodine intake could

lead to an increase in the incidence of endemic goitre and subsequently increase the incidence of thyroid nodules, global countries generally began to add a certain amount of iodine in their diet, mainly in salt. China began to implement the iodization policy of salt in 1995, and in 2011 the national iodine deficiency disease test results showed that iodine deficiency disorder (IDD) was being eliminated at the national level (1). The Shaanxi province was originally one of the provinces with the most serious iodine deficiency disease (2). After the implementation of the iodized salt policy, the iodine nutritional status in Shaanxi Province was at a slightly excessive level in 2011 (1). Shaanxi province has a salty diet, so this study can understand the current iodine content of people in Shaanxi Province, and provide a certain basis for further regulating the policy of iodized salt for people. In addition, there is still no conclusion on the relationship between iodine and thyroid disease, this study aimed to analyze the association between iodine intake level and thyroid diseases among adults in Shaanxi Province, and to explore whether iodine intake level is correlated with benign and malignant thyroid diseases. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-4928).

Methods

Samples

This study retrospectively analyzed the clinical data of patients with thyroid disease and healthy volunteers. Participants' basic information, urinary iodine (UI), and pathological reports were collected. Finally, a total of 1,159 patients with thyroid disease and 182 healthy volunteers were included in our study. All participants were aged ≥18 years old, residents of Shaanxi Province, had been admitted to Xijing Hospital from January 2016 to December 2020, and agreed and signed informed consent. All participants with thyroid disease diagnosis underwent UI testing at the same time as the healthy volunteers, who for 2 weeks prior to testing did not consume any iodine-containing substances that may have influenced the results, including drugs (amiodarone, compound iodine solution, or iodine-containing drugs) and excessive iodine-containing foods (kelp, seafood, and others). in addition, the healthy participants were not taking anti-thyroid drugs, and had no history of thyroid disease health check-up. According to the Chinese Guidelines for the Diagnosis and Treatment of Thyroid Diseases (3), the observation population was classified into the groups of hyperthyroidism, Hashimoto's thyroiditis (HT), papillary thyroid cancer (PTC), and the benign nodules, and those with disease whose morbidity was less than 10% of the total number of observers were grouped as others. All samples were confirmed by pathology. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of the local hospital (Xijing hospital), and because it was a retrospective study, permission for the exemption of informed consent was obtained.

Detection and evaluation of UI

The UI content detection was conducted as follows: urine samples were collected randomly once during the day. The UI content was determined by arsenic-cerium catalytic spectrophotometry in WS/T 107-2006 standard issued by the Ministry of Health of China. Iodine intake status assessment method was based on the recommended method in the Guidelines for the Assessment of Iodine Deficiency Disorders and Their Elimination issued by the World Health Organization, UNICEF, and the Global Iodine Intake Alliance in 2001. Iodine intake assessment was based on UI: <100 μg/L, insufficient; 100–199 μg/L, moderate; 200–299 μg/L, mild overdose; and >300 μg/L, excessive.

Statistical analysis

The chi-square test was used to compare the classified variables and continuous variables in the basic characteristics of participants. All confidence intervals (CIs) were stated at the 95% confidence level, non-normally distributed data were presented as median and quartile (P25, P75), and Kruskal-Wallis-H multi-group rank sum test was used for comparison between groups. A value of $P<0.05$ was considered statistically significant. The software SPSS 19.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis.

Results

Analysis of urinary iodine value

A total of 1,341 patients [mean age 39.94±12.10 years old, male 327, female 1,014, median urinary iodine (MUI) 233.20 μg/L, range, 142.55 to 355.20], including 353 hyperthyroidism participants, 148 cases of HT, and 285 cases of PTC. There were 244 cases of benign thyroid nodules, 129 cases of other groups (hypothyroidism, thyroid

Table 1 Comparison of urinary iodine (UI) (μg /L)

Sectionalization	n (%)	Urinary iodine (UI) ($\bar{x} \pm s$)	Median urinary iodine (MUI) (P25, P75)
Hyperthyroidism	353 (26.3)	278±225[a]	215 (119.10, 346.00)
HT	148 (11.0)	305±193[a]	256 (169.43, 404.98)
PTC	285 (21.3)	284±184[a]	238 (155.45, 364.50)
Benign nodules	244 (18.2)	280±177[a]	232 (155.18, 350.20)
Others	129 (9.6)	300±178[a]	268 (166.25, 391.10)
Control	182 (13.6)	211±144	191 (96.95, 284.40)

[a], Kruskal-Wallis-H multi-group rank sum test, P<0.05. HT, Hashimoto's thyroiditis; PTC, papillary thyroid carcinoma; UI, urinary iodine; MUI, median urinary iodine.

tumor, thyroid cyst, and so on), and 182 cases in the control group. Compared with the control, there was statistical difference in UI in the hyperthyroidism, HT, PTC, benign nodules, and others (P<0.05) (*Table 1*).

Features of thyroid disease

The odds ratio (OR) value of the group with insufficient iodine intake was 0.431 compared with that of the moderate iodine intake (P<0.05). The incidence of thyroid disease with excessive iodine intake was 1.55 times that in the moderate iodine intake (P=0.04). Compared with age <45 years and men, age ≥45 years and women were risk factors for thyroid disease (OR =1.59 and 4.48, respectively) (*Table 2*).

Comparison of thyroid nodule and PTC

The correlation between iodine intake level, age, and gender in benign and PTC was compared, and the results showed no statistical difference (P>0.05) (*Table 3*). The OR value of the group with insufficient iodine intake was 0.423 compared with that of the moderate iodine intake group (P<0.05). The incidence of PTC in the overdose group was 1.595 times that in the moderate dose group (P=0.07). Compared with age <45 years and men, age ≥45 years and women were risk factors for thyroid cancer (OR =1.84 and 4.46, respectively) (*Table 4*).

Features of benign thyroid disease

Compared with moderate iodine intake, the prevalence of hyperthyroidism was decreased (OR =0.58, P=0.03). When iodine intake was excessive, the morbidity of HT increased, and the OR value of HT was 2.36 (P<0.01) compared with the moderate group. The risk of benign nodules was shown to increase with age ≥45 years old (OR =3.56, P<0.01). In terms of gender, there were significant differences between men and women in thyroid diseases, with P<0.05, indicating a statistical difference (*Table 5*).

Discussion

Iodine is an important synthetic raw material for the synthesis of thyroxine in the human body, which is closely related to human health. Both iodine deficiency and excess lead to thyroid diseases. Approximately 80–90% of human iodine comes from food, 10–20% from drinking water, and 5% from air. About 5% is excreted through sweat glands, hair, and lungs. All the iodine absorbed by the human body is excreted except for a small portion (about 50–75 μg) which is absorbed by the thyroid gland. Excess iodine is not stored in the body, and the kidneys are the main organ of iodine excretion (4). Therefore, UI can reflect the level of iodine intake to some extent.

This study found that the median of urinary iodine intake in Shaanxi Province was 233.20 μg/L, which reflected a state of slight iodine overconsumption, consistent with the results of national iodine deficiency monitoring in 2011 (1). Compared with other regions in China, the level of UI in Shaanxi was higher, which may be related to the high-salt diet of people in Shaanxi. In this study, it was found that the incidence of thyroid diseases was lower when iodine intake was insufficient, which may be due to changes in the disease spectrum of thyroid diseases and the decline of thyroid diseases caused by iodine deficiency after the implementation of salt iodization policy for more than 10 years.

It was shown that hyperthyroidism patients had a higher

Table 2 Thyroid disease compared with the control group

Sectionalization	Thyroid disease	Control	OR (95% CI)	P value
Iodine intake, n (%)				
Moderate	329 (28.4)	48 (26.4)		
Insufficient	139 (12.0)	47 (25.8)	0.43 (0.27 to 0.67)	<0.01[a]
Mild overdose	264 (22.8)	47 (25.8)	0.82 (0.53 to 1.26)	0.36[a]
Excessive	427 (36.8)	40 (22.0)	1.55 (1.00 to 2.42)	0.04[a]
Age, years, n (%)				
<45	700 (60.4)	129 (70.9)		
≥45	459 (39.6)	53 (29.1)	1.59 (1.13 to 2.24)	<0.01[a]
Gender distribution, n (%)				
Male	231 (19.9)	96 (52.7)		
Female	928 (80.1)	86 (22.0)	4.48 (3.24 to 6.21)	<0.01[a]

[a], chi-square test. OR, odds ratio; CI, confidence interval.

Table 3 The benign thyroid disease was compared with PTC

Sectionalization	PTC	Benign thyroid	OR (95% CI)	P value
Iodine intake n (%)				
Moderate	82 (28.8)	247 (28.3)		
Insufficient	34 (11.9)	105 (12.0)	0.97 (0.61 to 1.54)	0.91[a]
Mild overdose	60 (21.1)	204 (23.3)	0.88 (0.60 to 1.29)	0.53[a]
Excessive	109 (38.2)	318 (36.4)	1.03 (0.74 to 1.438)	0.85[a]
Age, years n (%)				
<45	162 (56.8)	530 (60.6)		
≥45	123 (43.2)	344 (39.4)	1.17 (0.89 to 1.53)	0.25[a]
Sex distribution n (%)				
Male	57 (20.0)	174 (19.9)		
Female	228 (80.0)	700 (80.1)	0.99 (0.71 to 1.39)	0.97[a]

[a], chi-square test. PTC, papillary thyroid cancer, OR, odds ratio; CI, confidence interval.

UI level than the normal control group, indicating that excessive iodine intake is a risk factor for hyperthyroidism, with some researchers asserting that long-term excessive iodine intake will lead to increased hyperthyroidism (5-10). The thyroid has a certain capacity for adjustment, within a certain range of iodine deficiency or iodine excess normal thyroid function can be maintained; when iodine intake exceeds the adaptive capacity of the thyroid, some people will manifest disease, with hypothyroidism may occur due to the thyroid losing its inhibitive ability (11), "researches has been shown that when iodine intake is excessive, it is mainly manifested as iodine detoxification dysfunction, which leads to an increase in the prevalence of hypothyroidism (12,13)"; this is consistent with the results of this study. However, another expert has proposed that iodine intake has nothing to do with the incidence of hyperthyroidism. In the 3 different areas of Panshan (mild iodine deficiency areas), Zhangwu (abundant iodine area), Huanghua (iodine excess areas), a 5-year prospective epidemiological study of thyroid disease researched by Teng Xiao-chun found that the areas

Table 4 The PTC was compared with the control

Sectionalization	PTC	Control	OR (95% CI)	P value
Iodine intake n (%)				
Moderate	82 (28.8)	48 (26.4)		
Insufficient	34 (11.9)	47 (25.8)	0.42 (0.24 to 0.74)	<0.01[a]
Mild overdose	60 (21.1)	47 (25.8)	0.74 (0.44 to 1.26)	0.24[a]
Excessive	109 (38.2)	40 (22.0)	1.59 (0.96 to 2.65)	0.07[a]
Age, years				
<45	162 (56.8)	129 (70.1)		
≥45	123 (43.2)	53 (29.9)	1.84 (1.24 to 2.74)	<0.01[a]
Gender distribution				
Male	57 (20.0)	96 (52.7)		
Female	228 (80.0)	86 (47.3)	4.46 (2.96 to 6.73)	<0.01[a]

[a], chi-square test. PTC, papillary thyroid cancer; OR, odds ratio; CI, confidence interval.

Table 5 Hyperthyroidism, HT, and benign nodules compared with the control

Sectionalization	Sectionalization			Control	Hyperthyroidism, OR (95% CI), P value	HT, OR (95% CI), P value	Benign nodules, OR (95% CI), P value
	Hyperthyroidism	HT	Benign nodules				
Iodine intake n							
Moderate	115	31	68	48			
Insufficient	55	18	23	47	0.88 (0.49 to 1.57), 0.67	1.07 (0.50 to 2.27), 0.85	0.62 (0.31 to 1.22), 0.61
Mild overdose	66	38	67	4	0.58 (0.35 to 0.97), 0.03	1.25(0.67 to 2.33), 0.49	1.00 (0.59 to 1.70), 0.98
Excessive	117	61	86	40	1.22 (0.74 to 1.99), 0.42	2.36 (1.29 to 4.31), <0.01	1.51 (0.89 to 2.56), 0.12
Age, years							
<45	257	104	145	129			
≥45	96	44	99	53	0.90 (0.61 to 1.35), 0.63	1.03 (0.64 to 1.65), 0.90	3.56 (2.36 to 5.36), <0.01
Gender distribution							
Male	93	18	47	96			
Female	260	130	197	86	3.12 (2.12 to 4,54), <0.01	8.06 (4.54 to 14.29) <0.01	7.62 (3.80 to 18.85), <0.01

HT, Hashimoto's thyroiditis; OR, odds ratio; CI, confidence interval.

had no statistically significant differences compared with hyperthyroidism prevalence and incidence of a disease (14).

Some animal studies have found that the thyroid has a stronger tolerance to iodine excess than iodine deficiency (15), which may be the reason why the prevalence and morbidity of hyperthyroidism does not increase when iodine intake is excessive. The increase of iodine intake will lead to changes in the spectrum of thyroid diseases. Yan *et al.* found that the incidence of thyroid nodules increases in areas with high iodine levels (16). An epidemiological study conducted by

Shan *et al.* (17) showed a significant rise in the incidence of thyroid nodules in areas with iodine excess (P=0.001), which is consistent with the results of this study. The increase of iodine intake will also lead to growth in the incidence of HT. Epidemiological investigations conducted by Teng *et al.*, Shan *et al.*, and other scholars have confirmed this view (13,18). Part of the reason for HT due to high iodine may be that high iodine thyroxine is more immunogenic (19).

In this study, participants with thyroid cancer had higher UI levels than those in the control group (P<0.05), and the incidence of PTC was 1.595 times higher when iodine intake was greater than moderate. Guan *et al.* (20) found that the incidence of thyroid cancer in a high iodine area was significantly increased compared with other areas (P<0.01), when comparing the incidence of thyroid diseases in high iodine areas, low iodine areas, and suitable iodine areas. However, a survey conducted on iodine-rich and iodine-poor areas in Italy found that the incidence of thyroid cancer in iodine-poor areas was 2–3 times higher than that in iodine-rich areas (21). However, surveys in Iceland (22) and Hawaii (23) have shown that thyroid cancer levels remain quite high (well above the average incidence). An investigation of 2 iodine-poor and iodine-rich areas in eastern and western Denmark did not show a significant difference in the incidence of thyroid cancer (24). The relationship between iodine intake and thyroid cancer remains unclear, but the results of this study suggest that excess iodine intake is associated with PTC.

In this study, the comparison of UI between malignant thyroid disease and benign thyroid disease showed that there was no statistical difference in UI. Liu *et al.* (25) also held the same view, but some researchers have shown that UI is higher in malignant thyroid disease than in benign disease (26). The results of this study showed a clear correlation between gender and the incidence of thyroid disease, with an incidence ratio of 1:4.484. We speculated that the reason for this may be due to the levels of various hormones, mental physiological environment of males and females, or that women paying more attention to their health leads to a higher detection rate. Among the thyroid disease participants in this study, the incidence of thyroid disease in those older than 45 years was 1.514 times that of those younger than 45 years. The risk of PTC increased with age. At this stage, the crowd of iodine on the high side, this with our ten years of iodized salt policy is by the relationship, we should pay more attention to individual iodized salt policy. we can test our urinary iodine in the relevant inspection agencies, to judge our own iodine situation by the doctor, make us appropriately increase or decrease the iodine intake, and regular check, keeping our iodine intake at the moderate level can reduce the risk of thyroid disease to some extent.

This study reviewed thyroid disease-related research conducted in Xijing hospital in the recent 5 years to roughly reflect the current level of iodine nutrition in Shanxi Province, and it was found to belong to the super sufficient condition category. The occurrence of thyroid disease may be associated with high iodine intake, which may have a unique impact on thyroid disease. We believe that iodine supplementation should follow scientifically individualized strategy.

Acknowledgments

Funding: Health Research Fund of Shaanxi Province (CATEGORY D); Project Number: 2018D070.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/atm-21-4928

Data Sharing Statement: Available at https://dx.doi.org/10.21037/atm-21-4928

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-4928). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of the local hospital (Xijing hospital), and because it was a retrospective study, permission for the exemption of informed consent was obtained.

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Cite this article as: Yu Z, Yu Y, Wan Y, Fan J, Meng H, Li S, Wang Y, Wang T, Ling R. Iodine intake level and incidence of thyroid disease in adults in Shaanxi province: a cross-sectional study. Ann Transl Med 2021;9(20):1567. doi: 10.21037/atm-21-4928

