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IODINE INTAKE AND PREVALENCE OF THYROID DISORDERS IN DIFFERENT POPULATIONS OF ZHOUSHAN, CHINA

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Abstract

Background. To evaluate iodine status and the prevalence of thyroid disorders in different populations of Zhoushan Island, China.

Methods. A total of 3284 inhabitants of Zhoushan Island were surveyed, including 1389 urban residents, 737 salt workers, 502 peasants, 362 fishermen, and 294 monks from Mount Putuo. All subjects, except for salt workers, consumed iodized salt. A thyroid ultrasound was performed and serum levels of thyroid hormones and thyroid peroxidase antibody were measured.

Results. The median urinary iodine concentration was significantly higher in subjects who consumed iodized salt than in those who consumed non-iodized salt. No significant differences were noted in the prevalence of thyroid ultrasound abnormalities and functional thyroid disorders between subjects who consumed non-iodized and iodized salt except between salt workers and monks from Mount Putuo. The prevalence of thyroid ultrasound abnormalities differed significantly between males and females and was positively correlated with advanced age ($r=0.212$, $P<0.001$).

Conclusions. Iodine intake is considered adequate, more than adequate, or excessive amongst the study populations. The prevalence of both thyroid ultrasound abnormalities and functional thyroid disorders is extremely high in Zhoushan Island. Advanced age and female gender are significant predictors of thyroid ultrasound abnormalities.

Keywords: Goiter; iodine intake; hyperthyroidism; thyroid disorder; universal salt iodization.

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INTRODUCTION

Iodine is an essential element for the synthesis of thyroid hormones and inadequate intake is associated with an increased incidence of a wide spectrum of iodine deficiency disorders, such as goiter, hypothyroidism, and mental retardation (1,2). The World Health Organization (WHO) previously estimated that more than 30% of the worldwide population had insufficient iodine intake (3). To eliminate iodine deficiency, a strategy of universal salt iodization has been adopted in many countries and has resulted in a significant improvement in the correction of iodine deficiency on a global level (4-6).

In spite of the apparent benefits, iodine supplementation is also associated with a variety of complications. An increase in the incidence of iodine-induced hyperthyroidism has been reported as a consequence of many iodine supplementation programs (7-10). Excessive iodine intake also correlates with a higher risk of goiter (11,12), hypothyroidism (13-15), autoimmune thyroiditis (14,15), and thyroid carcinoma (16). It has been proposed that there is a U-shaped relationship between iodine intake level and the occurrence of thyroid diseases: both low and high iodine intake are linked to a higher risk of thyroid disorders (17). Therefore, the suggestion is now that iodine supplementation should be tailored to the different levels of iodine intake of specific demographic groups rather than a standardized preparation (14).

Zhoushan Island is situated in the East China Sea. Since its inhabitants consume large amounts of iodine-rich seafood on a daily basis, the prevalence of thyroid diseases caused by iodine deficiency has traditionally been low. However, since the strategy of universal salt iodization was adopted in China in 1995, the number of patients on the island with thyroid disorders has increased significantly. According to the data collected from various hospitals in Zhoushan City, the number of patients with thyroid disorders increased 2.3-fold from 1996 to 2006. At our center, the prevalence of thyroid cancer detected in 2006 increased 3.44-fold when compared to the figure for 1996. In particular, the number of people that were found to have a thyroid nodule, which is the main clinical sign of thyroid diseases, increased 14.3-fold from 1996 to 2006. These observations suggest that the inhabitants of Zhoushan Island may now have an excessive iodine intake.

To investigate the correlation between iodine status and the prevalence of thyroid disorders on Zhoushan Island, we conducted a survey of five different island populations between July 2007 and November 2008. The groups assessed were classified as urban residents, salt workers, peasants, fishermen and monks from Mount Putuo. Furthermore, other potential risk factors for the development of thyroid disorders were analyzed. The results obtained will provide new information with regard to the advantages and disadvantages of the universal salt iodization program.

PATIENTS AND METHODS

Study populations

A total of 3284 inhabitants of Zhoushan Island, comprising 1,389 urban residents, 737 salt workers, 502 peasants, 362 fishermen, and 294 monks from Mount Putuo, were included in this study. The participants had all lived in the area for more than 10 years and included 1426 males and 1858 females, with an age range from 10 to 89 years (mean: 46 years). Pregnant women and subjects using oral contraceptive or with a history of radiation exposure were excluded. The urinary iodine level was also measured in 1638 children (range: 8-10 years) with a male to female ratio of approximately 1:1. All adult subjects were interviewed by trained research assistants who completed a standardized questionnaire that had been validated in previous pilot studies. The questionnaire involved the collection of personal information, including age, sex, blood pressure, body weight, and height, and living habits, such as diet, smoking, and drinking. It also established whether or not there was a personal or family history of thyroid disease. The study protocol was approved by the medical ethics committee of Zhoushan Hospital. Informed consent was obtained from each subject prior to the start of any study procedure.

Assays

Thyroid ultrasound was performed using the Sonoscape SSI-1000 ultrasound system (7-10 MHz; SonoScape, Shenzhen, China). The thyroid gland volume was calculated from ultrasound data using the ellipsoid formula (18). Urinary iodine was measured by As^{3+}-Ce^{4+} catalytic spectrophotometry using ammonium persulfate digestion (19). Serum levels of thyroid stimulating hormone (TSH), free triiodothyronine (FT_3), free thyroxine (FT_4), and thyroid peroxidase antibody (TPOAb) were measured by chemiluminescence assay using commercial kits (Beckman-Coulter, USA). The sensitivity and reference range of these assays are as follows: FT3= 0.88 pg/mL and 2.5-3.9 pg/mL; FT4=2.5 pg/mL and 6.1-11.2 pg/mL; TSH=0.01 μIU/mL and 0.34-5.60 μIU/mL; TPOAb 1.0 IU/mL and 0-5.61 IU/mL. For the diagnosis of subclinical hypothyroidism and subclinical hyperthyroidism, the measurement of TSH and peripheral thyroid hormones was repeated at least three times. The evaluation criteria for iodine status, diagnostic criteria for thyroid disease, and the thyroid ultrasound abnormalities are listed in Tables 1 and 2.

Statistical analysis

All statistical analyses were performed using the SPSS 15.0 software package. Numerical data that were not normally distributed were converted into ranked data for the purpose of comparison. The chi-square, Mann-Whitney, or Kruskal-Wallis tests were used to compare possible differences between the groups. The correlation between age and the prevalence of thyroid ultrasound abnormalities was evaluated by the Spearman test. The potential risk factors for thyroid ultrasound abnormalities were evaluated by a multiple logistic regression. A P-value of <0.05 was considered to be statistically significant.

Table 1. Evaluation criteria for iodine status and diagnostic criteria for thyroid diseases

	Criteria
Iodine status	
Deficient	Median urinary iodine (MUI) <100 μg/L
Adequate	100 μg/L ≦ MUI < 200 μg/L
More than adequate	200 μg/L ≦ MUI < 300 μg/L
Excessive	MUI ≦300 μg/L
Thyroid diseases	
Clinical hyperthyroidism	TSH <0.35 μIU/mL and FT3 >3.9 pg/mL or FT4 >19.8 pg/mL
Subclinical hyperthyroidism	TSH <0.35 μIU/mL; FT3 ≦ 3.9 pg/mL and 7.1 pg/mL ≦ FT4 ≦ 19.8 pg/mL
Clinical hypothyroidism	TSH >5.50 μIU/mL; and FT3 <2.5 pg/mL or FT4 <7.1 pg/mL
Subclinical hypothyroidism	TSH >5.5 μIU/mL; 2.5 pg/mL ≦ FT3 ≦ 3.9 pg/mL; and 7.1 pg/mL ≦ FT4 ≦ 19.8 pg/mL
Autoimmune thyroiditis	TPOAb >5.61 IU/mL

RESULTS

Iodine nutritional status

Iodine-rich seafood is one of the main ingredients in the daily diet of the inhabitants of Zhoushan Island. The percentages of subjects who ate seaweed, laver, oyster, jellyfish, marine fish and salted fish more than three times per week were approximately 68.3%, 76.4%, 53.2%, 86.7%, 98.5% and 87.6%, respectively. All subjects, except for the salt workers, consumed iodized salt on a daily basis. The monks from Mount Putuo followed a strict vegetarian diet and avoided the consumption of animal products.

Urinary iodine excretion

The median urinary iodine (MUI) concentrations for urban residents, salt workers, peasants, fishermen and monks from Mount Putuo were 320.7, 122.2, 188.9, 193.6 and 271.7μg/L, respectively. The results differed significantly on all comparisons apart from the comparison between peasants and fishermen (among all five populations, χ^2=928.5, P<0.001; peasants vs. fishermen, P>0.05; all other comparisons were P<0.001). Similar results were obtained in children between the different groups. Notably, although the MUI concentration for salt workers was significantly lower than those for other populations (all P<0.001), their iodine intake is still considered adequate according to the WHO criteria (Table 3).

Thyroid ultrasound abnormalities

The prevalence of thyroid ultrasound abnormalities ranged from 30.5% to 42.3% in the study population (Table 4). Significant differences were noted in the prevalence of thyroid ultrasound abnormalities among the five populations (χ^2=37.6, P<0.001) and between urban residents and peasants (χ^2=12.8, P<0.01), urban residents and salt workers (χ^2=28.5, P<0.01), urban residents and fishermen (χ^2=12.0, P<0.01), and salt workers and monks from Mount Putuo (χ^2=5.3, P<0.05). It

Table 2. Evaluation criteria for thyroid ultrasound abnormalities

	Criteria
Colloid goiter	Thyroid volume increases by 3-10 times; the follicular lumen is expanded and filled with colloid, and appears as an anechoic area; color Doppler flow imaging (CDFI) reveals spotty or a few bar-like flow signals.
Nodular goiter	Thyroid enlargement; multiple nodules throughout the thyroid; the nodules appear as anechoic areas, or hypoechoic or isoechoic areas in the presence of cystic changes; CDFI reveals spotty or bar-like flow signals in the periphery of the nodules.
Thyroid adenoma	Presence of a round or oval mass within the thyroid; the lesion has a capsule and a sharp and smooth boundary, and appears as a hypoechoic area; CDFI reveals spotty or bar-like flow signals in the periphery of the lesion.
Thyroid cancer	The lesion has an irregular boundary and appears as a heterogeneous hypoechoic area, with the presence of microcalcifications in some cases; CDFI reveals neovascularization and arteriovenous fistulas within the lesion.

Table 3. Demographic characteristics and urinary iodine (UI) in the study population

	Urban residents	Salt workers	Peasants	Fishermen	Monks	Total
Number	1389	737	502	362	294	3284
Sex (M:F)	1:1.64	1:1.37	1:1.46	1:0.54	1:0.96	1:1.30
Age (yr)						
Mean	45.88±14.48	50.5±12.77	51.0±13.40	42.41±9.2	35.44±12.36	46.23±13.1
Range	23-85	20-84	23-74	15-76	16-89	15-89
Adult UI (μg/L)						
Median	320.7	122.2	188.9	193.6	271.7	226
Interquartile range	210.1-504.0	76.2-182.0	114.4-297.1	122.0-271.0	159.2-450.7	153.4-331.7
Child UI (μg/L)						
Median	259.0	123.7	130.9	156.8	147.6	192.6
Interquartile range	180.0-384.6	73.0-177.3	87.8-218.1	107.9-238.7	103.4-236.8	141.5-273.6

was notable that no significant differences were found in the prevalence of thyroid ultrasound abnormalities between subjects who consumed non-iodized and iodized salt (all P>0.05), except between the salt workers and the monks from Mount Putuo (χ^2=10.1, P<0.01).

Table 4. Prevalence of thyroid disorders in the study population

	Urban residents	Salt workers	Peasants	Fishermen	Monks	Total
Number	1389	737	502	362	294	3284
Thyroid disorders % (n)	5.90 (82)	4.21 (31)	4.58 (23)	6.35 (33)	5.44 (16)	5.33 (175)
Hyperthyroidism	0.50 (7)	0.41 (3)	0.40 (2)	0.55 (2)	0.34 (1)	0.46 (15)
Subclinical hyperthyroidism	0.79 (11)	0.68 (5)	0.80 (4)	0.83 (3)	0.68 (2)	0.76 (25)
Hypothyroidism	0.07 (1)	0	0	0	0	0.03 (1)
Subclinical hypothyroidism	1.01 (14)	0.81 (6)	0.80 (4)	1.66 (6)	1.36 (4)	1.04 (34)
Autoimmune thyroiditis	3.53 (49)	2.30 (17)	2.59 (13)	3.31 (12)	3.06 (9)	3.05 (100)
Thyroid cancer % (n)	0.22 (3)	0.68 (5)	0.40 (2)	0.83 (3)	0.34 (1)	0.43 (14)
Thyroid ultrasound abnormalities (%)	30.7	42.3	39.4	41.7	31.6	35.7

Some subjects underwent surgery as a result of thyroid ultrasonography and, of these, 0.43% were diagnosed to have thyroid cancer following pathological examinations (Table 4). The prevalence of thyroid cancer amongst urban residents, salt workers, peasants, fishermen and monks was 0.2%, 0.7%, 0.4%, 0.9% and 0.3%, respectively. There were no significant differences in the prevalence of thyroid cancer between the five groups (χ^2=4.0, P=0.407).

The multiple logistic regression revealed that gender and age were both risk factors for thyroid ultrasound abnormalities (P<0.001 for both). A further chi-square analysis confirmed the significant differences in the prevalence of thyroid ultrasound abnormalities between males and females in urban residents, salt workers, peasants and fishermen (all P<0.01 or 0.05), but not in the monks from Mount Putuo (P=0.385) (Fig. 1A). To further analyze the impact of age on the prevalence of thyroid ultrasound abnormalities, all subjects were divided into five groups according to age. As shown in Fig. 1B, the prevalence of thyroid ultrasound abnormalities increased significantly with age among different populations. A Spearman correlation analysis revealed a significantly positive correlation between age and the prevalence of thyroid ultrasound abnormalities (r=0.212, P=0.000) in the whole study population. Moreover, significant correlations were also observed between age and the prevalence of thyroid ultrasound

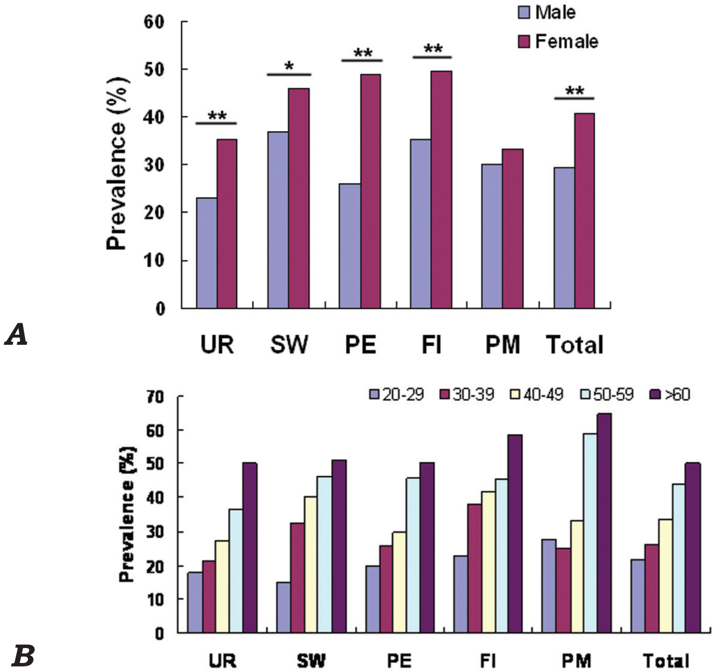

Figure 1. Gender- and age-specific prevalence of thyroid ultrasound abnormalities in the study populations. A, Comparison of the prevalence of thyroid ultrasound abnormalities between males and females of urban residents (UR), salt workers (SW), peasants (PE), fishermen (FI), monks from Mount Putuo (PM), and the whole study population (Total). * denotes $P<0.05$, ** denotes $P<0.01$. B, Prevalence of thyroid ultrasound abnormalities among different age groups in urban residents (UR), salt workers (SW), peasants (PE), fishermen (FI), monks from Mount Putuo, and the whole study population (Total).

abnormalities in urban residents (r=0.240, P=0.000), salt workers (r=0.154, P=0.000), peasants (r=0.198, P=0.000), fishermen (r=0.130, P=0.013), and monks from Mount Putuo (r=0.163, P=0.005). Taken together, these data suggest that advanced age and female gender are likely to be independent predictors of thyroid ultrasound abnormalities in these populations.

Functional thyroid disorders

The overall prevalence of functional thyroid disorders in the total population was 5.76% (Table 4). The prevalence of each thyroid disorder was as follows: subclinical hyperthyroidism (0.68% to 0.83%), overt hyperthyroidism (0.34% to 0.55%), subclinical hypothyroidism (0.80% to 1.66%), overt hypothyroidism (0.00% to 0.07%), autoimmune thyroiditis (2.30% to 3.53%), and thyroid cancer (0.22% to 0.68%). No significant differences were noted in the prevalence of hyperthyroidism (χ^2=0.3, P=0.989), subclinical hyperthyroidism (χ^2=0.1, P=0.998), hypothyroidism (χ^2=1.4, P=0.85), subclinical hypothyroidism (χ^2=2.3, P=0.679), and autoimmune thyroiditis (χ^2=2.9, P=0.575) among urban residents, salt workers, peasants, fishermen and the monks from Mount Putuo.

DISCUSSION

In the present study, an epidemiological survey of the iodine status and prevalence of thyroid disorders in five different populations that reside on Zhoushan Island in China was performed. This region was selected on the basis that its inhabitants consume large quantities of seafood daily. Moreover, a program of iodine supplementation has been implemented in this region since 1995. As a result, iodine nutrition can be described as adequate, more than adequate, or excessive in these populations, which makes them an ideal study population for the investigation of the impact of iodine supplementation in a population with adequate iodine nutrition. The investigation revealed that the prevalence of both thyroid ultrasound abnormalities and functional thyroid disorders was extremely high in these groups, which suggests that there is a link between iodine supplementation and the risk of thyroid disorders in such populations.

A previous study (20) demonstrated that the MUI concentration amongst the rural residents of Zhoushan Island who consumed non-iodized salt was significantly lower than those that consumed iodized salt (90 μg/L vs. 194 μg/L). As a result, the authors suggested that salt iodization was necessary in the region. The data from the present study also revealed a significant difference in MUI concentration between residents who consume non-iodized (salt workers) and iodized salt (urban residents, peasants, fishermen and monks from Mount Putuo). However, these results demonstrated that the level of iodine in the diet was adequate in salt workers. Such a discrepancy may be caused by differences in the study populations (rural residents vs. salt workers), which further suggests the importance of evaluating the level of iodine in nutrition prior to iodine supplementation in a given population. This will be an important consideration for future studies in this field.

Excessive iodine ingestion from the drinking water system results in a marked increase in the prevalence of goiter, while removal of excessive iodine decreases its prevalence (21), which suggests that excessive iodine intake can cause goiter. Our data revealed that the prevalence of thyroid ultrasound abnormalities in the thyroid gland ranged from 30.5% to 42.3%. In particular, the prevalence of nodular goiter was significantly higher than those reported in other areas of China where the level of dietary iodine is comparable (14). Such a high prevalence of goiter cannot simply be explained by high iodine ingestion: the MUI level in this region is not excessively high according to WHO criteria, and the prevalence of goiter in salt workers (having a minimum UI level among the five groups) was higher than those in other inhabitants. This may be attributable to other factors whose effects are currently unknown, such as the possible ingestion of radioactive iodine-rich seafood that could damage thyroid cells.

In addition to iodine intake, other environmental and genetic factors may be associated with thyroid disorders. Previous studies have demonstrated that smoking, advanced age, gender and family history of goiter are associated with a higher risk of goiter (22,23). In the present study, advanced age and female gender were found to be risk factors for the development of space-occupying lesions of the thyroid gland. In contrast, a history of smoking was not found to be a significant predictor of thyroid abnormalities on ultrasound. A possible reason for this difference is that the diagnostic criteria for goiter are different between the current survey and earlier studies.

Our data revealed a high prevalence of hyperthyroidism (0.3%-0.57%) and subclinical hyperthyroidism (0.7%-0.8%) amongst the different populations of Zhoushan Island; these were between three and ten times higher than those obtained in other epidemiological studies (7,24). Although there is still controversy over whether high iodine intake induces hyperthyroidism, it is generally believed that iodide-induced hypothyroidism only causes a transient increase in the incidence of hyperthyroidism, which peaks between 1-3 years after exposure and normalizes within 3-10 years (7,25). Given that there are no significant differences in the prevalence of hyperthyroidism and subclinical features between the salt workers (who consume non-iodized salt) and the other populations (who consume iodized salt), high iodine intake may not be the main cause of the high prevalence of hyperthyroidism in this study. The true reasons for the high prevalence of hyperthyroidism on Zhoushan Island remain elusive.

The high prevalence of subclinical hypothyroidism (0.81%-1.66%) on Zhoushan Island could be explained in two ways. Firstly, high iodine availability has been demonstrated to be able to inhibit the thyroid and induce subclinical hypothyroidism (25,26). Secondly, evidence from earlier epidemiological surveys has confirmed a strong association between autoimmune thyroiditis and hypothyroidism (14,25,26). Therefore, autoimmune thyroiditis could be a potential cause for the subclinical hypothyroidism observed in the present study since the prevalence of autoimmune thyroiditis can reach 2.3-3.5% in the various populations of Zhoushan Island (Table 4).

In conclusion, the present study has demonstrated that, according to the WHO criteria, iodine nutrition is adequate, more than adequate, or excessive amongst the different populations of Zhoushan Island. In addition, it has been demonstrated that the prevalence of thyroid ultrasound abnormalities, and nodular goiter in particular, and functional thyroid disorders is high. It therefore follows that iodine supplementation in the diet may be unnecessary on the island, and that its addition may result in the development of thyroid abnormalities. Although high iodine intake may partly explain the increased prevalence of thyroid disorders in the region, other contributing factors are probably involved. Further studies are needed to discover exactly why there is such an unusually high prevalence of thyroid disorders in this region.

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