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ORIGINAL ARTICLE

Iodine nutrition and thyroid nodules among children and adolescents in a coastal area of China

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Abstract
Aim This study aims to assess iodine nutritional status and investigate the prevalence of thyroid nodules in children and adolescents in Ningbo city, China.
Subject and methods A cross-sectional survey was conducted in Ningbo, China, in 2011. Salt iodine, urine iodine concentration (UIC) and thyroid nodules (by ultrasonography) were measured in 329 participants aged 6–17 years.
Results The median UIC of all participants was 167.23 μg/L. No significant differences in UICs were observed between boys and girls ($Z=-1.06$, $P=0.29$), children and adolescents ($Z=-1.88$, $P=0.06$), iodized salt users and noniodized salt users ($Z=-0.10$, $P=0.92$). A total of 114 nodules with maximum diameters between 1.5 and 12 mm were found among 51 (15.50 %) participants, the prevalence of thyroid nodules between children and adolescents has no significant difference ($\chi^2=0.29$, $P=0.59$), and there were no significant differences in age ($t=1.56$, $P=0.12$), gender ($\chi^2=0.13$, $P=0.72$), type of salt ($\chi^2=0.14$, $P=0.71$), family history of thyroid diseases ($P=0.46$, Fisher's exact test) and UICs ($Z=-1.12$, $P=0.26$) between the participants with thyroid nodules and those without.
Conclusion The iodine nutrition was adequate in children and adolescents in Ningbo city, but the prevalence of thyroid nodules among children and adolescents was high.

Keywords Iodine · Urinary iodine concentration · Thyroid nodules · Iodized salt

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Introduction

Iodine is an essential element of thyroid hormones and and it must be provided in the diet, its sufficient intake is crucial for the prevention of iodine deficiency disorders (IDD; Puig-Domingo and Vila 2013; Santos et al. 2015). In China, IDD has long been a significant public health problem. Since 1995, a universal salt iodization (USI) program has been carried out to fight this problem, and the goal of IDD elimination was achieved in 2000 (Zou et al. 2012). However, with the elimination of IDD, higher incidences of thyroid disorders, such as thyroid nodules, thyroid cancer, and hyperthyroidism, have been reported during the same period. Many endocrinology experts subjectively perceive that iodine intake has been excessive among the Chinese population (Chen et al. 2013).

Do Chinese people eat too much iodine? Numerous studies have been conducted to explore this problem. In 2001, WHO/UNICEF/ICCIDD reported that iodine intake in a part of China's population was more than adequate or excessive (WHO 2001); however, as Wu et al. (2012) reported, the iodine intake of Chinese residents in 2007 and that of residents of China's coastal areas and Beijing in 2009 was safe. However, most of these studies were conducted in adults, and less of them focused on children and adolescents, especially those living in coastal areas; herefore, the aim of this study is to assess iodine nutritional status and investigate the prevalence of thyroid nodules in children and adolescents in Ningbo city, China.

Subjects and methods

Subjects

This study was conducted in Ningbo (120.55°～122.16°E, 28.51°～30.33°N), a coastal city which is located in the middle of the mainland coast-line and the south of Yangze River Delta, bordering on the east China Sea. A cross-sectional survey was conducted from August 2011 to September 2011.

A total of 341 healthy residents aged 6–17 years, and living for more than 5 years at their present residence, were selected randomly from six districts and five counties of Ningbo. Of these, 329 participants completed the investigation and were included in this study, yielding a response rate of 96.48 %. All participants (parents or legal guardians) in this study signed an informed consent approved by Institutional Review Board of Ningbo Center of Disease Control and Prevention.

According to a national surveillance results, the pubic hair development (PH 2) of Chinese boys was 11.24 years (Sun et al. 2012); and the median ages of onset of Tanner stages 2 and 3 for pubic hair development in Chinese girls were 11.16 years and 12.40 years, respectively (Ma et al. 2009). For the purposes of this study, 'children' are defined as persons aged <12 years, and 'adolescents' are persons aged 12–17 years.

Methods

Demographic information including age, gender, nationality, length of residence in Ningbo, and family history of thyroid diseases, was collected at the time of interview from each participant. The iodine concentrations in table salt and urine were measured for all participants. Each participant provided a household salt sample of at least 100 g, and a spot urine sample of at least 20 ml. The household salt samples were then sealed and stored at room temperature (at 20 °C) away from light before measurements. The salt iodine concentrations were measured by the colorimetric titration method (GB/T 13025.7-1999), in which the iodine concentrations in iodized salt was set as ≥5 mg/kg and that in non-iodized salt it was under 5 mg/kg. The urine samples were sealed and stored at −20 °C until the assay. Iodine concentration in urine (urinary iodine concentration, UIC) was measured by arsenic cerium catalytic spectrophotometry (WS/ T107-2006), a median concentration of urinary iodine of 100–199 μg/L was defined as 'adequate', <100 μg/L as 'insufficient', 200–299 μg/L as 'above requirements', and ≥300 μg/L as 'excess'.

Thyroid ultrasonography (US) was performed to detect goiter and thyroid nodules, using equipment with 7.5-MHz linear transducers. Examinations were conducted and recorded by specially trained ultrasound doctors. The following ultrasound parameters were assessed in all nodules: nodule size (maximum diameter as evaluated by sagittal and transverse scans), nature (solid, mixed or cystic), echogenicity (hyperechoic, isoechoic or hypoechoic), margins (regular or irregular), spot calcifications (macro or microcalcifications), vascular pattern (type I, absence of blood flow; type II, perinodular and absent or slight intranodular blood flow; type III, marked intranodular and absent or slight perinodular flow; Scacchi et al. 2009).

Data analysis

Normally distributed data were shown as mean±SD, and the comparison between groups was performed by t test. Non-normally distributed data were shown as the median with the 25th and 75th percentiles, and the comparison between groups was done via the Mann–Whitney U test. Categorical variables were described as percentage, and the associations between categorical data were tested using the chi-square test or Fisher's exact test. Differences were considered statistically significant if $p<0.05$ in two-tailed tests. All statistic analyzes were performed by SPSS 10.0 software.

Results

The demographic characteristics of the participants

The mean age of the 329 participants was 11.40 ± 3.22 years, of which 156 (47.42 %) were boys, and 173 (52.58 %) were girls. Children accounted for the 54.41 % (179/329) of the total participants with a mean age of 8.85 ± 1.63 years, and adolescents accounted for the 45.59 % (150/329) of the total participants with a mean age of 14.43 ± 1.64 years. The gender ratio between children and adolescents has no significant difference ($\chi^2=0.00$, $P=0.98$; Table 1).

Urine iodine concentration

The median UIC of all participants was 167.23 μg/L. The proportions with a UIC <100 and ≥300 μg/L were 24.01 and 15.50 %, respectively. The proportions with a UIC in the range 100 ~ 199 μg/L and in the range 200 ~ 299 μg/L were 38.91 and 21.58 %, respectively, with onnly about 5.17 % of the participants having a UIC <50 μg/L. Furthermore, the median UIC in children was 152.77 μg/L, and in adolescents was 177.14 μg/L. No significant differences in UICs were observed between boys and girls: in children+adolescents ($Z=-1.06$, $P=0.29$), children ($Z=-0.70$, $P=0.48$), and adolescents ($Z=-0.79$, $P=0.43$), and there was no significant difference in UICs between children and adolescents ($Z=-1.88$, $P=0.06$; Table 1).

Among the participants, 238 (72.34 %) were using iodized salt, whereas 91 (27.66 %) were using non-iodized salt. There were no significant differences in UICs between iodized salt users and non-iodized salt using group: in children+adolescents ($Z=-0.10$, $P=0.92$), children ($Z=-0.28$, $P=0.78$), and adolescents ($Z=-0.78$,$P=0.44$; Table 1).

Table 1 Distribution of UICs in children and adolescents of Ningbo city

	N	Age (years)	The urine iodine concentration (UIC)				
			Median (25th, 75th percentiles) (μg/L)	<100 μg/L(%)	100–199 μg/L(%)	200–299 μg/L(%)	≥300 μg/L(%)
Gender							
Children+adolescents							
Male	156	11.17 ± 3.20	175.95 (113.58, 250.91)	21.15	39.10	25.64	14.10
Female	173	11.60 ± 3.24	151.10 (97.47, 251.35)	26.59	38.73	17.92	16.76
Total	329	11.40 ± 3.22	167.23 (105.01, 250.46)	24.01	38.91	21.58	15.50
Children							
Male	85	8.64 ± 1.59	162.37 (106.23, 224.35)	22.35	42.35	23.53	11.76
Female	94	9.05 ± 1.64	141.29 (92.63, 230.12)	28.72	40.43	15.96	14.89
Total	179	8.85 ± 1.63	152.77 (99.07, 224.48)	25.70	41.34	19.55	13.41
Adolescents							
Male	71	14.20 ± 1.58	193.46 (129.75, 268.39)	19.72	35.21	28.17	16.90
Female	79	14.63 ± 1.67	167.67 (101.17, 274.32)	24.05	36.71	20.25	18.99
Total	150	14.43 ± 1.64	177.14 (109.95, 272.33)	22.00	36.00	24.00	18.00
Type of salt							
Children+adolescents							
Non-iodized	91		167.23 (96.35, 241.26)	25.27	38.46	18.68	17.58
Iodized	238		166.80 (109.95, 254.67)	23.53	39.08	22.69	14.71
Children							
Non-iodized	63		150.58 (96.12, 213.71)	25.40	42.86	17.46	14.29
Iodized	116		154.40 (99.20, 231.73)	25.86	40.52	20.69	12.93
Adolescents							
Non-iodized	28		192.47 (98.69, 298.66)	25.00	28.57	21.43	25.00
Iodized	122		171.62 (112.89, 266.80)	21.31	37.70	24.59	16.39

The prevalence of thyroid nodules

Ultrasound evaluation showed that, 114 thyroid nodules with maximum diameters between 1.5 and 12 mm (mean size, 3.58 ± 1.75 mm) were found among 51(15.50 %) participants: 23 (45.10 %) had solitary nodules and 28 (54.90 %) had multiple nodules. Among these 114 nodules, only 1 nodule had a maximum diameter >10 mm, the remaining 113 had maximum diameters under 10 mm. 42(36.84 %) nodules were echoless, 69(60.53 %) were hypoechoic, 2(1.75 %) had mixed echogenicity and 1 (0.88 %) showed hyperechoic appearance. Margins were regular in 98 nodules (85.96 %) and irregular in the other 16 nodules (14.04 %). Microcalcifications were detected in 31 (27.19 %) nodules and 5 (4.39 %) nodules had macrocalcifications. Ninety-seven nodules (85.09 %) displayed type I flow, 16 nodules (14.04 %) displayed type II flow, and 1 nodule (0.88 %) displayed type III flow.

Table 2 showed that, the prevalence of thyroid nodules between children and adolescents has no significant difference ($\chi^2 = 0.29$, $P = 0.59$). Further analysis found that, the mean age of participants with thyroid nodules was not different from those without thyroid nodules ($t = 1.56$, $P = 0.12$). Similarly, there were no significant differences in gender ($\chi^2 = 0.13$, $P = 0.72$), type of salt ($\chi^2 = 0.14$, $P = 0.71$), family history of thyroid diseases ($P = 0.46$, Fisher's exact test) and UICs ($Z = -1.12$, $P = 0.26$) between the two groups; however, in the children's group, those who had thyroid nodules were older ($t = 2.76$, $P < 0.01$).

The prevalence of goiter

Only four (1.22 %) of the participants examined had grade I goiter (diffuse goiter, no nodule founded), of these 2 were children (2 boys) and 2 were adolescents (2 girls), and 3 of them had UIC below 100 μg/L.

Discussion

Urinary iodine reflects dietary iodine intake directly because more than 90 % of dietary iodine is excreted in the urine (Patrick 2008). The median UIC is the most commonly used as an indicator of population iodine nutrition (Ristic-Medic et al. 2009). For a population of school-aged children or

Table 2 The distributions of age, gender, type of salt, family history of thyroid diseases and UICs among participants with thyroid nodules and non-nodules group

Variables	Nodules	Non-nodules	*P* value
Age (years)			
Children+adolescents	12.04 ± 2.91	11.28 ± 3.27	=0.12
Children	9.65 ± 1.62	8.72 ± 1.59	<0.01
Adolescents	14.52 ± 1.50	14.41 ± 1.67	=0.76
Gender [*n* (%)]			
Children+adolescents			
Male	23 (14.74)	133 (85.26)	=0.72
Female	28 (16.18)	145 (83.82)	
Total	51 (15.50)	278 (84.50)	
Children			
Male	12 (14.12)	73 (85.88)	=0.88
Female	14 (14.89)	80 (85.11)	
Total	26 (14.53)	153 (85.47)	
Adolescents			
Male	11 (15.49)	60 (84.51)	=0.71
Female	14 (17.72)	65 (82.28)	
Total	25 (16.67)	125 (83.33)	
Type of salt [*n* (%)]			
Children+adolescents			
Non-iodized	13 (14.29)	78 (85.71)	=0.71
Iodized	38 (15.97)	200 (84.03)	
Children			
Non-iodized	8 (12.70)	55 (87.30)	=0.61
Iodized	18 (15.52)	98 (84.48)	
Adolescents			
Non-iodized	5 (17.86)	23 (82.14)	=0.79
Iodized	20 (16.39)	102 (83.61)	
Family history of thyroid diseases [*n* (%)][a]			
Children+adolescents			
Yes	3 (21.43)	11 (78.57)	=0.46
No	48 (15.24)	267 (84.76)	
Children			
Yes	2 (40.00)	3 (60.00)	=0.15
No	24 (13.79)	150 (86.21)	
Adolescents			
Yes	1 (11.11)	8 (88.89)	=1.00
No	24 (17.02)	117 (82.98)	
UIC [median (25th, 75th percentiles) (μg/L)]			
Children+adolescents	157.39 (119.61, 193.61)	169.38 (99.45, 259.80)	=0.26
Children	159.88 (112.48, 194.34)	149.88 (96.67, 232.58)	=0.84
Adolescents	152.78 (120.55, 193.80)	187.90 (106.83, 283.64)	=0.15

[a] Fisher's exact test

non-pregnant adults to be iodine sufficient, median UIC should be greater than 100 μg/L and no more than 20 % of the population should have values lower than 50 μg/L (WHO 2007). In the present study, the rate of goiter prevalence was 1.22 %, while the median UIC of all participants was 167.23 μg/L, and 152.77 μg/L in children and 177.14 μg/L in adolescents, respectively; therefore, the iodine nutrition was adequate in children and adolescents in Ningbo city. However, it is worth noting that in the present study, no significant differences in UICs were observed between iodized salt group and non-iodized salt group, this may be due to the fact that all the participants were students and most diets were taken in schools; thus, the consumption status of non-iodized salt may be inconsistent with the actual situation.

In children and adolescents, iodine deficiency can lead to goitre, psychomotor and growth retardation and hypothyroidism (García-García et al. 2012). School-aged children in iodine-deficient areas show poorer school performance, lower IQs, and a higher incidence of learning disabilities (Food and Nutrition Board, Institute of Medicine 2001). Artificial iodine supplementation via iodized salt has been recognized as one of the best strategies to ameliorate the incidence of IDD (Taga et al. 2008; Chen and Zou 2004).

Ningbo, a big coastal city in China, had been considered a non-IDD-endemic area; however, a survey in 1995 showed that the median UIC in children aged 8 ~ 10 years was 81.20 μg/L, and the goiter prevalence rate was 8.86 %. Therefore, iodized salt has been supplied in Ningbo since 1996, and the goal of IDD elimination was achieved in 1999. Although the iodine salt supply and IDD situation now are basically stable in Ningbo and the current iodine nutrition status of population was adequate, some problems still existed such as non-iodized salt competition (Zhao et al. 2013). Our previous study showed that, the residents who using non-iodized salt in Ningbo city were in the status of iodine deficiency with a median UIC of 90.36 μg/L (Zhao et al. 2015). This situation highlights the necessity of consolidating the USI in Ningbo city.

Thyroid nodules are a common clinical problem, and present as various conditions, including thyroid cysts, thyroid adenomas and thyroid cancers (Lawrence and Kaplan 2002). Most thyroid nodules are benign hyperplastic lesions, but 1–20 % of thyroid nodules are malignant (Anil et al. 2011; Pak et al. 2013; Mitra et al. 2010). Previous study demonstrated that thyroid nodules were found in 19~67 % of randomly selected individuals by high-resolution sonography (Yan et al. 2015). In the present study, the prevalence of thyroid nodules was 15.50 % among the participants, higher than a previous report: 10.59 % in Chinese children (Xu et al. 2014), lower than in Chinese adults (30.0 %; Chen et al. 2013).

Although thyroid nodules are less frequent in children than in adults, they have importance because of the high rate of malignancy (Önder and Aycan 2014). Compared to adults, children have a four times higher risk of malignancy when a thyroid nodule is diagnosed (Vaisman et al. 2011). The evaluation of thyroid nodules includes history collection, physical examination, laboratory examination, imaging and fine-needle aspiration biopsy (FNAB; Önder and Aycan 2014). Although a thyroid US cannot accurately discriminate between benign and malignant nodules, it does provide very useful information regarding the risk of malignancy. Among US parameters, hypoechoic, microcalcifications, irregular margins and increased intranodular vascular flow are all findings indicating a high suspicion for malignancy (De Luca et al. 2014). Thus, the possibility of malignancy should be considered in all the nodules with the presence of hypoechoic, microcalcifications, irregular margins or increased intranodular vascular flow in present study, and in need of further evaluation.

The prevalence of thyroid nodules in a given population is dependent on a variety of factors that include iodine intake, age, gender, diet, family history, and deficiency of selenium, even therapeutic and environmental radiation exposure (Neki and Kazal 2006; Beland et al. 2011; Rasmussen et al. 2011). In the present study, the associations between age, gender, type of salt, family history of thyroid diseases, UICs and thyroid nodules were estimated among the participants; however, there were no significant differences in age, gender, type of salt, family history of thyroid diseases and UICs between the participants who had thyroid nodules and those who did not. This could, at least partly, be explained by the relatively small number of subjects of the present study. In addition, the reasons for the high incidence of thyroid nodules in the studied population have not been explored in the present study, and need to be explored further.

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Compliance with ethical standards This study was approved by Institutional Review Board of Ningbo Center of Disease Control and Prevention, and all the participants signed informed consent forms.

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Conflict of interest The authors declare that they have no conflict of interest.

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