

Original Article

A comparative study on urinary iodine concentration and goitre prevalence between coastal and inland areas with low and high coverage of iodized salt: a cross-sectional study in Zhejiang province, China

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Background and Objectives: WHO recommended that iodized salt are more than 90% of households in USI programs, which may not be suitable for all regions, especially in coastal areas. This study intended to find out levels of iodine nutrition and give advice from the USI programs for areas with different iodized salt coverage. **Methods and Study Design:** Coastal and inland areas were selected according to geographical regions in Zhejiang Province, China. The water iodine concentration (spectrophotometer analysis), salt iodine concentration (the colorimetric titration method), salt intake, urinary iodine concentration (spectrophotometer analysis), and thyroid volume examination (ultrasonography), as well as questionnaire, were measured in the two areas. **Results:** Mean Urinary Iodine concentration (MUIs) of children in coastal areas was 149 $\mu\text{g/L}$, which was significantly lower than that in inland areas (191 $\mu\text{g/L}$). MUIs of pregnant women in coastal and inland areas were 111 and 138 $\mu\text{g/L}$, respectively. Pregnant women who consumed iodine-containing supplements had higher MUIs (207 $\mu\text{g/L}$) than those did not (134 $\mu\text{g/L}$) in inland areas. Prevalence of goiter in children reached 7.0% and 6.6% in coastal and inland areas, respectively. The lowest prevalence of goiter was reached when the urinary iodine concentration was approximately 120-160 $\mu\text{g/L}$ in coastal areas. **Conclusion:** Iodine levels of coastal and inland areas were in the adequate range. Advice from the USI program should be specialized for different areas to appropriately reduce the salt iodine concentrations in inland areas and to determine an appropriate proportion of households using iodized salt in coastal areas. Moreover, iodine supplement intake during pregnancy should officially be recommended.

Key Words: urinary iodine concentration, goitre prevalence, children, pregnant women, generalized additive models

INTRODUCTION

In China, severe iodine deficiency, resulting in diseases, such as cretinism and goiter, was prevalent in most regions. Universal salt iodization (USI) programs have been carried out to prevent iodine deficiency disorder (IDD) since 1995, and National Iodine Deficiency Disorders Surveillance Reports¹ appeared to reach national IDD control standards and resulted in a striking decline in goiter prevalence (GP). However, recent studies²⁻⁴ reported that the iodine status in some regions of China was above adequate levels. Consequently, there is controversy regarding whether it is necessary to carry out the USI programs throughout all of China.^{5,6}

The World Health Organization (WHO) Technical Consultation suggested determining whether the sustainable elimination of iodine deficiency as a public health problem has been achieved based on a threshold of 90% of households in USI programs using adequately iodized salt.⁷ However, this criterion may not be suitable for all regions, especially in coastal areas where the local diet contains iodine-rich food. Therefore, coastal and inland

areas with a low and high coverage of iodized salt were selected for the measurement of iodine status to propose reasonable policy adjustments to the USI program.

MATERIAL AND METHODS

Survey area

This study was conducted in Zhejiang Province, the east coastal region of China, which includes 11 cities. We selected Zhoushan city, which is near the eastern coastline, as the coastal area and Huzhou city, which is far from the eastern coastline, as the inland area. The cluster

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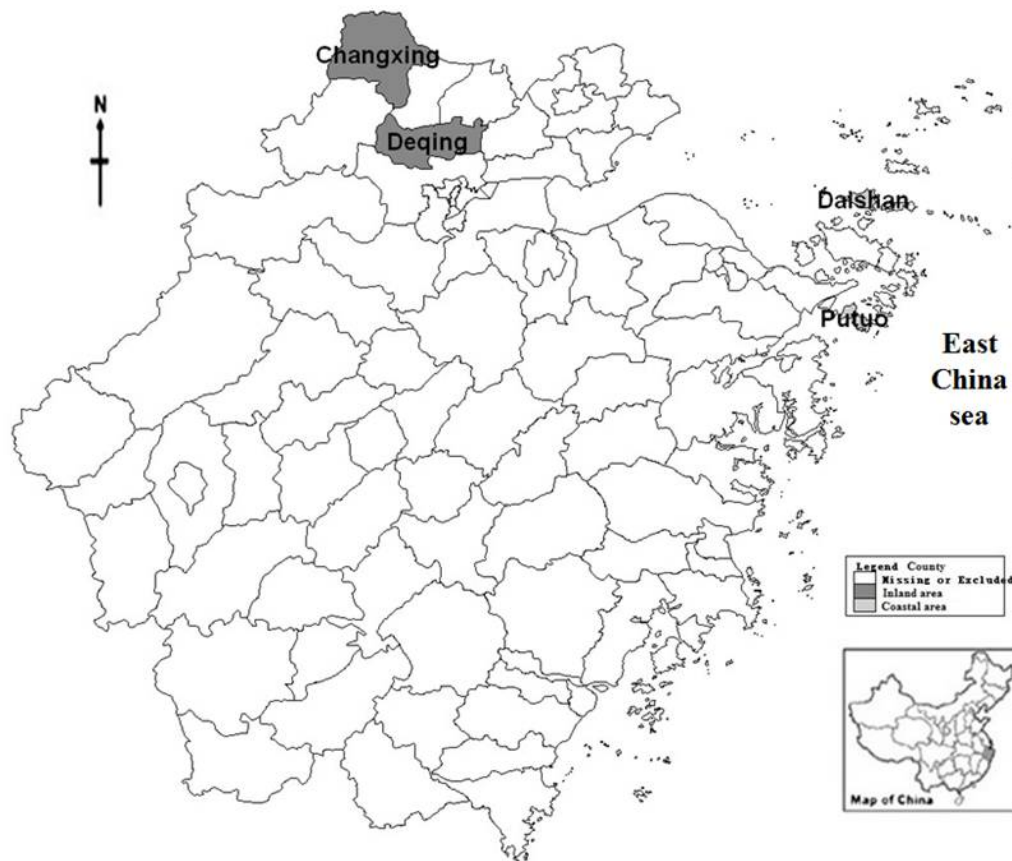


Figure 1. Location of the survey areas in Zhejiang Province, China. Putuo and Daishan counties were selected from Zhoushan city and were defined as Coastal areas according to their distance from the East China Sea; Changxing and Deqing counties were selected from Huzhou city and were defined as inland areas according to their distance from the East China Sea.

sampling method was applied to select 2 counties from each city; 5 sub-districts or towns were randomly picked in each county according to the east, south, west, north and central directions; and 1 community or village was randomly picked in each sub-district or town. The 4 selected counties are shown on the map of Zhejiang Province in Figure 1.

Subjects

Thirty school children aged 8-10 years from local elementary schools and 20 pregnant women were randomly selected from each included community or village. The sample size was estimated using the formula: $N = Z_{\alpha}^2 \times GP \times (1-GP) / \epsilon^2$ (assuming that $\alpha=0.05$, $Z_{\alpha}=1.96$, $GP=5.00\%$, $\epsilon=0.04$). Individuals who had lived in the survey areas for more than 6 months and did not suffer from thyroid disease were included in our study. Finally, 711 children and 402 pregnant women were included as interview subjects. The researchers introduced the study objectives and obtained informed consent from each subject. The study was carried out by well-trained public health doctors from March to May 2014.

Household and salt intake survey

A structured questionnaire was used to collect information about the type of salt used in the household and the awareness of IDD. Meanwhile, a weighed method recorded salt intake over 3 days to estimate the salt intake per day per person in the households of 10 school children that were randomly selected from 30 households in

each community or village. A survey regarding iodine-containing supplements in pregnancy was conducted in the coastal areas.

Measurements

Ten grams of edible salt samples in 60 households and 50 ml drinking water were collected from east, south, west, north and central directions in each selected community or village. The samples were stored at room temperature and kept out of light. The iodine concentrations in the edible salt and drinking water were measured using a colorimetric titration method (GB/T 13025.7-2012)⁸ and the spectrophotometer method (GB/T 8538-2008),⁹ respectively. Instant urine samples were collected from all subjects and were placed at -4°C before being sent to the laboratory. The measurement of urinary iodine concentrations (UICs) was performed using a spectrophotometer method (WS/T107-2006).¹⁰ All of the samples were tested in the Zhejiang Provincial CDC laboratory, which had been successfully certified through a quality control assessment program carried out by a national reference laboratory (China) since this program started.

Thyroid volume

Thyroid ultrasonography was performed on the school children by a single experienced operator with a portable ultrasound machine (PICO, SonoAce, Korea) with a 7.5-MHZ, 60mm transducer. The thyroid volume was the sum of the right and left thyroid lobe volumes, and the thyroid capsule was not included. The lobe volume was

calculated using the following formula: width (cm)×depth (cm)×length (cm)×0.479.¹¹

Definition of variables

The proportion of households using adequately iodized salt: the number of households using adequately iodized salt (18-33 mg/kg)¹²/the number of households selected×100%. Gestation was categorized into 3 groups: ≤12 weeks was defined as the first trimester, 12-17 weeks was defined as the second trimester, and >27 weeks was defined as the third trimester.¹³ Based on age, pregnant women were categorized into 3 groups: <20, 20-30, and >30 years. Based on the question about the type of salt consumed, the subjects were classified into 3 groups: consistently consumed iodized salt, occasionally consumed iodized salt, and consistently consumed non-iodized salt. However, because the sample sizes of the occasionally consumed iodized salt group and the consistently consumed non-iodized salt group were both small, the type of salt variable was merged into 2 groups: the iodized salt group, including those who consistently consumed iodized salt, and the non-iodized salt group, including those who occasionally consumed iodized salt and consistently consumed non-iodized salt. Awareness of IDD was categorized into 2 groups: the “Yes” group included those who knew the hazards of IDD, and the “No” group included those who did not know the hazards of IDD. According to the recommended iodine nutrition status evaluation criteria of the WHO/United Nations International Children’s Emergency Fund (UNICEF)/International Council for Control of Iodine Deficiency Disorders (ICCIDD), iodine deficiency was indicated by median urinary iodine concentrations (MUIs) of school children <100 µg/L, and adequate iodine nutrition was described as MUIs of 100-199 µg/L; MUIs in the range of 200-299 µg/L were considered above the requirements, and MUIs greater than 300 µg/L were considered to be excessive.⁷ The iodine nutrition status of pregnant women was determined as follows: MUIs <150 µg/L were considered deficient, MUIs within the range of 150 to 250 µg/L were considered adequate, MUIs within the range of 250 to 500 µg/L were considered above the requirements, and MUIs greater than 500 µg/L were considered excessive.⁷ The thyroid volume defined as goiter used the reference of the endemic goiter diagnostic standard (WS276-2007): over 4.5, 5.0, and 6.0 ml in children aged 8, 9, and 10 years old, respectively.¹⁴

Statistics

The water iodine concentrations (WICs), salt iodine concentrations (SICs) and UICs were presented as medians (inter quartile range); salt intake, age and gestation were presented as mean±SD. The Chi-square test was used to compare the categorical variables; and the *t* test, Wilcoxon’s test and the Kruskal-Wallis test were used to compare continuous variables that were or not normally distributed according to the Shapiro-Wilk test. The associations between UICs values ranging from 100-300µg/L and goiter were adjusted for age, sex and type of salt and were estimated using generalized additive models (GAM) stratified by area, and local polynomial regression (LO-ESS) analysis was used for scatter plot smoothing of the

UICs. Generalized additive models, as defined by Hastie and Tibshirani,¹⁵ are powerful tools for nonparametric regression and smoothing. Nonparametric regression relaxes the usual assumption of linearity and uncovers relationships between the independent variables and the dependent variable that might otherwise be missed. In all of the analyses, the level of significance was set at *p*<0.05. Epidata 3.1 software (Association, Odense, Denmark) was used for data entry, and all statistical analyses were performed using SAS 9.2 software (Cary, NC, USA).

RESULTS

Baseline characteristics of the two areas

In the coastal and inland areas, 300 and 411 school children aged 8.9±0.81 years and (9.1±0.81) years, with sex ratios of 0.961 and 0.995, respectively, and 200 and 202 pregnant women aged 28.1±4.5 years and (27.5±4.3) years, at gestations of 22.9±9.1 weeks and 22.8±8.3 weeks, respectively, were included in this study (all *p*≥0.05). The median water iodine concentration (MWIs) in the coastal areas was 12.5 (4.41) µg/L, which was higher than that in the inland areas [6.96 (5.31) µg/L]. However, the median salt iodine concentration (MSIs) was 21.4 (24.3) µg/L and proportion of households using adequately iodized salt was 61.3%, which were lower compared with the inland areas [23.5 (2.58) µg/L, 95.5%], respectively (all *p*<0.05). Compared with the subjects living in inland areas, those living in coastal areas had less consistent consumption of iodized salt, lower awareness of IDD (all *p*<0.05) and were more likely to take salt (*p*≥0.05) (Table 1).

The urinary iodine concentration and goiter prevalence of the two areas

The school children in the coastal areas had lower MUIs [149 (120) µg/L] compared with the school children in the inland areas [191 (140) µg/L]. The proportion with MUIs less than 100 µg/L was 25% in the coastal areas, which was greater than the corresponding proportion (13.4%) in the inland areas. Additionally, the proportion of MUIs above 300 µg/L was 8.67% in the coastal areas, which was less than the corresponding proportion in the inland areas (18.5%). The MUIs were significantly higher among children in coastal areas compared with children in inland areas in all groups (all *p*<0.05), except for the 8-year-old group and the non-iodized salt group (all *p*≥0.05). However, there was no statistically significant difference in GP between children in the coastal areas and those in the inland areas for all of the groups (all *p*≥0.05). The MUIs were higher in boys than in girls. Meanwhile, children consuming iodized salt had a higher MUIs than those consuming non-iodized salt in the coastal areas, but the difference between the children with iodized salt and those with non-iodized salt in the inland areas was not significant (*p*=0.05). Boys had more goiter than girls in the coastal areas [OR (95% CI): 2.78 (1.05-7.38)], and children 9 years of age had more goiters than children 10 years of age in the inland areas [OR (95% CI): 6.15 (1.75-21.6)] (Table 2).

The MUIs were slightly higher among pregnant women in the coastal areas than for those in the inland areas in all of the groups, except the <20 years-old group, but there

Table 1. Baseline characteristics of the two areas[†]

Index	Coastal areas		Inland areas		<i>t</i> / <i>Z</i> / <i>x</i> ²	<i>p</i>
	<i>n</i>	Mean±SD/ M (QR)/% (n1/n2)	<i>n</i>	Mean±SD/ M (QR)/% (n1/n2)		
Region Index						
Water iodine concentration (µg/L)	10	12.5 (4.41)	10	6.96 (5.31)	2.87	<0.01
Salt iodine concentration (mg/kg)	600	21.4 (24.3)	600	23.5 (2.58)	-10.9	<0.01
Proportion of households using adequately iodized salt (%)	600	61.3 (368/600)	600	95.5 (573/600)	207	<0.01
Household Index						
Consistent consumption of iodized salt rate (%)	300	51.3 (154/300)	300	92.0 (276/300)	122	<0.01
Awareness rate of IDD (%)	300	74.3 (223/300)	300	86.7 (260/300)	14.5	<0.01
Salt intake (g/person*d)	100	7.54±2.66	100	7.74±2.84	-0.510	0.610
School children aged 8-10 years Index						
Age (year)	300	8.93±0.809	411	9.05±0.811	-1.97	0.049
Sex (boy: girl)	300	0.961 (147:153)	411	0.995 (205:206)	0.0535	0.817
Pregnant women Index						
Age (year)	200	28.1±4.48	202	27.5±4.25	1.37	0.173
Gestation (week)	200	22.9±9.05	202	22.8±8.34	0.160	0.869

IDD: iodine deficiency disorder.

[†]Values are mean±SD, or % (n1/n2), or median (interquartile range).

was no statistically significant difference in the MUIs between pregnant women in the coastal areas and those in the inland areas in all of the groups ($p \geq 0.05$). The proportion with MUIs less than 150 µg/L was 64.0% in the coastal areas, which was greater than the 56.9% in the inland areas; and the proportion with MUIs above 500 µg/L was 9.50% in the coastal areas, which was also greater than 0.99% in the inland areas. Meanwhile, there was no statistically significant difference in the MUIs of pregnant women by age or gestation groups in either area (all $p \geq 0.05$). In addition, pregnant women who consumed iodine-containing supplements had higher MUIs compared with those who did not consume supplements ($p < 0.05$) (Table 3).

Adjusted associations between urinary iodine concentrations and goiters

Table 4 shows that UICs in the range of 100-300 µg/L had a significant but nonlinear association with goiters in the coastal areas, while the relationship was non-significant in the inland areas. Figure 2 shows that in the coastal areas, the partial predictions of goiter number corresponding to UICs in the range of 100 to 300 µg/L had a wavy pattern: the goiter number was at lower levels when the UICs was approximately 120-160 µg/L, while in the inland areas, this relationship had an ultimately non-significant pattern, which is presented in Figure 3.

DISCUSSION

Zhejiang Province is an area of mild iodine-deficiency disorders. In 2011, by determining iodine concentrations in household salt and urine, we conducted a population-based survey to understand iodine nutritional status in households of Zhejiang Province. As a result,¹⁶ this study showed that a total of 64.7% of households in coastal areas used adequately iodized salt, which was significantly lower than those households in inland areas (86.8%). Furthermore, in 2014, we choose key populations (such as pregnant women and school children) from coastal and inland households in order to know their iodine deficiency

status.

In our study, there was low coverage of iodized salt and high WICs in the coastal areas, where food in the regular diet has a high iodine content from iodine-rich seafood, such as laver and fish.¹⁷ These conditions were opposite of those in the inland areas. Meanwhile, the dietary salt intake in the two areas was similar, suggesting that the influence of salt intake on the iodine status could be eliminated in our study.

The iodine concentration, measured in a spot sample, is the most recommended biochemical marker for population surveillance of iodine nutrition, and low median values suggest that the population is at high risk of developing thyroid disorders⁷. Because of their representative nature and vulnerability, school-aged children and pregnant women were important target groups in the surveillance of iodine nutrition in populations during the USI program.^{7,18} The MUIs from the coastal and inland children were 149 and 191 µg/L, respectively, falling approximately within the range of the WHO recommendations. The MUIs of the coast were far lower than those of children in Sudan coastal areas (464 µg/L),¹⁹ where the food is also rich in iodine but also has a high coverage of iodized salt,²⁰ indicating that the high coverage of iodized salt in areas with high-iodine food is unnecessary.

On the other hand, the inland MUIs with 95.5% iodized salt coverage and a MSIs of 23.5 (2.58) mg/kg were relatively lower than those of Brazil (360 µg/L), which had 95.7% coverage²¹ and a MSIs of 24-65 mg/kg,²² and were higher than Iran (141 µg/L), which had 98.2% coverage²¹ and a MSIs of 21.2 (3.20-31.7) mg/kg.²³ Moreover, 18.5% of children in the inland areas had a high UICs (≥ 300 µg/L) compared with 8.67% in the coastal areas. These trends suggest a positive correction between MUIs and MSIs, although an adjustment is required to reduce the SICs to reach more appropriate iodine nutrition levels in the inland areas. In addition, the MUIs in areas with a low coverage of iodized salt and high WICs were lower than the MUIs of areas with high coverage and low WICs for almost all of the groups, suggesting that iodized salt

Table 2. Urinary iodine concentrations and goiter prevalence among school children in the two areas[†]

Area	Group	n	MUIs (QR) [µg/L]	Z (p)	The frequency distribution of UICs (%)				GP [% (n)]	OR (95% CI) [¶]
					0 µg/L-	100 µg/L-	200 µg/L-	300 µg/L-		
Coastal areas	Age (year) [*]			0.767 (0.682)						1.68 (0.551-5.10)
	8 [§]	109	154 (146)	-1.70 (0.0885)	24.8	43.1	20.2	11.9	9.17 (10)	1.03 (0.302-3.49)
	9 [§]	103	149 (110)	-4.38 (<0.01)	21.4	50.5	22.3	5.83	5.83 (6)	1.48 (0.561-3.89)
	10 [§]	88	139 (126)	-3.50 (<0.01)	29.6	40.9	21.6	7.95	5.68 (5)	0.479 (0.181-1.27)
	Sex [‡]			4.67 (<0.01)						2.87 (0.670-12.3)
	Boy [§]	147	169 (140)	-2.52 (0.0118)	15.7	43.5	27.2	13.6	10.2 (15)	2.78 (1.05-7.38)
	Girl [§]	153	126 (99.6)	-5.38 (<0.01)	34.0	46.4	15.7	3.92	3.92 (6)	1.44 (0.680-3.05)
	Type of salt [‡]			3.91 (<0.01)						0.660 (0.242-1.80)
	Iodized salt [§]	154	163 (127)	-2.88 (<0.01)	14.9	47.4	26.0	11.7	7.79 (12)	1.29 (0.525-3.15)
	Non-iodized salt [§]	146	128 (110)	-1.49 (0.136)	35.6	42.5	16.4	5.48	6.16 (9)	1.14 (0.539-2.42)
Total ^{**}	300	149 (120)	-5.55 (<0.01)	25.0	45.0	21.3	8.67	7.00 (21)	1.51 (0.183-12.5)	
Inland areas	Age (year) [*]			2.43 (0.296)						1.07 (0.593-1.93)
	8	125	191 (137)	-	20.8	37.6	24.0	17.6	6.40 (8)	3.26 (0.846-12.6)
	9	140	191 (126)	-	6.43	46.4	29.3	17.9	11.4 (16)	6.15 (1.75-21.6)
	10	146	190 (155)	-	13.7	39.7	26.7	19.9	2.05 (3)	1.00
	Sex [‡]			2.25 (0.0250)						1.00
	Boy	205	197 (135)	-	10.7	39.5	28.3	21.5	7.32 (15)	1.28 (0.582-2.79)
	Girl	206	183 (139)	-	16.0	43.2	25.2	15.5	5.83 (12)	1.00
	Type of salt [‡]			1.95 (0.0513)						1.70 (0.217-13.3)
	Iodized salt	276	192 (128)	-	11.6	42.0	27.2	19.2	6.88 (19)	1.00
	Non-iodized salt	24	147 (97.9)	-	25.0	45.8	12.5	16.7	4.17 (1)	1.00
Total	411	191 (140)	-	13.4	41.4	26.8	18.5	6.57 (27)	1.00	

MUIs: median urinary iodine concentrations; UICs: urinary iodine concentrations; GP: goiter prevalence; CI: confidence interval.

[†]Values are median (inter-quartile range), or % (n).

^{*}Compared at age or gestation or supplement contained iodine groups in coastal or inland areas.

[§]Compared between coastal and inland areas in different age or gestation or supplement contained iodine groups.

[¶]OR (95% CI) upper in age was 8 vs 10 years group, and then number down was 9 vs 10 years group.

Table 3. Urinary iodine concentrations among pregnant women in the two areas[†]

Area	Group	n	MUIs (QR)[$\mu\text{g/L}$]	Z/ χ^2 (p)	The frequency distribution of UICs (%)			
					0 $\mu\text{g/L}$ -	150 $\mu\text{g/L}$ -	250 $\mu\text{g/L}$ -	500 $\mu\text{g/L}$ -
Coastal areas	Age (year) [*]			5.93 (0.0516)				
	<20 [§]	7	215 (242)	-0.912 (0.362)	14.3	42.9	28.6	14.3
	20-30 [§]	149	111 (132)	-1.47 (0.142)	66.4	15.4	8.05	10.1
	>30 [§]	44	96.3 (125)	-0.661 (0.509)	63.6	15.9	13.6	6.82
	Gestation (week) [*]			3.86 (0.145)				
	≤ 12 [§]	33	111 (99.6)	0.655 (0.513)	57.6	27.3	6.06	9.09
	13-27 [§]	84	133 (195)	-0.412 (0.680)	59.5	14.3	14.3	11.9
	>27 [§]	83	95.9 (127)	0.917 (0.359)	71.1	14.5	7.23	7.23
	Total ^{**}	200	111 (135)	-1.29 (0.198)	64.0	16.5	10.0	9.50
Inland areas	Age (year) [*]			0.281 (0.869)				
	<20	3	161 (228)	-	33.3	33.3	33.3	0.000
	20-30	154	137 (104)	-	57.1	32.5	9.74	0.650
	>30	45	141 (95.1)	-	57.8	31.1	8.90	2.22
	Gestation (week) [*]			2.82 (0.244)				
	≤ 12	24	145 (88.5)	-	54.2	33.3	12.5	0.00
	13-27	116	146 (107)	-	51.7	35.3	12.1	0.860
	>27	62	132 (101)	-	67.7	25.8	4.84	1.61
	Supplement contained iodine [*]			3.72 (<0.01)				
	Yes	29	207 (138)		27.6	37.9	31.0	3.45
No	173	134 (90.7)		61.9	31.2	6.36	0.580	
Total	202	138 (111)	-	56.9	32.2	9.90	0.990	

MUIs: median urinary iodine concentrations; UICs: urinary iodine concentrations.

[†]Values are median (inter-quartile range), or % (n).

^{*}Compared at age or gestation or supplement contained iodine groups in coastal or inland areas.

[§]Compared between coastal and inland areas in different age or gestation or supplement contained iodine groups.

Table 4. Adjusted associations between the urinary iodine concentrations and goiter prevalence adjusted for age, sex and type of salt stratified by area using generalized additive models

Areas	n	Smoothing parameter	df	GCV	Sum of squares	χ^2	p
Coastal areas	199	0.455	2.22	0.0162	11.1	11.1	<0.01
Inland areas	205	0.485	2.65	0.0289	0.515	0.515	0.879

GCV: Generalized cross validation.

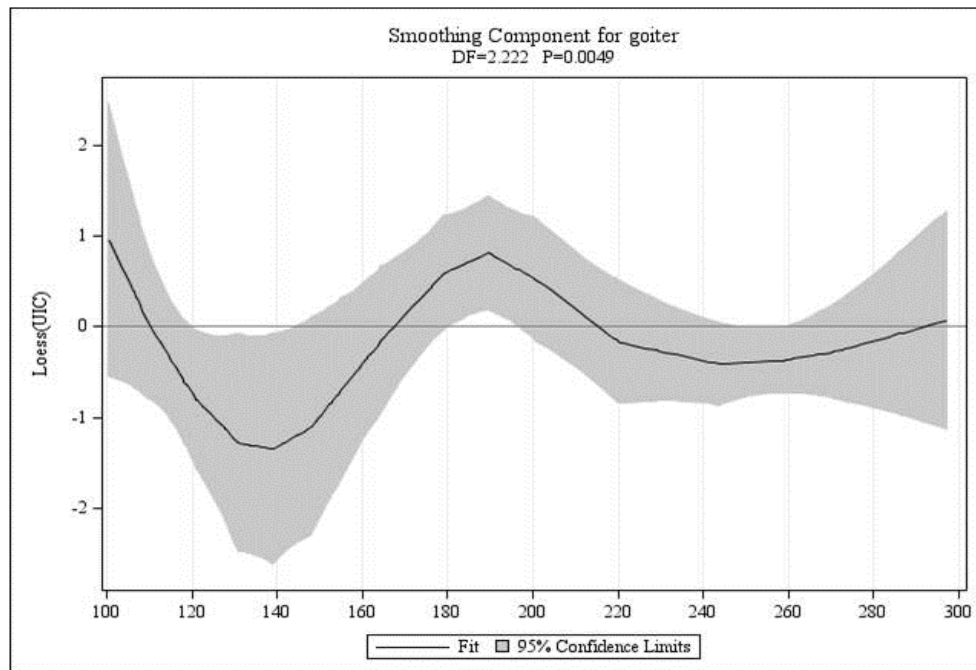


Figure 2. The result of GAM smoothing for the association between goiter and UICs adjusted for age, sex and type of salt in coastal areas

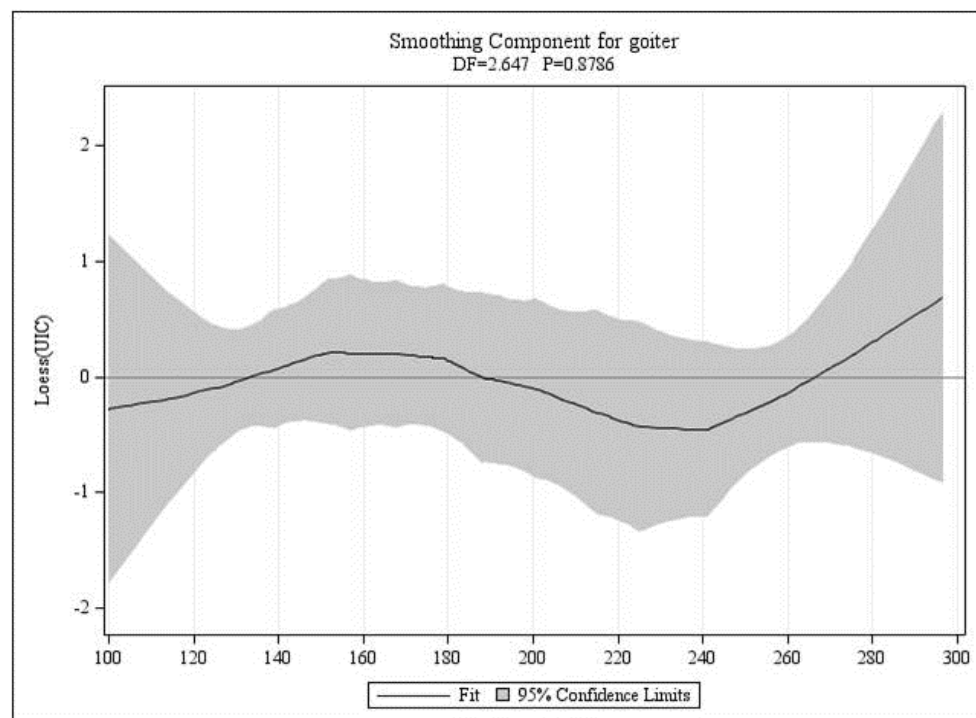


Figure 3. The result of GAM smoothing for the association between goiter and UICs adjusted for age, sex and type of salt in inland areas

played a more important role in iodine nutrition compared with water iodine from the external environment in Zhejiang Province, which is also demonstrated by the difference in MUIs between iodized and non-iodized salt groups in the coastal areas.

Adequate intake of iodine in pregnancy is important as the iodine requirement rises to meet demands for neurological development and fetal growth during pregnancy. In the present study, the MUIs from the coastal and inland pregnant women were 111 and 138 $\mu\text{g/L}$, respectively, which were below WHO recommendations and were in line with those reported²⁴⁻³⁰ from iodine-sufficient areas.

Moreover, 64.0% and 56.9% of the pregnant women in coastal and inland areas, respectively, had low UICs ($<150 \mu\text{g/L}$). Therefore, most pregnant women appear to not be protected against iodine deficiency from the current iodine concentrations in salt regardless of whether they live in areas with high or low coverage of iodized salt. In addition, approximately 9.50% of the pregnant women in coastal areas had a high UICs ($\geq 500 \mu\text{g/L}$) compared with 0.99% in inland areas, which was closely related to the local dietary patterns. In contrast to children, the differences in MUIs of all of the groups between the coastal and inland areas were not significant. However,

in the coastal areas, the mean MUIs from pregnant women who consumed iodine-containing supplements was 207 µg/L, which is an appropriate level and is significantly higher than that of those who did not consume supplements (134 µg/L, or a deficient level), suggesting that iodine supplement intake during pregnancy was very important for improving iodine nutrition. This finding was similar to the results from studies in the UK,³⁰ Belgium,²⁹ the United States,²⁸ Denmark²⁷ and Spain.²⁶

In the current study, the GP in children reached 7.00% (27/300) and 6.57% (21/411) in the coastal and inland areas, respectively. According to the WHO criteria, GP poses a threat to public health when it is greater than 5%.⁷ These results could be caused by a variety of reasons, except for the iodine status, such as goitrogens in the drinking water that may contain various chemical compounds interfering with thyroid hormone synthesis,³¹ which could not be investigated in our study. Meanwhile, the growth indicators, such as height and weight, which had a positive correlation with thyroid volume independent of age,³² were not included in our country reference for the definition of goiter. Although a new international reference was established in 2004,³³ the recommendations also suggested that in-country population-specific references may be more accurate than a single international reference. Hence, further research on a country thyroid volume reference is needed.

A recent report³⁴ found that the relationship between UICs and the risk of the occurrence of goiter has a U-shaped curve and that the cumulative incidence of diffuse goiter was 7.1%, 4.4%, and 6.9% and was higher in iodine deficient areas than in areas with appropriate iodine levels ($p=0.013$ and $p=0.015$). In our study, because of the small sizes of the iodine deficient and iodine excess groups, we selected subjects whose UICs ranged from 100 to 300 µg/L in an attempt to explore which acceptable UICs range is most effective at reducing the risk of goiter. When the UICs were approximately 120-160 µg/L, the goiter number was lowest in the coastal areas with a low coverage of iodized salt, while in the inland areas, this relationship had a non-significant pattern. However, we have no abundant evidence in this study to address the consequences of UICs on the risk of goiter. To clarify this association, further research in larger samples is required.

There were some limitations to this study. First, goitrogens in the drinking water that may contain various chemical compounds interfering with thyroid hormone synthesis could not be investigated in our study. Second, the sample size was not large enough for subgroup analyses. Third, as mentioned earlier, the survey regarding iodine-containing supplements in pregnancy was only studied in the coastal areas. Fourth, the causal association between UICs and goiter could not be established because of the cross-sectional study design. Moreover, UICs in addition to the use of food frequency questionnaires (FFQs) can more accurately reflect individual iodine status and FFQs were not used in our study.

Overall, the conclusions from these data can be outlined as follows:

1. The iodine nutrition status of the populations in the Zhejiang coastal and inland areas were at appropriate and safe levels, and the MUIs of areas with high cov-

erage of iodized salt were higher than areas with low coverage.

2. Furthermore, USI program recommendations should be area-specific to appropriately reduce SICs in inland areas and to maintain an appropriate use of iodized salt among households in coastal areas. However, more evidence regarding the required coverage of iodized salt in coastal areas is needed.
3. Most pregnant women appear to not be protected against iodine deficiency from the current iodine concentration in salt, regardless of whether they live in high or low iodized salt coverage areas. They should be given advice on how to improve their iodine status through dietary behaviors. Iodine supplement intake during pregnancy should be officially recommended.

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AUTHOR DISCLOSURES

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REFERENCES

1. Sun DJ, Xiao DL, Liu SJ, Shen HM, Li X, Su Xh, Zhang S, B. China National IDD Surveillance in 2011. Beijing: People's Health Publishing House; 2014. (In Chinese)
2. Meng F, Zhao R, Liu P, Liu L, Liu S. Assessment of iodine status in children, adults, pregnant women and lactating women in iodine-replete areas of China. *PLoS One*. 2013;8:e81294. doi: 10.1371/journal.pone.0081294.
3. Yang J, Zheng H, Li X, Zhu L, Hao Z, Chen G, Liu Y, Wang Y. Assessment of iodine status and associated factors in vulnerable populations in Henan Province, China, in 2012. *Asia Pac J Clin Nutr*. 2014;23:626-33. doi: 10.6133/apjcn.2014.23.4.03.
4. Yin JZ, Feng YM, Wu SX, Zhang XH, Wang SM, Wang Q, Li Y, Qi DL. Assessment of the iodine status of the Wa national boarding school students in Southwest China. *Biol Trace Elem Res*. 2014;160:316-20. doi: 10.1007/s12011-014-0072-y.
5. Li S, Zheng Q, Xu J, Gorstein J, Wang H, Dong H. Iodine excess or not: analysis on the necessity of reducing the iodine content in edible salt based on the national monitoring results. *Asia Pac J Clin Nutr*. 2011;20:501-6.
6. Li WH, Dong BS, Li P, Li YF. Benefits and risks from the national strategy for improvement of iodine nutrition: a community-based epidemiologic survey in Chinese schoolchildren. *Nutrition*. 2012;28:1142-5. doi: 10.1016/j.nut.2012.04.014
7. WHO/UNICEF/ICCIDD. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for program managers. Geneva: WHO; 2007.
8. Bureau SQS. General test method in salt industry-Determination of iodine.GB/T 13025.7-2012. Beijing: China Criterria Publishing House; 2012. p. 1. (In Chinese)
9. Bureau SQS. Methods for examination of drinking natural mineral water.GB/T 8538-2008. Beijing: China Criterria Publishing House; 2008. p. 95. (In Chinese)

10. Bureau SQS. Method for determination of iodine in urine by As³⁺-Ce⁴⁺ catalytic spectrophotometry. WS/T 107-2006. Beijing: China Criterria Publishing House; 2006. p. 1. (In Chinese)
11. Brunn J, Block U, Ruf G, Bos I, Kunze WP, Scriba PC. Volumetric analysis of thyroid lobes by real-time ultrasound (author's transl). *Dtsch Med Wochenschr.* 1981;106:1338-40. doi: 10.1055/s-2008-1070506.
12. MOHC. Iodine content in edible salt. GB 26878-2011. Beijing: China Criterria Publishing House; 2011. p. 1. (In Chinese)
13. Le J. *Obstetrics and Gynecology.* Beijing: People's Health Publishing House; 2008. (In Chinese)
14. MOHC. Diagnostic criteria for endemic goiter. WS 276-2007. Beijing: China Criterria Publishing House; 2008. pp. 1-2. (In Chinese)
15. Hastie TJ, Tibshirani R. *Generalized Additive Models.* New York: Chapman & Hall; 1990.
16. Mao G, Ding G, Lou X, Zhang R, Zheng P, Mo Z et al. Survey of iodine nutritional status in 2011, Zhejiang, China. *Asia Pac J Clin Nutr.* 2015;24:234-44. doi: 10.6133/apjn.2015.24.2.08.
17. Mo Z, Xu PW, Wang XF, Lou XM, Zhou JS, Mao GM, Zhu WM, Ding GQ. Dietary iodine intake level of adult population in coastal and inland areas of Zhejiang province. *Chinese Journal of Endemiology.* 2011;30:598-601. doi: 10.3760/cma.j.issn.1000-4955.2011.06.003. (In Chinese)
18. Schaafsma A, Deurenberg P, Calame W, van den Heuvel EG, van Beusekom C, Hautvast J et al. Design of the South East Asian Nutrition Survey (SEANUTS): a four-country multistage cluster design study. *Br J Nutr.* 2013;110(Suppl 3):S2-10. doi: 10.1017/S0007114513002067.
19. Medani AM, Elnour AA, Saeed AM. Excessive iodine intake, water chemicals and endemic goitre in a Sudanese coastal area. *Public Health Nutr.* 2013;16:1586-92. doi: 10.1017/S1368980012004685.
20. Hussein IS, Min Y, Ghebremeskel K, Gaffar AM. Iodine status and fish intake of Sudanese schoolchildren living in the Red Sea and White Nile regions. *Public Health Nutr.* 2012;15:2265-71. doi: 10.1017/S1368980012000833.
21. Zimmermann MB, Andersson M. Update on iodine status worldwide. *Curr Opin Endocrinol Diabetes Obes.* 2012;19:382-7. doi: 10.1097/MED.0b013e328357271a.
22. Maihara VA, Moura PLC, Fávoro DIT, Vasconcellos MBA. Assessment of iodine content in Brazilian duplicate portion diets and in table salt. *Journal of Radioanalytical and Nuclear Chemistry.* 2008;278:391-93. doi: 10.1007/s10967-008-0806-4.
23. Nazeri P, Mirmiran P, Mehrabi Y, Hedayati M, Delshad H, Azizi F. Evaluation of iodine nutritional status in Tehran, Iran: iodine deficiency within iodine sufficiency. *Thyroid.* 2010;20:1399-406. doi: 10.1089/thy.2010.0085.
24. Marchioni E, Fumarola A, Calvanese A, Piccirilli F, Tommasi V, Cugini P, Ulisse S, Rossi Fanelli F, D'Armiento M. Iodine deficiency in pregnant women residing in an area with adequate iodine intake. *Nutrition.* 2008;24:458-61. doi: 10.1016/j.nut.2008.01.015.
25. Tahirovic H, Toromanovic A, Balic A, Grbic S, Gnat D. Iodine nutrition status of pregnant women in an iodine-sufficient area. *Food Nutr Bull.* 2009;30:351-4.
26. Murcia M, Rebagliato M, Espada M, Vioque J, Santa Marina L, Alvarez-Pedrerol M et al. Iodine intake in a population of pregnant women: INMA mother and child cohort study, Spain. *J Epidemiol Community Health.* 2010;64:1094-9. doi: 10.1136/jech.2009.092593.
27. Andersen SL, Sorensen LK, Krejbjerg A, Moller M, Laurberg P. Iodine deficiency in Danish pregnant women. *Dan Med J.* 2013;60:A4657.
28. Gahche JJ, Bailey RL, Mirel LB, Dwyer JT. The prevalence of using iodine-containing supplements is low among reproductive-age women, NHANES 1999-2006. *J Nutr.* 2013;143:872-7. doi: 10.3945/jn.112.169326.
29. Vandevijvere S, Amsalkhir S, Mourri AB, Van Oyen H, Moreno-Reyes R. Iodine deficiency among Belgian pregnant women not fully corrected by iodine-containing multivitamins: a national cross-sectional survey. *Br J Nutr.* 2013;12:2276-84. doi: 10.1017/S0007114512004473.
30. Bath SC, Walter A, Taylor A, Wright J, Rayman MP. Iodine deficiency in pregnant women living in the South East of the UK: the influence of diet and nutritional supplements on iodine status. *Br J Nutr.* 2014;109:1622-31. doi: 10.1017/S0007114513004030.
31. Gaitan E. Goitrogens in food and water. *Annu Rev Nutr.* 1990;10:21-39. doi: 10.1146/annurev.nu.10.070190.000321.
32. Svensson J, Nilsson PE, Olsson C, Nilsson JA, Lindberg B, Ivarsson SA. Interpretation of normative thyroid volumes in children and adolescents: is there a need for a multivariate model? *Thyroid.* 2004;14:536-43. doi: 10.1089/1050725041517066.
33. Zimmermann MB, Hess SY, Molinari L, De Benoist B, Delange F, Braverman LE et al. New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. *Am J Clin Nutr.* 2004;79:231-7.
34. Yu X, Fan C, Shan Z, Teng X, Guan H, Li Y et al. A five-year follow-up study of goiter and thyroid nodules in three regions with different iodine intakes in China. *J Endocrinol Invest.* 2008;31:243-50.