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ORIGINAL ARTICLE

An assessment of iodine nutritional status and thyroid hormone levels in children aged 8–10 years living in Zhejiang Province, China: a cross-sectional study

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Abstract Iodine is an essential nutrient for the synthesis of thyroid hormones that are critical for brain development. Iodine deficiencies were prevalent in China until the introduction of universal salt iodization (USI) in 1995. USI has been considered as the world's best achievements. This study aims to assess children's iodine nutrition and goiter status in Zhejiang Province in order to provide reasonable suggestions to the government for policy-making under the USI period. A cross-sectional survey in Zhejiang Province was conducted to children aged 8–10 years by stage cluster random sampling method. Spot urine samples were collected and analyzed. Thyroid ultrasonography examination was performed by special trained technicians using a 7.5-MHz transducer. Fasting venous blood samples were collected and analyzed for thyroid functional status. The median urinary iodine concentration was found to be 173.3 μg/L. The percentage of urine samples with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 15.5, 42.0, and 13.3 %, respectively. Goiter prevalence rate with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 6.8, 10.0, and 14.9 %, respectively, with no significant difference. Children with goiter have lower serum FT3 and T3 concentrations compared to those without goiter ($p<0.05$). *Conclusions*: The median urinary iodine concentration of children aged 8–10 years falls in optimal iodine status as recommended by WHO/UNICEF/ICCIDD. Maintaining USI at an appropriate level is an important part of preventing iodine deficiency disorders and should always be based on routine monitoring urinary iodine concentration by the province.

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Introduction

Iodine is an essential nutrient for the synthesis of thyroid hormones that are critical for brain development. Iodine deficiency is defined by the World Health Organization (WHO) as a population median urinary iodine concentration that falls below 100 μg/L [13]. Urinary iodine concentration does not provide direct information on thyroid function, but it is a reliable measure of exposure. Urinary iodine concentration surveys are usually done in school-aged children because they are a convenient population, easy to reach through school-based surveys, and usually a representative of the general population.

Iodine deficiencies were prevalent in China until the introduction of universal salt iodization (USI) in 1995. USI has been considered as the world's best achievements because it contributes significantly to the world's disease and mortality burden [2]. In the early 1980s, surveys identified 831,000 individuals with iodine deficiency disorders (IDD) manifesting as goiter and an additional 134 individuals with typical cretinism in Zhejiang Province [1]. USI proved to be very effective; a provincial survey in 2000 found the virtual elimination of IDD [1].

In 2011, household coverage of adequately iodized salt (35±15 mg/kg) reached 97.2 % [1]. On the other hand, excess iodine consumption may also have adverse public health impacts [4, 14]. Careful monitoring of population iodine status is recommended according to the literatures. The measurement of the urinary iodine concentration (UIC) is the most commonly used index to assess iodine status in schoolchildren. In addition, blood constituents such as thyroglobulin antibodies (TGAb), thyroid peroxidase antibodies

Table 1 Median urinary iodine concentration and distributions by age and sex in school-age children aged 8–10 years in Zhejiang Province, China

	Number	Median (range) (μg/L)	<100 μg/L		100–300 μg/L		>300 μg/L		χ^2	*p* value
			N	%	*N*	%	*N*	%		
Age										
8-year-old	140	169.1 (1,338.1)	26	18.6	86	61.4	28	20	1.523	0.823
9-year-old	160	168.7 (1,042.6)	39	24.4	92	57.5	29	18.1		
10-year-old	151	192.3 (674.9)	34	22.4	90	59.2	28	18.4		
Gender										
Boys	225	174.3 (1,345.1)	46	20.4	133	59.1	46	20.4	1.073	0.585
Girls	226	171.8 (1,035.6)	53	23.5	134	59.3	39	17.3		

(TPOAb), free triiodothyronine (FT3), free thyroxine (FT4), total triiodothyronine (T3), total thyroxine (T4), and thyroid-stimulating hormone (TSH) can also be measured. Moderated iodine deficiency lowers circulating T4 concentrations, resulting in a subsequent rise in TSH [3, 12]. This paper aims to compare children's iodine nutrition and goiter status by age and sex in Zhejiang Province in order to provide reasonable suggestions to the government for policy-making under the USI period.

Subjects and methods

This survey was a cross-sectional survey of a representative sample of children aged 8–10 years in Zhejiang Province. The study was approved by the Ethical Review Board of the Zhejiang Provincial Center for Disease Control and Prevention. Research protocols were approved by Zhejiang Provincial Center for Disease Control and Prevention. All subjects provided a written informed consent after the research protocols were carefully explained to them.

A cluster sampling technique, probability proportional to size sampling, in which the probability that a particular sampling unit will be selected in the sample is proportional to the population size of the sampling unit [14], was employed in the present study. With county as the sampling unit, first, 22 counties were selected from 89 counties. One primary school was then randomly selected from each county chosen. Finally, about 20 schoolchildren aged 8–10 years from each school were selected. The child's sex and age were recorded. Informed written consent was obtained from parents or guardians of the children.

Spot urine samples were collected and delivered to the local Center for Disease Control and Prevention (CDC) laboratory for measuring urinary iodine concentration. Urinary iodine concentration was determined by the modified acid-digestion method (method for determination of iodine in urine by $As3+-Ce4+$catalytic spectrophotometry, WS/T 107–2006, Ministry of Health of the People's Republic of China). Blood samples of 131 children were collected from a subset of urban and rural children of two counties and stored at −80 °C until measuring TGAb, TPOAb, FT3, FT4, T3, T4, and TSH. These indexes were analyzed by chemiluminescent immunoassay (Abbott GmbH & Co. KG, Germany).

Height and weight were measured by child health nurses using standardized procedures. Thyroid ultrasonography was performed by a single operator using a 7.5-MHz transducer with the child lying supine and the neck hyperextended. The

Table 2 Comparison of goiter status according to urinary iodine concentration by age and sex in school-age children aged 8–10 years in Zhejiang Province, China

	Number	<100 μg/L			100–300 μg/L			>300 μg/L			χ^2	*p* value
		N	Goiter	%	*N*	Goiter	%	*N*	Goiter	%		
Age												
8-year-old	121	23	2	8.7	76	8	10.7	24	5	21.7	2.092	0.351
9-year-old	145	35	1	3	88	8	9.3	22	3	13.6	2.031	0.154
10-year-old	134	32	3	9.4	79	8	10.1	23	2	9.1	0.029	0.986
Gender												
Boys	193	42	1	2.5	118	15	12.7	34	2	6.1	5.099	0.078
Girls	207	48	5	10.4	124	9	7.3	35	8	23.5	6.259	0.044

volume of each lobe was calculated by the formula V(ml)= 0.479×width×length×thickness. The thyroid volumes were the sum of the volumes of the two lobes. In accordance with the Chinese national criteria for thyroid measurement, goiter was defined by age-specific thyroid volume. The upper limit of thyroid volume for children aged 8, 9, and 10 years was 4.5, 5.0, and 6.0 ml, respectively. If the child's thyroid volume exceeded the relevant value, the child was judged as goitrous [10].

Data processing and statistical analyses were performed using spss13.0 software. All tests were two-sided and the level of significance set at $P<0.05$. As continuous variables were not normally distributed, they were described as median and range. The difference between boys and girls were evaluated by nonparametric test (Mann-Whitney test). In order to compare blood constituents among different intervals of urinary iodine concentration, we divided the urinary iodine concentration into three intervals (<100 μg/L, 100–300 μg/L, >300 μg/L). The difference among different ages and different urinary iodine concentration intervals was evaluated by nonparametric test (Kruskal-Wallis H test).

Results

Iodine concentration in urine sample of children aged 8–10 years

A total of 460 children participated in the study, and 451 urine samples were collected from children aged 8–10 years and analyzed for iodine concentration. The median (range) urinary iodine concentration found to be 173.3 (1,345.1) μg/L. The percentage of urine samples with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 15.5, 42.0, and 13.3 %, respectively. There were no statistically significant differences by age and sex (Table 1).

Goiter distribution of children aged 8–10 years

Of the 451 children whose urine samples were collected and analyzed, 400 underwent ultrasonography (193 boys and 207 girls). Among the 400 children aged 8–10 years examined by ultrasound, 40 were found to have goiter accounting for 10 % of the group. The goiter prevalence rate with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 6.8, 10.0, and 14.9 %, respectively, with no significant difference ($\chi^2=2.758$, $p=0.252$). There were no statistically significant differences by age (Table 2). In girls, the goiter prevalence rate with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 10.4, 7.3, and 23.5 %, respectively, with significant difference ($\chi^2=6.259$, $p=0.044$).

Table 3 Comparison of thyroid volume according to urinary iodine concentration by age and sex in school-age children aged 8–10 years in Zhejiang Province, China

	<100 μg/L				100–300 μg/L				>300 μg/L			
	N	Height Median (range) (cm)	Weight Median (range) (kg)	Thyroid volume Median (range) (ml)	*N*	Height Median (range) (cm)	Weight Median (range) (kg)	Thyroid volume Median (range) (ml)	*N*	Height Median (range) (cm)	Weight Median (range) (kg)	Thyroid volume Median (range) (ml)
Age												
8-year-old	22	127.5 (40.0)	25.5 (22.0)	2.77 (4.07)	74	130.0 (75.0)	26.0 (36.7)	2.87 (7.07)	20	131.0 (50.0)	27.0 (49.2)	3.36 (6.03)
9-year-old	30	135.5 (34.0)	30.0 (25.0)	2.95 (3.44)	79	132.0 (66.0)	29.0 (54.0)	3.09 (7.17)	19	140.0 (56.0)	31.5 (52.0)	3.22 (11.71)
10-year-old	28	142.5 (45.0)	34.0 (35.5)	3.83 (6.53)	75	141.0 (61.0)	34.0 (71.0)	3.75 (7.70)	12	140.0 (32.0)	37.0 (19.5)*	3.69 (5.62)
Gender												
Boys	36	132.0 (52.0)	30.9 (30.0)	2.72 (4.19)	112	135.0 (68.0)	30.3 (68.0)	3.23 (7.59)	22	135.0 (51.0)	30.0 (37.5)	3.13 (5.82)
Girls	45	136.0 (44.0)	31.0 (37.0)	3.45 (6.94)*	115	134.0 (71.0)	28.1 (59.0)	2.92 (8.21)*	29	138.0 (53.0)	30.8 (57.5)	3.85 (12.35)*

*$p=0.016$ (chi-square=8.270, nonparametric test, Kruskal-Wallis H test)

Thyroid volume of children aged 8–10 years

Of the 451 children whose urine were collected and analyzed, 359 underwent ultrasonography as well as height and weight measurement (170 boys and 189 girls). The median (range) of thyroid volume for 8, 9, and 10-year-old children was 2.87 (7.29), 3.09 (12.5), and 3.75 (7.72), respectively. There were significant differences on thyroid volume by different urinary iodine concentration group in girls (chi-square= 8.270, p=0.016) (Table 3).

Blood constituents of children aged 8–10 years

Of the 451 children whose urine samples were analyzed, 131 underwent blood constituents' analysis (69 boys and 62 girls), and 120 underwent blood constituents' analysis as well as ultrasonography. Among the 131 children aged 8–10 years, the median (range) of blood FT3 of children with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 5.8 (3.2), 6.0 (5.0), and 6.1 (3.2), respectively, with no significant difference (chi-square=5.346, p=0.069). There were no statistically significant differences among different urinary iodine concentration on blood constituents (Table 4). Among the 120 children aged 8–10 years, the median (range) of blood FT3 and T3 concentration of children with goiter was 6.2 (5.0) and 2.7 (2.8), respectively, with significant difference (p<0.05) when compared to children without goiter whose blood FT3 and T3 concentration was 5.6 (3.4) and 2.2 (1.6), respectively. But there were no statistically significant differences on TGAb, TPOAb, FT4, T4, and TSH in children with or without goiter (Table 4).

Discussion

Because more than 90 % of dietary iodine eventually appears in the urine, the urinary iodine concentration is an excellent biomarker of recent iodine intake [17]. Because of the large intraindividual and interindividual variations in urinary iodine concentration [8], a limitation of urinary iodine concentration is that it can only be used to assess the iodine status of a population, but not of the individual in that population. Based on the result of the present study, the median urinary iodine concentration of children aged 8–10 years was 173.3 μg/L, which falls between 100 and 199 μg/L. According to WHO/ UNICEF/ICCIDD, children were in optimal iodine status. Since 2009, China's government has been considering lowering the salt iodization standard from the then mandatory mean of 35 mg/kg. In 2012, China's government decided that while USI remains mandatory, provinces may now iodize salt to a median within the range of 20–30 mg/kg depending on iodized salt coverage and urinary iodine concentration [9]. Combined with this new public health policy and the result of this study, it is urgent to monitor the urinary iodine concentration regularly to assess the iodine status and give suggestion to the government for policy-making.

Goiter is a functional biomarker that can be applied to both individuals and populations, but it is subjective. The goiter prevalence rate with iodine concentration <100 μg/L, 100–300 μg/L, and >300 μg/L was 6.8, 10.0, and 14.9 %, respectively, with no significant difference (χ^2=2.758, p=0.252). This is consistent with the previous findings for both urinary iodine concentrations and relative lack of correlation with thyroid volume [5]. In fact, the goiters were previously examined by palpation, until the recent years when thyroid ultrasonography was performed. Thyroid ultrasonography examination has better resolving power. So, the thyroid ultrasonography

Table 4 Comparison of blood constituents according to urinary iodine concentration and goiter prevalence rate in school-age children aged 8–10 years in Zhejiang Province, China

	Number	TGAb Median (range) (IU/L)	TPOAb Median (range) (IU/L)	FT3 Median (range) (pmol/L)	FT4 Median (range) (pmol/L)	T3 Median (range) (nmol/L)	T4 Median (range) (nmol/L)	TSH Median (range) (μIU/L)
Urine iodine concentration								
<100 μg/L	37	12.2 (140.0)	10.1 (193.4)	5.8 (3.2)	19.1 (13.1)	2.6 (2.4)	128.4 (102.3)	2.5 (8.8)
100–300 μg/L	56	10.7 (150.0)	8.5 (236.6)	6.0 (5.0)	18.3 (14.1)	2.7 (2.8)	125.6 (122.8)	2.9 (7.2)
>300 μg/L	38	14.0 (201.0)	12.0 (34.3)	6.1 (3.2)	18.7 (9.5)	2.7 (2.1)	123.6 (129.5)	2.8 (6.4)
Chi-square		5.406	5.841	5.346	1.240	0.742	0.210	0.310
p		0.067	0.054	0.069	0.538	0.690	0.900	0.857
Goiter								
Yes	16	12.1 (140.0)	10.0 (236.6)	6.2 (5.0)	18.8 (16.4)	2.7 (2.8)	127.1 (134.4)	2.7 (19.6)
No	104	12.6 (14.0)	14.2 (24.2)	5.6 (3.4)	18.6 (8.6)	2.2 (1.6)	122.5 (53.5)	2.3 (5.9)
Z		−0.331	−1.245	−2.748	−0.301	−3.802	−1.783	−0.861
p		0.740	0.213	0.006	0.763	0.000	0.075	0.389

examination may be an influencing factor for the goiter prevalence rate in this study. On the other hand, there had been three times adjustments on standard salt iodine concentration since 1995. In year 2000, the standard salt iodine concentration was 35±15 mg/kg, and in year 2012, the standard salt iodine concentration was adjusted to 20–30 mg/kg. This study was carried out in year 2011 before the third adjustment on standard salt iodine concentration. And the goiter rate reflects chronic iodine deficiency or iodine overdose and will be inconsistent with measurements of urinary iodine. Provided the goiter rate in year 2011 and combined with the result of urinary iodine concentration, the results of this study would provide suggestions to the government for policy-making. We had revised the discussion on this part on the manuscript. But in girls, both goiter prevalence rate and thyroid volume with different iodine concentration (<100 μg/L, 100–300 μg/L, >300 μg/L) have significant differences. Limited by the sample size of this current study, further studies on this topic should be carried out to explore the difference.

Iodine deficiency has multiple adverse health effects, all due to inadequate thyroid hormone production that are termed the IDD. Given the role of thyroid hormones in the brain, a lack of iodine in childhood could affect the developing brain. A study of Mexican schoolchildren found that moderate iodine deficiency was associated with a 4.26 times higher risk of low IQ [11]. An intervention study found that iodine supplementation improved perceptual reasoning in mildly iodine-deficient children and suggests that mild iodine deficiency could prevent children from attaining their full intellectual potential [6]. In this study, there were no statistically significant differences among different urinary iodine concentration on blood constituents including TGAb, TPOAb, FT3, FT4, T3, T4, and TSH. The mean FT3 concentration of children in this survey was similar to other study [7]. But children with goiter have lower serum FT3 and T3 concentrations compared to those without goiter. Iodine deficiency in certain geographical regions had been determined by goiter prevalence rate in the population [15]. Changes in goiter prevalence lay behind changes in iodine nutrition status after a salt iodization program has been initiated [16]. Goiter, when accurately assessed, remains an important and sensitive long-term indicator of the success of an iodine program. So, the finding of this study suggested that the changes of serum FT3 and T3 may be the biomarkers that lag behind urinary iodine concentration but superior to goiter.

Conclusions

This study has comprehensively examined the iodine status of a representative sample of 8–10-year-old children using a wide range of blood constituents. The median urinary iodine concentration of children aged 8–10 years falls in optimal iodine status as recommended by WHO/UNICEF/ICCIDD, but a part of children were mildly iodine-deficient or at risk of adverse health consequences. Maintaining USI at an appropriate level is an important part of preventing IDDs and should always be based on routine monitoring urinary iodine concentration by the province. Studies on the impact and most appropriated level of salt iodization should also be carried out at the time the new local iodization policy will be put forward.

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Author contributions G.D. was responsible for the study design. Y.Z. was responsible for data collection and analysis, paper writing, and revision. X.L. and Z.M. took part in the field investigation and data collection. W.Z was in charge of laboratory detection. J.Z and G.M. did the thyroid measurements by ultrasound.

Conflict of interest The authors declare no conflict of interest.

References

1. Zhejiang provincial center for disease control and prevention. Annals of Zhejiang provincial center for disease control and prevention. 2000
2. Boy E, Mannar V, Pandav C et al (2009) Achievements, challenges, and promising new approaches in vitamin and mineral deficiency control. Nutr Rev 67:S24–S30
3. Ceviz N, Ozkan B, Olgun H et al (2004) Left ventricular systolic and diastolic functions in children living in a moderate-severe iodine deficiency area. J Pediatr Endocrinol Metab 17:197–201
4. Delange F, de Benoist B, Alnwick D (1999) Risks of iodine-induced hyperthyroidism after correction of iodine deficiency by iodized salt. Thyroid 9:545–556
5. Filipsson Nyström H, Andersson M et al (2010) Thyroid volume in Swedish school children: a national, stratified, population-based survey. Eur J Clin Nutr 64:1289–1295
6. Gordon RC, Rose MC, Skeaff SA et al (2009) Iodine supplementation improves cognition in mildly iodine-deficient children. Am J Clin Nutr 90:1264–1271
7. Kapelari K, Kirchlechner C, Högler W et al (2008) Pediatric reference intervals for thyroid hormone levels from birth to adulthood: a retrospective study. BMC Endocr Disord 8:15
8. König F, Andersson M, Hotz K et al (2011) Ten repeat collections for urinary iodine from spot samples or 24-hour samples are needed to reliably estimate individual iodine status in women. J Nutr 141:2049–2054
9. Ministry of Health. Announcement on food safety national standard "iodine content in edible salt;" 2011[cited 2012 Mar 15]. Available from: http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohwsjdj/s7891/201109/53064.htm
10. Ministry of Health (2007) Diagnostic criterion for endemic goiter. MOH, Beijing, in Chinese
11. Pineda-Lucatero A, Avila-Jiménez L, Ramos-Hernández RI et al (2008) Iodine deficiency and its association with intelligence quotient in schoolchildren from Colima, Mexico. Public Health Nutr 11:690–698

12. Simsek E, Safak A, Yavuz O et al (2003) Sensitivity of iodine deficiency indicators and iodine status in Turkey. J Pediatr Endocrinol Metab 16:197–202
13. Stanbury JB, Ermans AE, Bourdoux P et al (1998) Iodine-induced hyperthyroidism: occurrence and epidemiology. Thyroid 8:83–100
14. World Health Organization/UNICEF/International Council for Control of Iodine Deficiency Disorders (2008) Elimination of iodine deficiency disorders: a manual for health workers. WHO Regional Office for Eastern Mediterranean, Cairo
15. World Health Organization: WHO/UNICEF/ICCIDD (2007) Assessment of iodine deficiency disorders and monitoring their elimination, 3rd edn. Geneva: a guide for programme managers
16. Zimmermann MB, Hess SY, Adou P et al (2003) Thyroid size and goiter prevalence after introduction of iodized salt: a 5-y prospective study in schoolchildren in Côte d'Ivoire. Am J Clin Nutr 77:663–667
17. Zimmermann MB, Jooste PL, Pandav CS (2008) Iodine-deficiency disorders. Lancet 372:1251–1262