

BMJ Open Associations of adiposity measurements with thyroid nodules in Chinese children living in iodine-sufficient areas: an observational study

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ABSTRACT

Objectives Obesity has been found to be associated with an elevated risk of thyroid nodule(s), mainly in adults; however, evidence for this association in children was limited. The objective of this study was to investigate the association of adiposity and thyroid nodule(s) in children living in iodine-sufficiency areas.

Setting and participants We conducted a cross-sectional study of 1403 Chinese children living in the East Coast of China in 2014.

Outcome measures Anthropometric measures including height, weight and waist and hip circumferences were taken, and body mass index (BMI), body surface area (BSA) and waist-hip ratio (WHR) were then calculated. Thyroid ultrasonography was performed to assess thyroid volume and nodules.

Results Based on BMI, 255 (18.17%) children were overweight and 174 (12.40%) were obese. Thyroid nodule(s) was detected in 18.46% of all participants and showed little age and sex variations. As compared with normal-weight children, obese children experienced significantly higher risks for solitary (OR 2.07 (95% CI 1.16 to 3.71)) and multiple (OR 1.67 (95% CI 1.03 to 2.70)) thyroid nodules. Similar associations with thyroid nodule(s) were observed with adiposity measured by waist circumference and BSA, but not WHR. There were no notable differences in the associations between children consuming iodised and non-iodised salt.

Conclusions These findings provide further evidence that childhood obesity is associated with the risk for thyroid nodule(s).

INTRODUCTION

Thyroid nodule (TN) is a common thyroid disorder globally, and the incidence has been increasing in recent decades.^{1,2} Thyroid ultrasound investigations have documented very high prevalences (approaching 50%) of TNs worldwide.³⁻⁵ Potential risk factors for TNs include age, sex, iodine intake,^{3, 6-8} demographic parameters, clinical history and waist circumference (WC).^{2,9} Both mildly deficient iodine intake and excessive iodine intake are risk factors for TN(s) in normal subjects.¹⁰

Strengths and limitations of this study

- Large sample size, directly measured thyroid ultrasonography and various anthropometric measurements following a standardised protocol.
- Detailed information distinguishing solitary and multiple nodules and household iodised salt consumption status at the individual level.
- Lack of information on thyroid function.

Obesity is a known risk factor for a number of chronic conditions and may also increase the risk of thyroid cancer.¹¹⁻¹⁵ The recent increase in TNs and thyroid cancer may partly be due to the epidemic of obesity.^{9, 16, 17} Elevated thyroid-stimulating hormone levels and declined free thyroxine (FT4) levels have been observed in obese patients.¹⁶ However, previous studies of the associations between obesity and thyroid were mainly conducted in adults, and the results were not entirely consistent. Whether these observations from adults can be applied to children is not clear particularly because the incidence of TNs is lower but the risk for malignancy is greater in children as compared with adults.¹⁸

In the current study, we conducted a large-scale epidemiological study to determine the associations of a number of anthropometric measurements including body mass index (BMI), body surface area (BSA), WC and waist-hip ratio (WHR) with solitary or multiple TNs in school-age children.

METHODS

Study population

Randomised cluster sampling was used to selected subjects. Similar study methodologies have been reported in an earlier study.¹⁹ Briefly, three coastal cities in East China (Minhang District in Shanghai, Haimen City



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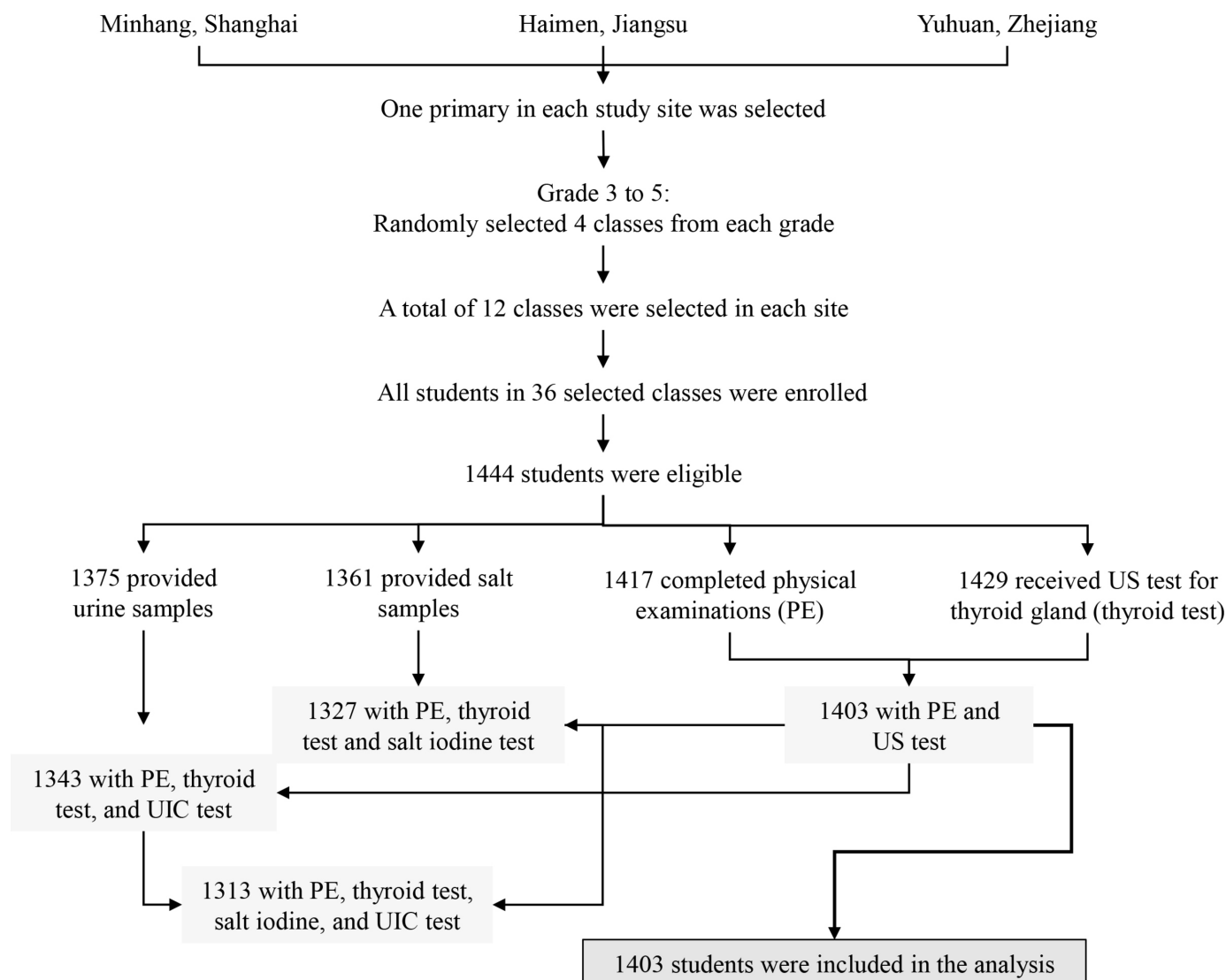


Figure 1 Flow chart for the study design. UIC, urinary iodine concentration; US, ultrasound.

in Jiangsu Province and Taizhou City in Zhejiang Province) were selected by purposive sampling. Previous studies have revealed an iodine-sufficient status^{20–22} along with distinguished iodised salt consumption proportions among three sites. One primary school (students were mainly local residents) was selected from each city to ensure a good representativeness. Four classes in each grade from grade 3 to grade 5 in these schools were randomly selected in 2014 and all students in 12 selected classes in each school were enrolled into this study (figure 1). Among 1444 eligible children, an ultrasound test for thyroid gland volume was performed on 1429 students and 1403 of them completed routine physical examinations. A total of 1375 students provided first morning urine samples. Based on data from 1403 students who completed physical examinations and thyroid test, we determined the prevalence of TN(s) and the influences of overweight and obesity. Written consent from parents or guardians of all participants were received, and the study was approved by the ethical review board of the School of Public Health of Fudan University.

Study variables

The outcome variables in this study were having TN(s) (no, yes) and number of TNs (no nodule, solitary nodule, multiple nodules). Adiposity measurements were explanatory variables, including BMI, BSA, WCs and WHR. Sex, age, urinary iodine concentrations (UICs) and iodised salt consumption status were covariates in the multivariate regression models.

Anthropometric measurements

Anthropometric measurements, including standing height (cm), weight (kg) and circumferences of the waist, hip and chest (cm) were taken by trained health professionals according to a standard protocol. The standing height was measured to the nearest 0.1 cm without shoes. Weight was measured to the nearest 0.1 kg using a digital weight scale. BMI was calculated as weight in kilograms divided by the square of height in metres, and all participants were categorised into three groups of under/normal weight, overweight and obesity status according to the BMI growth reference values for Chinese children.²³ The

cut-offs for overweight and obesity in boys were 17.8 and 20.1 for age 8, 18.5 and 21.1 for age 9, 19.5 and 22.2 for age 10 and 20.1 and 23.2 for age 11. The corresponding cut-offs for girls were 17.3 and 19.5, 17.9 and 20.4, 18.7 and 21.5, and 19.6 and 22.7, respectively. BSA was calculated by using the following formula: $BSA = (\text{Weight}^{0.425}) \times (\text{Height}^{0.725}) \times 0.007184$.²⁴ WHR was calculated as WC divided by hip circumference. BSA, WC and WHR were categorised into quintiles to assess their relations with TNs.

Thyroid ultrasonography

All participants received thyroid ultrasonography performed by experienced examiners at school using a real-time sector scanner with a 7.5 MHz/40mm probe linear transducer. The ultrasonographic examination was carried out on the children lying on a desk with the neck extended. Standardised thyroid ultrasound technique was adopted according to the method described by Fuse *et al.*²⁵ Discrete lesion(s) within the thyroid gland that was palpably and/or ultrasonographically distinct from the surrounding thyroid parenchyma was defined as TN(s).²⁶ In case of abnormality in the sonographic examination of the thyroid, parents of the children would receive a written note describing the abnormal results of the examination and be advised to take their children to visit a physician. All participants were categorised as having no nodule or having nodule(s) (solitary nodule and multiple nodules) according to their TN detection status.

Urine and salt samples collection and iodine concentration analyses

First, morning urine sample was collected for each participant. Students were also asked to bring a salt sample of more than 20g from home for iodine measurement.

UIC was determined following the method proposed by the Ministry of Health of the People's Republic of China (WS/T107.2006 and GB/T13025.7-1999).²⁷ Salt iodine content was also measured using a national standard method with a proper quality control²⁸ (GB/T13025.7-1999). Urine samples (10%) were assayed in duplicate, and no statistical differences were observed as compared with the primary results.

Iodine nutrition status was determined at a population level according to WHO/Unicef/International Council for Control of Iodine deficiency Disorders (ICCIDD): insufficient (UIC <100 µg/L), sufficient (100–199 µg/L), more than adequate (200–299 µg/L) and excessive (≥300 µg/L). Iodised salt consumption status was grouped into two categories: non-iodised salt (<5 mg/kg) and iodised salt (≥5 mg/kg).²⁹

Statistical analysis

χ^2 test was used to examine TNs in relation to sex, age, BMI, iodised salt consumption status, urinary iodine level and study area. Multinomial logistic regression analysis was used to examine the associations of various anthropometric measurements with the frequency of TNs (no

nodule, solitary nodule and multiple nodules). Due to a considerable day-to-day variation in iodine excretion, one-spot urinary iodine level was not a proper indicator of iodine status for individuals.^{30 31} Therefore, in current analysis, iodised salt consumption instead of iodine concentration in urine was included in the multivariate models. We also assessed the correlation between UIC and iodised salt consumption and observed a significantly higher level of UIC in children who consumed iodised salt at home, suggesting that iodised salt consumption status could be a good proxy for iodine nutrition at a population level. Multivariable logistic regression models were then used to adjust for age, sex and iodised salt consumption. Potential effect modifications by sex, age and iodised salt consumption on the associations of interest were also examined by including associated interaction terms into the multivariate analysis. We also reanalysed the data by using mixed effects with survey schools as random effect and observed no statistical significance of random effect in the generalized linear mixed model (GLMM) ($p=0.320$).

All analyses were performed by using SAS software, V.9.3 (SAS Institute), and all statistical significance was based on two-side probability.

RESULTS

Table 1 shows the demographic characteristics as well as iodine nutrition status for the 1403 participants included in the analysis. The mean age was 9.54 (± 0.98) years, the median BMI was 17.05 (IQR 15.55–19.35) kg/m² and the median UIC was 184.90 µg/L.

TN(s) were detected in 259 children, accounting for 18.46% of all the participants. Most nodules were accompanied by hypoechogenicity. Of the participants, 5.92% (83/1403) had solitary nodule and 12.54% (176/1403) had multiple TNs. The frequency of TNs showed no age-related or sex-related difference (**table 2**). The median UICs in children without nodules, with single nodule and multiple nodules were 187.80 µg/L, 195.55 µg/L and 160.45 µg/L, respectively (χ^2 7.44, $p=0.024$). The prevalence of multiple TNs was much higher in children consuming non-iodised salt than those consuming iodised salt.

Based on BMI, 255 (18.17%) were overweight and 174 (12.40%) were obese. Girls were more likely to be overweight than boys, and the prevalence of overweight/obese decreased with age in both sexes (p trend: 0.033 for boys and 0.010 for girls). The prevalences of solitary and multiple nodules in overweight subjects were 3.53% (9/255) and 15.29% (39/255), while the corresponding prevalences were 20.48% (17/174) and 14.77% (26/174) in obese ones, respectively.

Multivariable analysis revealed significant associations between obesity and the risk of TN(s) (**table 3**). As compared with normal-weight children, obese children experienced a significantly higher risks of TN(s) (OR 1.82 (95% CI 1.22 to 2.70)). We observed a similar association

Table 1 General characteristics for children from Shanghai, Haimen and Taizhou, China, in 2014

	Male		Female		χ^2	p Value
	n	%	n	%		
Total	739	52.67	664	47.33		
Age (years)					0.788	0.852
8	116	15.70	111	16.72		
9	246	33.29	215	32.38		
10	237	32.07	204	30.72		
11	140	18.94	134	20.18		
BMI					11.56	0.003
Normal	531	71.85	443	66.72		
Overweight	110	14.88	145	21.84		
Obese	98	13.26	76	11.45		
Area					6.182	0.046
Minhang	294	39.78	226	34.04		
Haimen	234	31.66	214	32.23		
Yuhuan	211	28.55	224	33.73		
UIC ($\mu\text{g/L}$)*					4.198	0.241
<100	122	17.35	132	20.63		
100–199	282	40.11	226	35.31		
200–299	171	23.14	158	24.69		
≥ 300	128	17.32	124	19.38		
Iodised salt consumption†					0.015	0.901
No	250	36.39	235	36.72		
Yes	437	63.61	405	63.28		

*A total of 60 missing: 36 (60.00%) were male and 24 (40.00%) were female.

†A total of 76 missing: 52 (68.42%) were male and 24 (31.58%) were female.

BMI, body mass index; UIC, urinary iodine concentration.

of obesity with the risk of either solitary nodule or multiple nodules (table 4). When stratified by sex, only obese girls experienced an increased risk for multiple nodules (OR 2.10 (95% CI 1.03 to 4.31)), but the interaction of obesity with sex was not significant ($p=0.494$). Associations of multiple nodules with overweight (OR 1.87, 95% CI 1.07 to 3.29) and obesity (OR 2.00, 95% CI 1.05 to 3.78) were observed in children aged 8 or 9 years, but not in older ones. Overweight was not significantly associated with solitary TN in general, which might be due to small number of children with this thyroid condition. Overweight children had an increased risk for multiple TNs (OR 1.76, 95% CI 1.03 to 3.02) only in iodised salt consumers.

Figure 2 presents multivariate-adjusted ORs and 95% CIs for solitary and multiple TNs associated with the quintiles of BSA, WC, BMI and WHR, respectively. After adjustment for sex, age and iodised salt consumption status, BSA and WC were positively related to the risks of solitary and multiple nodule(s) (p values for trend for all the nodules together were 0.0001 and <0.0001 , respectively). As compared with children in the lowest quintile, the ORs of solitary and multiple nodules were 2.45 (95% CI 1.24

to 4.87) and 2.76 (95% CI 1.54 to 4.97) for those in the highest quintile of BSA and 3.46 (95% CI 1.54 to 7.80) and 2.18 (95% CI 1.27 to 3.74) for those in the highest quintile of WC, respectively. The interaction between BSA and sex on TNs was not statistically significant (p interaction: 0.785 for solitary nodule and 0.600 for multiple nodules).

The results for BMI and WHR were less consistent. BMI was positively associated with the risk of multiple nodules (p trend=0.005), while WHR showed no association with either solitary or multiple nodules.

DISCUSSION

In this large cross-sectional study of children living in iodine-sufficient areas in East China, we observed a high prevalence of TNs and positive associations of obesity with both solitary and multiple TNs. Among several anthropometric measurements, BSA and WC were related to the risks for both solitary and multiple TNs. These findings were generally consistent across sex groups and independent of iodised salt consumption status.

Table 2 Comparison of the prevalence of thyroid nodules in different subgroups for children from Shanghai, Haimen and Taizhou, China, in 2014

Characteristics	n	Nodule(s)		χ ² , p Value*	χ ² , p Value†
		No nodule n (%)	Solitary nodule (n (%)) Multiple nodules (n (%)) Total		
All	1403	1144 (81.54)	83 (5.92) 176 (12.54) 259 (18.46)		
Sex				3.95, 0.047	4.264, 0.119
Male	739	617 (83.49)	37 (5.01) 85 (11.50) 122 (16.51)		
Female	664	527 (79.37)	46 (6.93) 91 (13.70) 137 (20.63)		
Age (years)				9.11, 0.028	11.61, 0.071
8	227	192 (84.58)	12 (5.29) 23 (10.13) 35 (15.42)		
9	461	359 (77.87)	34 (7.38) 68 (14.75) 102 (22.13)		
10	441	374 (84.81)	24 (5.44) 43 (9.75) 67 (15.19)		
11	274	219 (79.93)	13 (4.74) 42 (15.33) 55 (20.07)		
Iodised salt consumption‡				6.85, 0.009	12.46, 0.002
No	485	380 (78.35)	26 (5.36) 79 (16.29) 105 (21.65)		
Yes	842	708 (84.09)	52 (6.18) 82 (9.74) 134 (15.91)		
Urinary iodine (µg/L)§				13.00, 0.005	18.65, 0.005
≤100	254	204 (80.31)	12 (4.72) 38 (14.96) 50 (19.69)		
100–200	508	400 (78.74)	31 (6.10) 77 (15.16) 108 (21.26)		
200–300	329	268 (81.46)	25 (7.60) 36 (10.94) 61 (18.54)		
>300	252	225 (89.29)	12 (4.76) 15 (5.95) 27 (10.71)		
Area				142.11, <0.001	155.80, <0.001
Shanghai	520	344 (66.15)	49 (9.42) 127 (24.42) 176 (33.85)		
Haimen	448	426 (95.09)	20 (4.46) 2 (0.45) 22 (4.91)		
Taizhou	435	374 (85.95)	14 (3.22) 47 (10.80) 61 (14.02)		

*Comparison between participants with/without thyroid nodule(s).

†Comparison among participants without nodule/with solitary nodule/with multiple nodules.

‡A total of 60 missing: 36 (60.00%) were male and 24 (40.00%) were female.

§A total of 76 missing: 52 (68.42%) were male and 24 (31.58%) were female.

Table 3 Multinomial logistic regression analysis of obesity and thyroid nodule(s) for children from Shanghai, Haimen and Taizhou, China, in 2014

	Thyroid nodule(s)						
	No nodule	Normal		Overweight		Obesity	
	N	N	OR	N	OR (95% CI)*	N	OR (95% CI)*
All subjects†	1144	168		48		43	
Model 1			1.00		1.11 (0.78 to 1.59)		1.58 (1.07 to 2.31)
Model 2			1.00		1.00 (0.69 to 1.45)		1.82 (1.22 to 2.70)
Model 3			1.00		1.04 (0.71 to 1.51)		1.71 (1.13 to 2.59)
Sex‡							
Male	576	80	1.00	14	0.83 (0.45 to 1.54)	17	1.39 (0.77 to 2.52)
Female	512	79	1.00	29	1.21 (0.75 to 1.96)	20	2.10 (1.17 to 3.79)
Age (years)§							
8–9	519	76	1.00	27	1.37 (0.83 to 2.25)	25	1.87 (1.10 to 3.19)
10–11	569	83	1.00	16	0.77 (0.43 to 1.38)	12	1.39 (0.70 to 2.75)
Iodised salt consumption¶							
Yes	708	81	1.00	28	1.20 (0.75 to 1.93)	25	1.62 (0.98 to 2.68)
No	380	78	1.00	15	0.81 (0.43 to 1.50)	12	1.94 (0.92 to 4.09)

*95% confidence interval.

†Model 1, univariate analysis (n=1403); model 2, adjusted for sex, age, iodised salt consumption (n=1327); model 3, adjusted for sex, age, urinary iodine concentration (n=1343).

‡Adjusted for age and iodised salt consumption (n=1327).

§Adjusted for sex and iodised salt consumption (n=1327).

¶Adjusted for sex and age (n=1327).

TN(s) is common in adults, and its impact on thyroid cancer risk is still unclear.¹⁶ The prevalence of incidental TNs detected by ultrasound examinations is high in adults (close to 50%) as well as in iodine-deficient countries.^{3–5} However, few studies have investigated the prevalence and the spectrum of appearance of ultrasound-detected findings in children. TNs were identified in 1.65% of children aged 3–18 years in three Japanese prefectures, and the prevalence increased with age with a female predominance.³² The information released by Fukushima Prefecture indicated that 2014 (1.15%) of 75 216 Japanese children aged 0–18 had TNs.³³ Avula *et al* conducted a retrospective analysis in 287 Canadian children (mean age=6.2) and detected only 1 child with multiple TNs but 52 (18%) children with thyroid abnormalities.³⁴ In healthy Greek children living in an iodine-replete area, one or more nodules were observed in 5.1% of them.³⁵ For 2410 children aged 6–17 years living in Hangzhou, China, TNs were detected in 10.66% of them.³⁶ These results showed much lower frequencies than those observed in the current study, in which TNs existed in 18.46% of 1433 Chinese children with little age variations and sex variations. Influencing factors include age composition, interobserver variation, iodine intake, socioeconomic status and individual and/or family history, as well as detection sensitivity and image quality of ultrasound machine.³²

TN has multiple known risk factors, including demographic parameters, clinical history, age, sex,^{6–8} iodine deficiency³ and potentially milk consumption.³⁶ The association between TN(s) and obesity has been explored mostly in adults with inconsistent results.^{37,38}

Obesity is a risk factor for several chronic conditions, as well as goitre in adults.³⁹ Its impact on TNs has also been investigated by using different anthropometric parameters in adults. Among various parameters, BMI was most frequently used as a measure of general adiposity. It has been increasingly recognised that the adverse effects of obesity relate to the amount and to the distribution of excess body fat. Therefore, the use of BMI alone to infer health risks in Asians may underestimate the detrimental health effects of excess adiposity.⁴⁰ WHR and WC were good proxy measures of central adiposity. It has been suggested that WC is a better marker for total body adiposity than it is for visceral fat.⁴¹ Another study has shown that both WC and BMI appear to perform equally well for estimating children and adolescents's total adiposity.⁴² BSA is a better indicator of the circulating blood volume, oxygen consumption and basal energy expenditure than BMI³⁷ and has been shown to be the best independent predictor of the thyroid volume in both sexes.

Several studies have found significant associations between measures of obesity and the risk of TNs. For example, a study conducted in Hangzhou, China, observed a prevalence of

Table 4 Multinomial logistic regression analysis of obesity and solitary and multiple thyroid nodules for children from Shanghai, Haimen and Taizhou, China, in 2014

	Normal						Overweight						Obesity						
	No nodule		Solitary nodule		Multiple nodules		Solitary nodule		Multiple nodules		Solitary nodule		Multiple nodules		Solitary nodule		Multiple nodules		
	N	OR	N	OR	N	OR (95% CI)*	N	OR (95% CI)*	N	OR (95% CI)*	N	OR (95% CI)*	N	OR (95% CI)*	N	OR (95% CI)*	N	OR (95% CI)*	
All subjects†	1144	57	111	1.00	9	0.62 (0.30 to 1.26)	39	1.37 (0.92 to 2.03)	17	1.84 (1.04 to 3.25)	26	1.44 (0.91 to 2.30)							
Model 1				1.00		0.53 (0.25 to 1.13)		1.33 (0.88 to 2.03)		1.82 (0.99 to 3.36)		1.62 (0.98 to 2.70)							
Model 2				1.00		0.54 (0.25 to 1.16)		1.24 (0.82 to 1.88)		2.07 (1.16 to 3.71)		1.67 (1.03 to 2.70)							
Model 3				1.00															
Sex‡																			
Male	576	26	54	1.00	1	0.17 (0.02 to 1.28)	13	1.18 (0.61 to 2.26)	7	1.53 (0.63 to 3.71)	10	1.29 (0.62 to 2.70)							
Female	512	29	50	1.00	7	0.77 (0.33 to 1.82)	22	1.49 (0.86 to 2.59)	8	2.09 (0.89 to 4.89)	12	2.10 (1.03 to 4.31)							
Age (years)§																			
8–9	519	29	47	1.00	5	0.63 (0.24 to 1.68)	22	1.87 (1.07 to 3.29)	9	1.60 (0.71 to 3.57)	16	2.00 (1.05 to 3.78)							
10–11	569	26	57	1.00	3	0.46 (0.14 to 1.55)	13	0.95 (0.50 to 1.82)	6	2.05 (0.80 to 5.25)	6	1.05 (0.43 to 2.60)							
Iodised salt consumption¶																			
Yes	708	35	46	1.00	5	0.48 (0.18 to 1.27)	23	1.76 (1.03 to 3.02)	12	1.76 (0.88 to 3.54)	13	1.50 (0.78 to 2.90)							
No	380	20	58	1.00	3	0.59 (0.17 to 2.08)	12	0.88 (0.45 to 1.75)	3	1.84 (0.50 to 6.79)	9	1.97 (0.86 to 4.48)							

*95% confidence interval.

†Model 1, univariate analysis (n=1403); model 2, adjusted for sex, age, iodised salt consumption (n=1327); model 3, adjusted for sex, age, urinary iodine concentration (n=1343).

‡Adjusted for age and iodised salt consumption (n=1327).

§Adjusted for sex and iodised salt consumption (n=1327).

¶Adjusted for sex and age (n=1327).

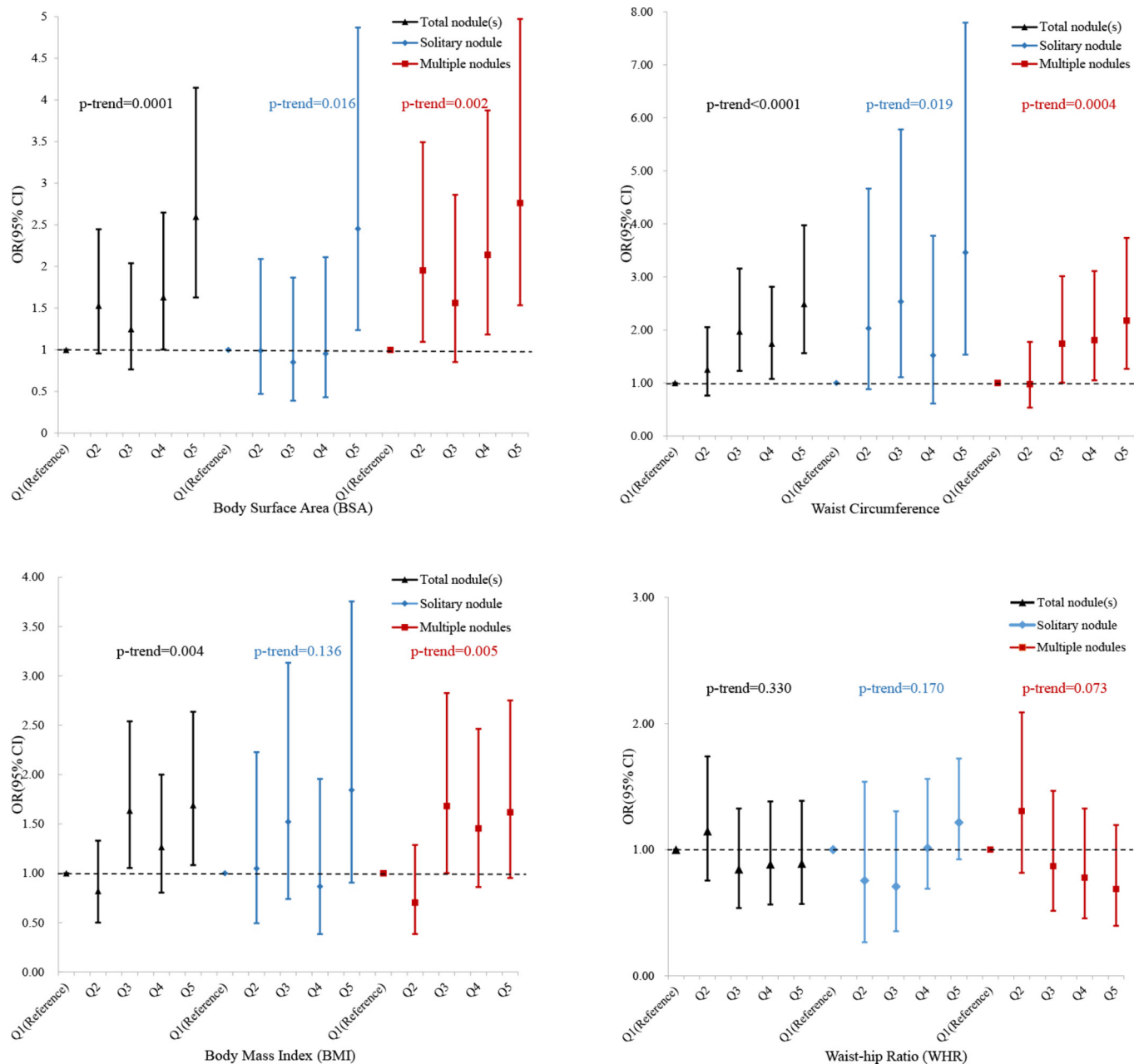


Figure 2 Associations of different physical measurements (body surface area, waist circumference, body mass index and waist-hip ratio) with thyroid nodule(s) for children from Shanghai, Haimen and Taizhou, China, in 2014.

TN being 34.97% (33.97 for men and 36.92% for women) and great WC as a risk factor for new TN in this iodine-adequate area.² Similar trends were observed for females and males, but the association was not statistically significant in men,² which was similar to our findings in children. Another study of postmenopausal women also revealed that WC and BMI were associated with TNs.⁴³ Large BMI was associated with nodule growth among older patients with multiple nodules and larger dominant nodules.¹⁷ A study conducted by Shin *et al* linked thyroid nodular disease to WC for males and glycated haemoglobin for females,⁴⁴ suggesting potential sex disparity. The presence of insulin resistance was associated with larger thyroid gland volume and an increased prevalence of TNs,^{45 46} which might be explained by obesity-related subclinical inflammation and

an associated increase in levels of insulin-like growth factor-1.⁴⁵ However, another study yielded conflicting results, which suggested that adult patients with normal weight or overweight based on BMI tended to have an increased risk of TNs, as compared with underweight or obese people.³⁸ Evidence in children had been relatively limited.

The prevalence of obesity and overweight in our study population was slightly higher than that in students from four Chinese megacities (25.6%)⁴⁷ but lower than urban students of similar age groups in the National Surveys on Chinese Students' Constitution and Health (37.0% for overweight and 20.3% for obesity).⁴⁸ Our findings of increased risk for TNs in obese children are generally consistent with those in obese adults of other studies. The association of BSA with thyroid volume in children

has been well established,³⁵ while its relation to TNs has been seldom explored. Kim *et al*³⁸ examined 7763 healthy Korean adults and observed a significantly smaller BSA in those with TNs compared with the others, which was opposite to our findings. Considering the great difference in BSA between adults and children, it needs to be cautious to generalise the results to children.¹⁶ Xu *et al*³⁶ conducted a cross-sectional study in Hangzhou, China, and reported an OR of 2.97 (95% CI 1.85 to 4.77) for TNs for children with average BSA or above as compared with those with less than average BSA. However, they did not collect the information on waist and hip circumferences and number of TNs. Therefore, it was not possible to determine different associations between WC, WHR and different kinds of nodules in that study. The potential interactive effects of iodised salt consumption and sex on the association between overweight and multiple nodules also need further investigations with a larger sample size.

The strengths of our study include large sample size, directly measured thyroid ultrasonography and anthropometric measurements following a standardised protocol and the abilities to distinguish solitary and multiple nodules and to adjust for household iodised salt consumption status. Our study has several limitations. First, we did not have any information on thyroid function. Therefore, we were unable to further search potential mechanisms that might explain the observed associations. Second, there were no information on the amount of salt and milk consumption. In the current study, the number of children with solitary or multiple nodules was small in some categories. In addition, the cross-sectional design prevents us from making causal inferences.

CONCLUSION

In this cross-sectional study of a relatively lean children population, we found that elevated levels of general or abdominal adiposity, measured by BMI, BSA and WC, were associated with a significant increase in the risk of TN(s), especially multiple nodules in girls and solitary nodule in boys. Our findings, along with those observed from adult populations, emphasise the importance of preventing excess adiposity for primary prevention of TNs.

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Contributors NW, HF, CF, PH, MS, QZ and QJ contributed to the study design; NW, HF, CF, PH, MS, FJ, QZ and QJ contributed to data acquisition and collection; NW, QZ and YC contributed to data analysis and interpretation; NW, QZ and YC drafted the

manuscript; all authors contributed to the preparation of the final document, read and approved the final manuscript.

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