INCREASED LEVELS OF MEDIAN URINARY IODINE EXCRETION OF PRIMARY SCHOOL CHILDREN IN THE SUBURBAN AREA, KHON KAEN, THAILAND

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Abstract. Iodine deficiency disorder (IDD) is associated with a low IQ in children and is an important public health problem in northeastern Thailand. Despite campaigns to reduce IDD in northeastern Thailand, studies showed people in this region continue to have the lowest median urinary iodine (UI) excretion and Intelligence Quotient scores. We conducted a cross sectional study of median urinary iodine excretion among primary school children in suburban Khon Kaen Province, in northeastern Thailand, during December 2012 to evaluate the current status of IDD in this population. We studied 377 school children. Urine samples were collected and measured for UI using a simple microplate method. The median UI level was 229.0 μg/l (range15.0-1,124.1). Forty school children (10.6%) had UI levels less than 100 μg/l and 10 children (2.7%) had UI levels less than 50 μg/l. One hundred nine children (28.9%) had UI levels greater than 300 μg/l. Our study shows that there are still children in the study population and study area with inadequate UI levels. Programs to prevent IDD need to include this population in this area.

Keywords: suburban area, urine iodine excretion, school children

INTRODUCTION

Iodine is an essential micronutrient needed for the synthesis of thyroxine (T4) and triiodothyronine (T3) (Kopp, 2005), needed to control energy production and oxygen consumption in cells, for normal growth, and neural and sexual development (Connolly *et al*, 1979; Bleichrodt and Born, 1994). Iodine is present naturally in soil, seawater and in salt water fish, seaweed, shellfish, cheese, cow's milk and yogurt (WHO, ICCIDD, UNICEF, 2001). Inadequate iodine intake can cause iodine deficiency disorder (IDD) and hypothyroidism causing short stature, goiter, mental retardation, decreased fertility rates and pregnancy-related complications (Zimmermann *et al*, 2006, 2008; WHO, ICCIDD, UNICEF, 2007). Children living in areas with severe iodine deficiency may have an intelligence quotient (IQ) of up to 13.5 points below that of comparable communities in areas where there is no iodine deficiency (Bleichrodt and Born, 1994).

Physical examination in IDD can reveal a goiter and laboratory testing can show abnormalities in urinary iodine (UI)

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excretion, thyroid stimulating hormone (TSH) and serum thyroglobulin (TG) levels (Delange, 1997; Knudsen *et al*, 2001). TSH and TG testings are impractical in the field for population-based studies. Morning UI levels are a good, cost-effective method for screening for IDD in the population (Ristic-Medic *et al*, 2009).

The Ministry of Public Health for Thailand has conducted campaigns to prevent IDD using iodized salt. IDD and low IQ in children are important public health problems in Thailand (Jaruratanasirikul *et al*, 2009). After a recent campaign to prevent IDD, two studies were conducted to evaluate iodine status in northeastern Thailand, one in urban Khon Kaen (Suesirisawad *et al*, 2013) and another in rural Sakon Nakhon (Kasuri, 2012). No studies have yet be conducted in suburban northeastern Thailand. Therefore, we conducted a cross sectional study of UI excretion among primary school children in the suburban Khon Kaen.

MATERIALS AND METHODS

This study was conducted in December 2012 at Bantum Primary School, located in a suburban area, 11 kilometers from the Mueang District of Khon Kaen Province, northeastern Thailand. Three hundred seventy-seven children, aged 6-12 years were included in the study. Informed consent was obtained from both the children and their parents. Exclusion criteria included children who had received iodized oil within the previous year, children who had a diagnosis of hyperthyroidism or hypothyroidism who were being treated with medication, radioactive iodine or surgery, children with an arrhythmia who took amiodarone and those from whom no consent from the parents or guardians were obtained. Demographic data collected included sex, age, parental occupation and education level, history of underlying disease, current medications and opinion about the need to consume iodized salt. A physical examination was carried out on all the study subjects to detect thyroid abnormalities, such as goiter or signs of hypo- or hyperthyroidism. Thyroid function tests, thyroid autoantibodies testing and an IQ test (using the Colored Progressive Matrices, performed by a psychologist) were performed on all children with a goiter. Spot urine samples were collected in the morning during 6:00-10:00 AM and transported on ice to the Laboratory unit of Regional Health Promotion Center 6, Department of Mental Health, Ministry of Public Health and stored at -20°C until analyzed. Iodine testing was performed using a simple microplate method described by Ohashi *et al* (2000). The study was approved by The Human Ethics Committee of Khon Kaen University in June, 2012.

IDD is defined as more than 10% of the school children in a population having goiter (Perez *et al*, 1960; Querido *et al*, 1974; Delange *et al*, 1986). The classification of goiters is shown in Table 1 (WHO/UNICEF/ICCIDD, 1994). The WHO cut-off criteria for median UI excretion were used in this study (Table 2) (WHO/ICCIDD/UNICEF, 2007). A median UI level of 100-199 μg/l was defined as adequate iodine intake.

Statistical analysis

The formula $n = p(1-p)/e^2/Z^2+p(1-p)/N$, (where $p = 0.348$, $e = 0.05$, $Z= 1.96$ for 95% confidence, $N = 15{,}102$) was used to determine the sample size of 345 subjects . All data processing was done with the Statistical Package for Social Sciences SPSS version 11.5 software for Windows

Table 1
WHO classification of goiter (WHO/UNICEF/ICCIDD, 1994).

Grade	Characteristics of goiter
0	No goiter found, the thyroid has no palpable enlargement and is not visible on inspection.
1	An enlarged thyroid that is palpable but not visible on inspection with the neck in a normal position. An enlarged thyroid is noticable during swallowing. Grade 1 also includes a nodular goiter if the thyroid is not visible on inspection.
2	An enlarged thyroid is visible when the neck is in a normal position, corresponding to an enlarged thyroid found with palpation.

Table 2
Epidemiologic criteria for assessing iodine nutrition based on a median urine iodine level among school children (WHO/UNICEF/ICCIDD, 1994 and WHO/ICCIDD/UNICEF, 2007).

Median UI (μg/l)	Iodine intake	Iodine nutrition
< 20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Optimal iodine level
200-299	More than adequate	Risk of iodine-induced hyperthyroidism within 5-10 years following introduction of iodized salt in susceptible groups
≥300	Excessive	Risk of adverse health consequences (iodine induced hyperthyroidism, autoimmune thyroid diseases)

UI: urine iodine.

(SPSS, Chicago, IL). Means, medians, proportions and percentages were used to analyze the data.

RESULTS

Three hundred seventy-seven school children aged 6-12 (mean ± SD = 9.4 ± 1.8) years were included in the study, 203 (53.8%) were boys and 174 (46.2%) were girls. Forty-one point nine percent of fathers and 50.9% of mothers had a secondary school education. Forty-eight point one percent of fathers and 46.9% of mothers worked as temporary workers. Most of school children were healthy; 5.3% had underlying diseases such as allergic rhinitis or mild anemia. Antihistamines or multiple vitamins were taken by 3.7%. Ninety-four percent of parents and children understood the importance of iodized salt. Iodized salt was used regularly by 29.2% and occasionally used 59.2%. Seventy-one percent of subjects had an iodine-rich diet during the previous week.

Urinary iodine excretion

For statistical analysis, the non-parametric data of UI levels are not normally

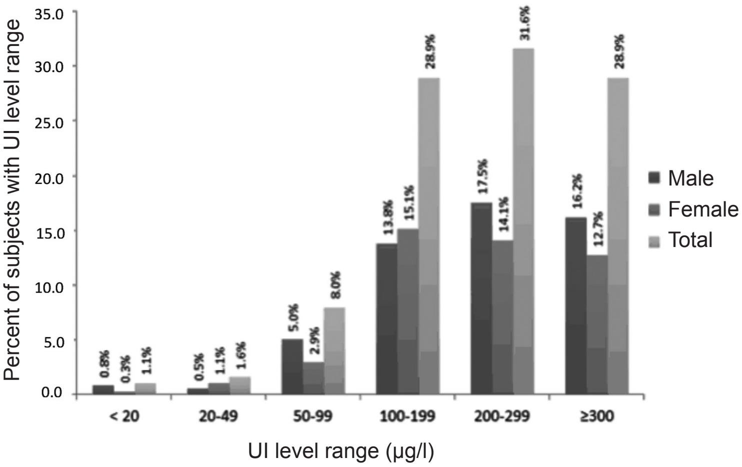

Fig 1–Distribution of study subjects with urine iodine (UI) level ranges.

distributed, therefore the median and interquartile range of UI levels were presented. The median UI level was 229.0 μg/l [interquartile range (IQR): 15.0-1,124.1 μg/l]. The median UI level among boys was 240 μg/l (IQR: 15.0-1,124.1 μg/l) and girls was 217.8 μg/l (IQR: 17.6-1,107.6 μg/l ($p = 0.54$)(Table 3). Forty subjects (10.6%) had a median UI level less than 100 μg/l, 10 (2.7%) had a UI level less than 50 μg/l and 109 (28.9%) had a UI level greater than 300 μg/l. More than adequate iodine intake (UI level 200-299 μg/l) was observed in 119 (31.6%) and adequate intake (UI level: 100-199 μg/l) was seen in 109 (28.9%) (Table 4, Fig 1).

Goiter

Physical examination revealed goiter in 4 subjects (1.1%), 3 had a grade 1 goiter and 1 had a grade 2 goiter. The median UI level among subjects with a goiter was 239.1 μg/l (IQR: 71.9-373.3 μg/l). All the goiter subjects were female; none had symptoms or signs of hyper- or hypothyroidism. One had a low UI level (71.9 μg/l); all had a normal or above normal IQ (range 90-117). All had normal thyroid function tests but one had autoimmune thyroiditis with positive thyroid autoantibodies (Table 5).

DISCUSSION

Iodine deficiency disorders (IDDs) is a serious public health problem in Thailand. Many studies have been conducted to determine the incidence and prevalence of IDD in Thailand using signs of goiter and biochemical testing. In iodine-rich areas such as Hat Yai municipality, Songkhla Province, southern Thailand, 6,035 school children, aged 8-17 years, were examined for goiter: goiter was detected in 355 children (6%) (Jaruratanasirikul *et al*, 1995); simple goiter being the most common. Iodine deficiency was not seen in that study. A study of school children, aged 7-12 years from 3 provinces in northern Thailand found median UI levels of 264.5, 998.6 and 137.0 μg/l (Jongjirasiri *et al*, 2000). In Bangkok and the surrounding metropolitan area, the median UI excretion among school children was 200 μg/l (range 25-835 μg/l) (Gowachirapant *et al*, 2009).

The Thai National Control and Prevention of IDD Project of the Ministry of Public Health established a program to eliminate IDD in 2000. A survey from the Health Systems Research Institute during 2008-2009 found the median UI level among Thai children aged 1-14 years was 146 μg/l, 34.8% had a UI level less than 100 μg/l, 27.8% had a UI level 50-99 μg/l, 5.7% had a UI level 20-49 μg/l and 1.2% had a UI level less than 20 μg/l (Pruenglampoo

Table 3
Urinary iodine (UI) levels among study subjects.

Sex	Median UI (μg/l)[a]	Range (μg/l)
Male	240.0	15.0-1,124.1
Female	217.8	17.6-1,107.6
Total	229.0	15.0-1,124.1

[a]No statistically significant differences in median urinary iodine concentration by gender ($p = 0.539$, Mann-Whitney test).

Table 4
Median urinary iodine level distribution among study subjects.

	Median UI (μg/l)						Total
	<20	20-49	50-99	100-199	200-299	≥300	
Number of children (%)	4 (1.1)	6 (1.6)	30 (7.9)	109 (28.9)	119 (31.6)	109 (28.9)	377 (100)
Male (%)	3 (0.8)	2 (0.5)	19 (5.0)	52 (13.8)	66 (17.5)	61 (16.2)	203 (53.8)
Female (%)	1 (0.3)	4 (1.1)	11 (2.9)	57 (15.1)	53 (14.1)	48 (12.7)	174 (46.2)

Table 5
Characteristics of 4 study subjects with goiter.

Number	Sex	Age (yrs)	Grade of goiter	Urine iodine level (μg/l)[a]	Thyroid autoantibodies	IQ[b]
1	Female	9	1	236.4	Positive	99
2	Female	9	2	241.7	Negative	117
3	Female	11	1	373.3	Negative	90
4	Female	12	1	71.9	Negative	94

[a]Median urinary iodine level = 239.1 μg/l.
[b]Median intelligence quotient (IQ): 96.5 (interquartile range 90-117).

and Aekplakorn, 2011). In northeastern Thailand, where there is a history of a high prevalence of IDD, one survey found the median UI level was 125 μg/l compared to the overall Thai country median UI level of 146 μg/l; 32.9% had a UI level less than 100 μg/l, 10.1% had a UI level less than 50 μg/l, and 9.1% had a UI level more than 300 μg/l (Pruenglampoo and Aekplakorn, 2011). The results of a study from Sakon Nakhon Province in rural northeastern Thailand found a median UI of 172.4 μg/l (range 21.8-296.1 μg/l)(Kasuri, 2012). A study among mothers and neonates from urban Khon Kaen found a maternal median UI of 208.4 μg/l and 29.3% had UI value less than 100 μg/l. The median neonatal TSH was 4.3 milliunits/l; 3.0% had TSH levels greater than 5.0 milliunits/l, indicating adequate iodine status in this population (Suesirisawad *et al*, 2013).

The present study was conducted in a suburban area of Khon Kaen using random urine samples collected in the morning during 6:00-10:00 AM, the time with the lowest UI level but the highest sensitivity; this represents recent iodine intake and is useful to determine IDD in the community but not for an individual. The median UI levels (299 μg/l) seen in our study were higher than the previous studies (125 μg/l) from northeastern Thailand (Pruenglampoo and Aekplakorn, 2011).

Excess iodine ingestion (UI level greater than 300 μg/l) was found in 109 children (28.9%), indicating recent excess iodine ingestion. Several studies have also reported iodine excess from central China (Li *et al*, 1987), Japan (Fuse *et al*, 2007), Brazil (Duarte *et al*, 2009), Dehli in India (Kapil, 2010) and Korea (Lee *et al*, 2014). Recent availability of iodine rich foods, such as dried seaweed and squid snacks have resulted in greater availability of these foods in suburban areas, school cafeterias and shops. Chronic exposure to foods with high iodine levels is associated with the development of goiter, increased serum thyrotropin levels and hyperthyroidism in some children (Andersson *et al*, 2005; Zimmermann *et al*, 2005; Duarte *et al*, 2009). Thyroid function tests were not performed in this study but no one had clinical symptoms of hyperthyroidism. UI level examinations should be performed at least every 2 to 5 years to evaluate for iodine excess in at risk populations.

Four children in our study (1.1%) had a goiter: 3 with grade 1 goiter and one with grade 2 goiter. All the subjects with goiter were female and none had a family history of thyroid disease, there were no signs of hyper- or hypothyroidism. One goiter subject had a low urine iodine level (71.9 μg/l), and 1 had a high UI level (373.3 μg/l); all of them had normal thyroid function tests and a normal or above normal IQ (range 90-117). Only 1 child with goiter had thyroid autoantibodies. Using WHO criteria of goiter prevalence to diagnose IDD (>10% of subjects) (Perez *et al*, 1960), suburban Khon Kaen may have IDD, but the clinical and laboratory findings in these children did not show IDD. This suggests a single UI level does not reflect individual iodine status.

The median UI level is often misinterpreted. Individual iodine intake and spot UI concentrations are highly variable from day-to-day. A common mistake is to assume all individuals with a spot UI of less than 100 μg/l are iodine deficient. To estimate iodine intake in an individual, a 24-hour urine collection is preferable and better represents hydration status, but is more difficult to obtain. An alternative method is to use the age-adjusted, sex-adjusted iodine to creatinine ratio, but this ratio also has limitations. The median UI concentration in the general population should be 100-199 μg/l. A good screening technique to evaluate deficiency, or excess is to screen a representative population for UI levels every 5 years (WHO/ ICCIDD/ UNICEF, 2007).

Ninety-four percent of parents and children in our study understood the importance of iodized salt. However, iodized salt was used regularly by only 29.2% and occasionally by 59.2% of our study subjects. Provision of iodine rich foods, such as seafood, to suburban areas may assist in eliminating IDD in these areas. Iodine status needs to be monitored regularly. Nutritional education to reduce IDD needs to be given regularly. Regular studies of IDD need to be conducted among at risk population in northeastern Thailand.

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