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Maternal iodine status and neonatal thyroid-stimulating hormone concentration: a community survey in Songkhla, southern Thailand

Somchit Jaruratanasirikul[1,]*, Pasuree Sangsupawanich[1], Ounjai Koranantakul[2], Prasin Chanvitan[1], Prasit Ruaengrairatanaroj[3], Hutcha Sriplung[4], Thanomjit Patanasin[5] and Siriporn Sukmee[5]

[1]Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Songkhla, 90110 Thailand: [2]Department of Obstetrics and Gynecology, Prince of Songkla University, Songkhla, Thailand: [3]Department of Pathology, Prince of Songkla University, Songkhla, Thailand: [4]Epidemiology Unit, Prince of Songkla University, Songkhla, Thailand: [5]Songkhla Provincial Public Health Service, Songkhla, Thailand

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Abstract

Objective: To determine iodine intake and urinary iodine excretion (UIE) in a group of pregnant Thai women and the concentration of thyroid-stimulating hormone (TSH) in their neonates.
Design: A prospective cohort study.
Setting: Three districts of Songkhla, southern Thailand.
Subjects: Two hundred and thirty-six pregnant women.
Results: A quarter of the participants lacked knowledge of iodine and the prevention of iodine deficiency, although 70 % used iodized salt. Those who did not use iodized salt stated that they had no knowledge about iodine (57 %) and no iodized salt was sold in their village (36 %). The median iodine intake in the three districts was 205–240 μg/d, with 53–74 % of pregnant women having iodine intake <250 μg/d. The median UIE in the three districts was 51–106 μg/l, with 24–35 % having UIE < 50 μg/l. The mean neonatal TSH was 2·40 (SD 1·56) mU/l, with 8·9 % of neonates having TSH > 5 mU/l.
Conclusions: The studied women and their fetuses were at risk of mild iodine deficiency. About a quarter of the participants lacked knowledge of the importance of iodine. Education regarding the importance of iodine supplements and the promotion of iodized salt should be added to national health-care policies in order to prevent iodine-deficiency disorders, diseases that are subclinical but have long-term sequelae.

Keywords
Iodine deficiency
Neonatal thyroid-stimulating hormone
Neonatal TSH screening
Urinary iodine excretion

Iodine-deficiency disorders (IDD) are a global public health problem [1–3]. Data from the WHO Regional Office for South-East Asia (SEARO) in 2004 showed that 600 million people worldwide were at risk of IDD and 172 million people were affected with goitre[4]. Nearly 20 million children born each year in this region are at some risk of mental impairment due to hypothyroidism in the mother and/or the fetus[4,5]. The three main indicators currently used for IDD monitoring to indicate iodine sufficiency are: (i) median urinary iodine excretion (UIE) >100 μg/l, with <20 % of the population having UIE < 50 μg/l; (ii) enlarged thyroid gland by palpation or ultrasonography (goitre) present in <5 % of the population; and (iii) thyroid-stimulating hormone (TSH) >5 mU/l in <3 % of neonates[1–3].

Thailand is one of the countries in South-East Asia where IDD is endemic[4,6]. In 1989, the 'National IDD Control Project' on household and industrial salt iodization was established as a strategy for IDD elimination. However, a survey in 1997 in the north and north-east, the major endemic areas of IDD in Thailand, found that the prevalence of goitre in schoolchildren was still as high as 20–30 % and the prevalence of neonatal TSH concentration >5 mU/l was 30–50 %[7,8]. In southern Thailand, a coastal region, IDD was less prevalent as indicated by the 3–5 % goitre prevalence in schoolchildren and the higher levels of UIE[9]. However, a recent 2004 study indicated the prevalence of neonatal TSH > 5 mU/l in the fourteen provinces of southern Thailand to be 10–30 %[10], indicating that pregnant women are at mild to moderate risk of IDD. A national survey of IDD during 2000–4 revealed a prevalence of UIE < 100 μg/l in pregnant women of 30–40 % all over the country[11]. In our own institution, the tertiary care centre in southern Thailand, we performed

*Corresponding author: Email somchit.j@psu.ac.th

a study in 2004 among pregnant women living in urban areas and found that 32 % of pregnant women had UIE < 100 μg/l and 36 % of neonates had TSH concentration >5 mU/l[12]. These various studies led to the implementation in 2006 of a national project providing iodized salt with a minimum of 30 ppm iodine to pregnant women who were attending antenatal clinics in every community hospital in the country. The present study collected data one year after the end of this 2006 project, with the aim to survey the current iodine status including iodized salt coverage, iodine intake and UIE in pregnant women attending community hospitals, along with TSH concentrations in their neonates.

Subjects and methods

Population

Songkhla is one of the southern provinces of Thailand, located on the eastern side of the Malay Peninsula. It is 950 km south of Bangkok, with a population of 1·2 million. It is subdivided into sixteen districts; each district has one district hospital, along with a number of smaller community hospitals. Three districts were chosen for our study: Sathing-Phra (population 50 000) to represent the seashore area; with Sadao (population 117 000) and Rattaphum (population 68 000) to represent the inland area. The delivery rate at each district hospital was 30–50 cases/month.

All pregnant women attending the antenatal clinic at these three district hospitals were invited to participate in the study. The inclusion criteria were pregnant women who: (i) were at 12–16 weeks of gestation at the first antenatal visit; (ii) lived in and intended to deliver at the district hospital; and (iii) agreed to participate in the study.

From October 2006 to March 2007, we recruited 272 pregnant women consistent with the above criteria: eighty-eight in Sathing-Phra, ninety-one in Sadao and ninety-three in Rattaphum district.

Protocol

After recruitment, the pregnant women were instructed on how to record details concerning the type and amount of food intake, including snacks, juice and milk, in the previous 24 h. They were also asked whether they had knowledge regarding iodine, as well as the importance of iodine for brain development for fetuses and infants. The subjects were scheduled to visit the antenatal clinic three times at 12–16 weeks, 24–30 weeks and 32–36 weeks of gestation. At each visit, each participant was asked about her health, any illnesses or medications used and any complications of the pregnancy, and was requested to fill out a 24 h food record and a food frequency checklist, including daily household salt use. The food frequency checklist was adapted for the present study to include items concerning the traditional diet of people in southern Thailand and was tested for validity. The food frequency checklist consisted of fourteen groups of foods and beverages which are commonly consumed in rural areas of southern Thailand, including six protein items (milk, dairy products, beans, meat and fish, eggs and seafood); four items on the traditional consumption of seaweeds; three items on common fruits and vegetables; and one question on juices and beverages. The 24 h food records and food frequency checklists were rechecked by an experienced dietitian. A morning urine sample was collected.

At delivery, the type and complications of delivery were recorded. Birth weight, length and head circumference of the newborn were measured by experienced nurses.

The protocol for the study was approved by the Ethics Committee of our institution, Songklanagarind Hospital. Written informed consent was obtained from all participants.

Calculation of iodine intake

Iodine intake was calculated on the basis of the 24 h food record and food frequency checklist using the INMUCAL software program (Mahidol University, Nakhon Pathom, Thailand) and associated food composition database[13].

Urinary iodine excretion measurement

Measurement of UIE was performed using a simple plate method as described previously by Ohashi *et al.*[14]. The intra- and inter-assay CV were both <10 %.

Thyroid-stimulating hormone measurement

As part of a national neonatal screening programme in effect during the time of the study, TSH measurements were routinely performed in all newborns at 60–72 h after birth. The blood samples of the present study were sent in filter paper to the Regional Medical Sciences Centre (Songkhla), Department of Science, Ministry of Public Health. TSH was determined using an immunoradiometric assay method which has a sensitivity of 0·2 mU/l, intra-assay CV of 4–6 % and inter-assay CV of 7–9 %[15].

Statistical analysis

Demographic data are expressed as percentages and means with their standard deviations. Iodine intake and UIE are reported as medians. Body weight, length, head circumference and TSH concentration are reported as means with their standard deviations. The Spearman rank test was used to identify the relationship between maternal iodine intake and maternal UIE, and between maternal UIE and neonatal TSH concentration.

Results

Of the total 272 pregnant women initially recruited, thirty-six were excluded due to moving to another province (twenty subjects) and failure to attend follow-ups as

Table 1 Characteristics of the study subjects: pregnant women from the three districts of Songkhla, southern Thailand, October 2006–March 2007

Characteristic	Rattaphum (*n* 81) Mean	SD	Sadao (*n* 82) Mean	SD	Sathing-Phra (*n* 73) Mean	SD	Total (*n* 236) Mean	SD
Age (years)	27·4	6·1	24·6	5·2	29·9	6·8	27·2	6·2
	%		%		%		%	
Religion								
Buddhist	60·5		45·1		87·7		63·6	
Muslim	39·5		54·9		12·3		36·4	
Level of education								
Primary school	48·1		31·7		21·9		34·3	
Secondary school	39·5		56·1		64·4		53·0	
College/university	12·4		12·2		13·7		12·7	
Family income (Baht/month)								
<10 000	72·8		76·8		84·9		88·0	
10 001–20 000	19·8		17·1		11·0		16·1	
>20 000	7·4		6·1		4·1		5·9	

Table 2 Household iodized salt use, iodine intake and urinary iodine excretion (UIE) in the study subjects: pregnant women from three districts of Songkhla, southern Thailand, October 2006–March 2007

	Rattaphum (*n* 81)	Sadao (*n* 82)	Sathing-Phra (*n* 73)	Total (*n* 236)
Iodized salt use (%)				
Gestational age 12–16 weeks	64·2	62·2	83·6	69·5
Gestational age 28–30 weeks	86·4	92·7	94·5	91·1
Gestational age 34–36 weeks	87.7	92·7	93·2	91·1
Median iodine intake (μg/d)				
Gestational age 12–16 weeks	236·6	240·2	222·5	234·4
Gestational age 28–30 weeks	218·1	210·9	221·2	215.2
Gestational age 34–36 weeks	205·7	210·5	217·4	209·5
Median UIE (μg/l)				
Gestational age 12–16 weeks	105·7	73·2	53·9	75·5
Gestational age 28–30 weeks	88·5	65·3	90·1	87·6
Gestational age 34–36 weeks	83·1	71·2	50·9	72·1
Subjects with UIE < 50 μg/l (%)				
Gestational age 12–16 weeks	23·5	30·5	32·9	28·8
Gestational age 28–30 weeks	34·6	35·4	30·1	33·5
Gestational age 34–36 weeks	24·7	26·8	32·9	28·0

scheduled in the research protocol (sixteen subjects). The demographic data of the remaining 236 pregnant women (seventy-three in Sathing-Phra, eighty-two in Sadao and eighty-one in Rattaphum district) who were followed-up until delivery are shown in Table 1.

Regarding their knowledge of iodine, we found that a quarter of the studied women lacked knowledge of iodine, IDD and the prevention of iodine deficiency. The household use of iodized salt in the three districts was 62–84 % in the first trimester and increased to 87–93 % in the third trimester. Of those who stated they did not use iodized salt, the reasons given were having no knowledge about iodine (57 %) and no iodized salt sold in their village (36 %). The median daily iodine intake of the subjects ranged from 205 to 240 μg according to district and was nearly the same amount at each trimester. The percentage of women whose iodine intake was <250 μg/d was 60–70 % in all three districts. The median UIE in the subjects at the three visits ranged from 50 to 105 μg/l, with 24–35 % of subjects having UIE < 50 μg/l. The percentage of household iodized salt use, daily iodine intake and UIE in the pregnant women are summarized in Table 2. The amount of iodine intake was significantly positively correlated with UIE ($R = 0{\cdot}15$, $P = 0{\cdot}023$), as shown in Fig. 1.

The 236 women delivered 236 neonates, 123 males and 113 females. The disinfectant routinely used during delivery was chlorhexidine, which is a non-iodine-containing antiseptic. The mean gestational age was 39·2 (SD 1·6) weeks. The mean birth weight was 3054 (SD 474) g, mean birth length was 50·7 (SD 2·4) cm and mean head circumference was 33·3 (SD 1·6) cm. All the neonates were in generally good health. Neonatal jaundice was found in twenty cases (8·5 %) which improved in all cases after 3–4 d of phototherapy. The mean age at the time of TSH blood collection for the present study was 65 (SD 4) h. The median neonatal TSH concentration in infants from all districts was 3·20 mU/l, slightly higher than the mean TSH concentration of 2·40 (SD 1·56) mU/l. Using a TSH concentration of 5 mU/l as a cut-off point, there were twenty-one (8·9 %) neonates having TSH > 5 mU/l: eleven (13·6 %) in Rattaphum, six (7·3 %) in Sadao and four (5·5 %) in Sathing-Phra. The characteristics of the neonates according to district are shown in Table 3. Neonatal TSH concentrations were negatively correlated with maternal UIE, but without statistical significance ($R = -0·10$, $P = 0·068$) as shown in Fig. 2. There were no correlations between neonatal TSH concentration and neonatal outcome, i.e. gestational age, birth weight, birth length or head circumference.

Discussion

In the present study we evaluated the iodine status of pregnant women in rural areas in southern Thailand by the use of four indicators: household iodized salt coverage, daily iodine intake, maternal UIE and neonatal TSH concentration. All of these indicators showed concordant results in that a majority of pregnant women in all studied areas, both inland and seashore, were iodine-insufficient as evidenced by household iodized salt coverage of <90 %, median iodine intake of <250 μg/d, median UIE of <100 μg/l with the proportion having UIE < 50 μg/l being >20 %, and TSH concentration of >5 mU/l in >3 % of neonates. Thus our results demonstrate that pregnant women in rural areas of Thailand are at risk of iodine deficiency as early as the first trimester and hence their children are at risk of growing up with impaired cognitive and intellectual functions.

Despite more than 15 years of a 'National IDD Control Project' in Thailand focusing on universal salt iodization (USI), household iodized salt coverage as reported by different recent studies is still only 60–70 %, substantially lower than the goal of 90 %. A national survey by the Thai Ministry of Public Health during 2000–4 found household iodized salt coverage of only 60 %[11]. The WHO/SEARO report in 2004 showed overall iodized salt coverage in Thailand of only 67 %[4]. Recently, a national survey by the Ministry of Information and Communication Technology, done in

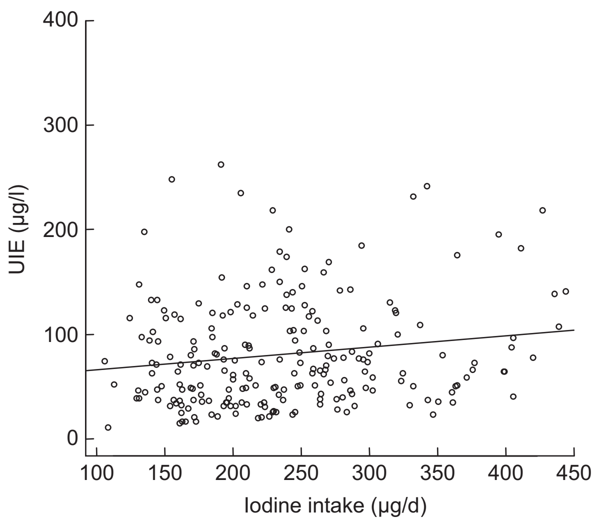

Fig. 1 Relationship between iodine intake (μg/d) and urinary iodine excretion (UIE, μg/l) among pregnant women (*n* 236) from three districts of Songkhla, southern Thailand, October 2006–March 2007. Daily iodine intake was significantly positively correlated with UIE ($R = 0·15$, $P = 0·023$)

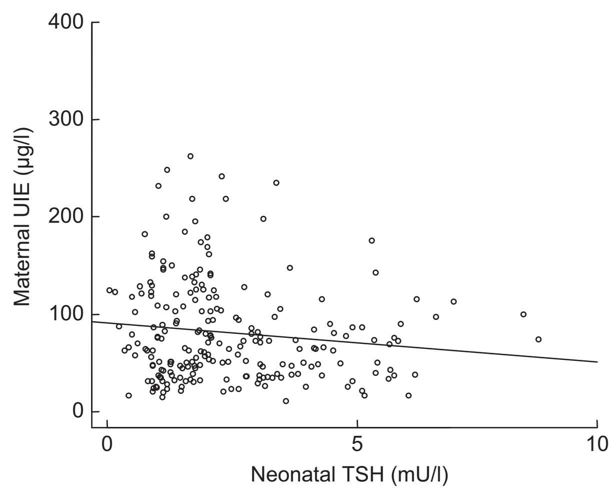

Fig. 2 Relationship between maternal urinary iodine excretion (UIE, μg/l) and neonatal thyroid-stimulating hormone (TSH) concentration (mU/l) among women (*n* 236) from three districts of Songkhla, southern Thailand, October 2006–March 2007. Neonatal TSH concentration was negatively correlated with maternal UIE, but without statistical significance ($R = -0·10$, $P = 0·068$)

Table 3 Characteristics of the neonates born to study women from three districts of Songkhla, southern Thailand, October 2006–March 2007

	Rattaphum (*n* 81)		Sadao (*n* 82)		Sathing-Phra (*n* 73)		Total (*n* 236)	
Characteristic	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Gestational age (weeks)	39·5	1·5	39·5	1·4	38·7	1·8	39·2	1·6
Birth weight (g)	3077	380	3068	422	3010	604	3054	474
Birth length (cm)	50·7	2·6	50·9	2·1	50·3	2·3	50·7	2·4
Head circumference (cm)	33·2	1·5	33·2	1·5	33·5	1·7	33·3	1·6
TSH concentration (mU/l)	2·76	1·74	2·41	1·37	2·00	1·45	2·40	1·56
TSH > 5 mU/l (%)	13·6		7·4		5·5		8·9	

TSH, thyroid-stimulating hormone.

2005–6, also revealed overall iodized salt coverage of only 60–67 %[16]. Despite the 2006 national campaign of iodized salt coverage for all pregnant women, the results of our study, which was carried out only one year after the end of this project, demonstrated that iodized salt coverage in rural communities was still only 70 %, indicating a failure to reach the goal of USI. This failure was explained in our study by two main reasons: lack of knowledge of iodine and no iodized salt sold in the communities. In rural areas of Thailand it is known that non-iodized salt, which is locally made by small producers, is widely sold, either in packaged or unpackaged form, inexpensively in many retail shops. Although potassium iodate has been provided freely by the government since the beginning of the IDD programme, the local salt producers pay little attention to the IDD prevention programme. An additional consideration is that even if some of the local producers use the potassium iodate supplement, iodine losses during low-quality processing or packaging, transportation and storage in retail shops could lead to sub-standard iodine content of the salt, particularly in the warm and humid climate in Thailand. Moreover, monitoring and surveillance for quality control of iodized salt has been done irregularly. In the present study, the increase in use of household iodized salt in the last trimester was likely related to the study itself in that the subjects were asked at each visit about the use of iodized salt and IDD. UIE in the third trimester, however, was still persistently lower than 100 μg/l, indicating that iodine intake was lower than the recommended level; thus it is evident that at least some participants learned of the health benefits of iodized salt without any actual corresponding behavioural changes.

To assess the mothers' iodine status, the iodine content of their diet was evaluated one day before the urine collection for determining their UIE. These assessments were performed three times for each individual at the three different times of gestation. The results showed a regular pattern for type of food intake, indicating the consistency of eating behaviour in each individual. The iodine intake in the study was calculated using the INMUCAL program, the standard program for calculating the macro- and micronutrient contents of Thai food[13]. The median iodine intake ranged from 205 to 240 μg/d in all studied areas, with 60–70 % of the subjects having an iodine intake of $<$250 μg/d. The calculated inadequate iodine intake corresponded well with the low UIE of $<$100 μg/l. As is already known, UIE is a highly sensitive indicator, a more precise and reliable parameter for evaluation of adequacy of iodine intake than the food record and food frequency checklist. However, UIE is widely variable within a single day as well as between days, and therefore a single urinary iodine measurement is not very informative at an individual level. However, at a population level, the median level of a large number of UIE tests provides an estimation of the average amount of iodine in the diet of the population[17]. In the present study, UIE was measured three times at different gestational ages, and many participants demonstrated a persistently low UIE of $<$100 μg/l.

Neonatal TSH screening concentration $>$5 mU/l in $>$3 % of newborns has been accepted to be one of the sensitive indicators and monitoring tools for control of IDD. It is known that iodine requirements are increased during pregnancy[18] because of an increased requirement for iodide and thyroid hormones to maintain physiological thyroid metabolism in the mother from increased thyroxine-binding globulin and increased renal blood flow, and an increased transfer of iodide and thyroid hormones from the mother to the fetus. The WHO/UNICEF/International Council for the Control of Iodine Deficiency Disorders recommends iodine intake during pregnancy of 250 μg/d[19,20], although some experts in thyroid metabolism suggest that iodine intake even in non-pregnant adults should be higher, up to 300–400 μg/d[21]. During the first half of gestation, the iodide and thyroid hormones available to the fetus are entirely of maternal origin. Iodide and thyroid hormones from the mother are important for fetal brain maturation and development. Moderate/severe iodine deficiency can result in both maternal and fetal hypothyroxinaemia, and is also associated with neurological and intellectual deficit during fetal development[22]. The severity of intellectual deficit is related not only to the degree of iodine deficiency, but also to the developmental phase during which the deficiency is suffered, the most severe such deficits arising from iodine deficiency during the first trimester of pregnancy[23].

In the present study, although the median neonatal TSH concentrations were within normal ranges, the proportion with TSH $>$ 5 mU/l ranged from 6 to 14 %, an indication of iodine insufficiency in both mothers and fetuses during pregnancy. In iodine deficiency areas, neonatal TSH concentrations should theoretically be negatively correlated to maternal UIE. However, this negative correlation was not observed in our study, likely due to the wide variation of maternal UIE results and the relatively small sample size.

In summary, the present study demonstrated that pregnant women in rural areas in southern Thailand are at substantial risk of iodine deficiency. Iodized salt is still not universally used despite almost 20 years of a 'National IDD Control Project' on household and industrial salt iodization in Thailand. To reach the goal of USI, emphasis on monitoring and surveillance is mandatory. Legislation on salt iodization should cover not only households and industrial food processing, but also be included in animal husbandry, dietary and locally made salt production regulations. National policies and efforts for monitoring and surveillance of the quality of salt, both from commercial factories and locally made production, should be a priority to eliminate this preventable public health hazard in the current generation; and moreover to protect future generations from the neurointellectual impairment caused by IDD. Knowledge regarding iodine and IDD should be provided to every community through public health programmes and health-care providers should be involved in monitoring the quality of iodized salt.

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