Asian Biomedicine Vol. 7 No. 6 December 2013;847-853
DOI: 10.5372/1905-7415.0706.249

Brief communication (Original)

Correlation between maternal and neonatal urine iodine with thyroid-stimulating hormone (TSH) levels in Srinagarind Hospital, Khon Kaen, Thailand

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Background: Thailand is an endemic area for iodine deficiency disorders (IDD) in Southeast Asia. More than 50% of pregnant women in northeast Thailand have low urine iodine levels. While rising thyroid- stimulating hormone (TSH) levels in neonates are particularly sensitive to IDD.

Objective: To establish the iodine status of postpartum mothers and neonates and its relationship with TSH in Khon Kaen Province.

Materials and Methods: A prospective study was conducted between June and October 2011. Three hundred postpartum mothers and their neonates were enrolled. Urine iodine was collected and measured using a simple microplate method. TSH assay was performed using an immunoradiometric assay. The optimum level of maternal urine iodine including children <2 years was >100 μg/L and neonatal whole blood TSH <5 mU/L (equivalent to serum TSH <11.2 mU/L).

Results: The median postpartum maternal urine iodine was 208.4 μg/L, 29.3% had values <100 μg/L and 42.3% <150 μg/L. The median neonatal urine iodine was 151.0 μg/L with 26.0% having urine iodine levels <100 μg/L and 49.7 % <150 μg/L. The median neonatal whole blood TSH was 4.3 mU/L, 3.0% had TSH >5 mU/L. There was no significant correlation between postpartum maternal urine iodine and neonatal TSH ($p = 0.340$, $r = 0.055$), but there was a significant positive correlation between maternal and neonatal urine iodine levels ($p = 0.013$, $r = 0.143$), neonatal urine iodine and TSH levels ($p = <0.01$, $r = 0.203$).

Conclusion: After a national campaign of iodized salt coverage and oral iodine supplement for all pregnant women, there was increasing median maternal and neonatal urine iodine and a weakly positive correlation between maternal and neonatal urine iodine levels, neonatal urine iodine and TSH levels, but no correlation between maternal urine iodine and TSH levels. The prevalence of IDD in pregnant women in northeast Thailand seems to have decreased, but intervention programs needs to be extended to reach populations that still have inadequate iodine intake.

Keywords: Khon Kaen, maternal urine iodine excretion, neonatal TSH screening, neonatal urine iodine, urine iodine

Around 31% (1,900.9 million) of the world's population is estimated to have insufficient iodine intake, with the most affected WHO regions being Southeast Asia and Europe [1]. Urinary iodine is the most useful indicator for iodine intake because it reflects the current intake of iodine in the diet [2, 3]. While rising thyroid-stimulating hormone (TSH) levels in neonates are particularly sensitive to iodine deficiency [4, 5]. The experts on iodine deficiency disorders (IDD) from three partner organizations, WHO, UNICEF, and ICCIDD recommended the use of urinary iodine (UI) to monitor IDD status, blood TSH, and thyroglobulin may also be useful [1]. Iodine

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deficiency is the single most important preventable cause of brain damage [6-9]. People with severe iodine deficiency may have an intelligence quotient (IQ) of up to 13.5 points below that of those from comparable communities in areas where there is no iodine deficiency [10]. The northeast of Thailand contains a high prevalence of IDD [11]. To prevent IDD in this rural area, we performed studies to evaluate the iodine status and prevalence of IDD in postpartum women and neonates and whether there was a correlation between maternal and neonatal UI with neonatal TSH concentration in the status of national campaign of iodized salt coverage for all pregnant women.

Materials and methods

Between June and October 2011, a cross-sectional prospective study was undertaken in postpartum mothers and their neonates born in Srinagarind Hospital, Khon Kaen University, Khon Kaen. All mothers were prescribed a drug containing iodine (Obimin-AZ, iodine 200 □g/tablet or tripherdine, iodine 150 □g/tablet) during pregnancy. Informed consent was obtained from the mothers and legal guardians. Mothers with history of thyroid diseases or the use of thyroid hormone or antithyroid drugs were excluded. Maternal and neonatal spot urine samples were collected at 06.00–11.00 am, 48–72 hours after delivery and iodine measurement was performed using a simple microplate method described by Ohashi et al. [12]. We used ammonium persulfate, arsenic trioxide, sulfuric acid sodium hydroxide, sodium chloride, ceric ammonium sulfate, and potassium iodate for analysis. The calorimetric measurements were performed by TECAN automatic analyzer (Roche, USA). The intra-assay and inter-assay coefficients of variation were <10%. As part of the national neonatal screening program, TSH measurement was routinely performed at 48–72 hours. The dried whole blood was sent in filter paper to the Department of Science, Ministry of Public Health and TSH was performed by immunoradiometric assay using kits manufactured in Thailand. The sensitivity of the assay for TSH is 0.2–0.9 mU/L. Data were collected by the status quo method. The demographic data of mothers including age, total maternal weight gain, education, family income, were recorded. For the neonates, sex, gestational age, mode of delivery, weight, length, and head circumference were recorded. For lactating women and children <2 years of age a median UI concentration of >100 µg/L was used to define adequate iodine intake [1]. While TSH assay is used on whole blood samples collected 48 to 72 hours after birth, TSH values <5 mU/L (equivalent to serum TSH <11.2 mU/L)[13] in <3% population indicates iodine sufficiency in a population [1]. The study was approved by The Human Ethics Committee of Khon Kaen University.

Statistical analysis

All data processing was conducted using the Statistical Package for Social Sciences, version 11.5 software for Windows. Commonly used statistical methods (means, medians, proportions) were applied to analyze the data. The level of significant in all statistical tests was set at $p \leq 0.05$. The Spearman rank test was used to identify the correlation between maternal UI and neonatal UI and TSH levels.

Results

The mean postpartum maternal age and total weight gain were 29.3 years and 14.6 kg, respectively. Fifty-one percent of mothers had secondary school education level and 49.7% had moderate family income (10,000–20,000 baht/month). The mean gestational age, birth weight, length and head circumference were 37.6 weeks, 3,115.2 g, 49.4, and 33.6 cm, respectively. Sixty-three percent of neonates were male and 54% were delivered by cesarean section (**Table 1**).

Maternal and neonatal urine iodine

The frequency distribution of UI concentrations in 300 mothers was shown in **Figure 1**. The median UI was 208.4 µg/L. Eighty-eight (29.3%) and 127 (42.3%) mothers had UI <100 µg/L and <150 µg/L, respectively.

The frequency distribution of UI concentrations in 300 neonates was shown in **Figure 2**. The median neonatal UI was 151.0 µg/L. Seventy-eight (26.0%) and 140 (49.7%) neonates had UI levels <100 and <150 µg/L, respectively.

Neonatal TSH concentration

The median neonatal TSH concentration was 4.3 mU/L and 10 (3.0%) neonates had TSH levels >5 mU/L.

Correlation between maternal and neonatal urine iodine and neonatal TSH concentration

There was no significant correlation between maternal UI and neonatal TSH ($p = 0.340$, $r = 0.055$)

(**Figure 3**). For the correlation between maternal and neonatal UI, there was weakly significant positive correlation (p = 0.013, r = 0.143) (**Figure 4**) and weakly significant positive correlation between neonatal UI and TSH levels (p < 0.01, r = 0.203) (**Figure 5**).

Table 1. Characteristics of the study population

Maternal variables (n = 300)	
Age (years)	29.3 ± 5.9
Total maternal weight gain (kg)	14.6 ± 4.6
Level of education	
Primary school	6.3%
Secondary school	51.7%
College/university	42.0%
Familial income (Baht/month)	
<10,000	19.7%
10,000–20,000	49.7%
>20,000	30.6%
Newborn variables (n = 300)	
Sex (% male)	63.0%
Gestational age (weeks)	37.6 ± 5.6
Mode of delivery	
Normal labor	43.0%
Cesarean section	54.0%
Birth weight (g)	3,115.2 ± 434.4
Birth length (cm)	49.4 ± 2.2
Head circumference (cm)	33.6 ± 1.7

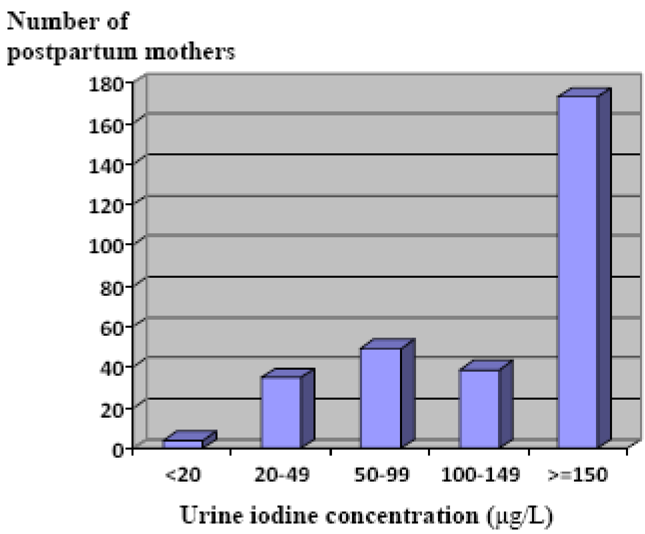

Figure 1. Number of postpartum mothers and urine iodine concentration

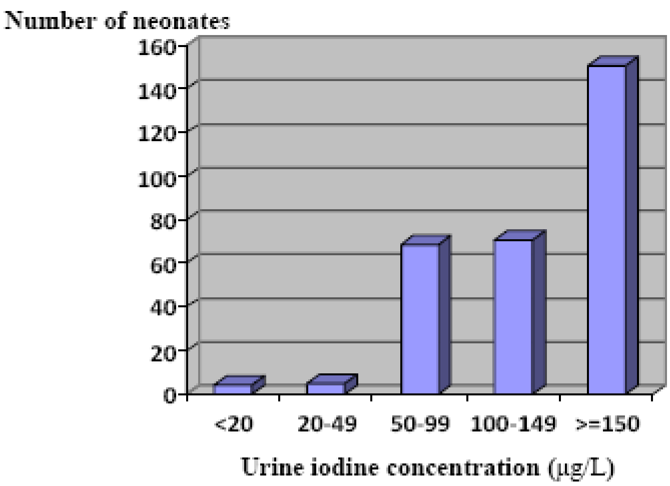

Figure 2. The numbers of neonates and urine iodine concentration

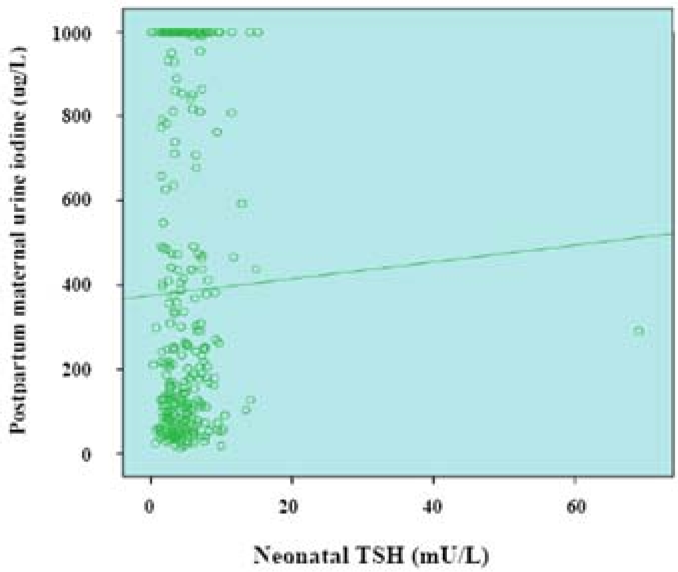

Figure 3. Correlation between maternal urine iodine and neonatal TSH concentration

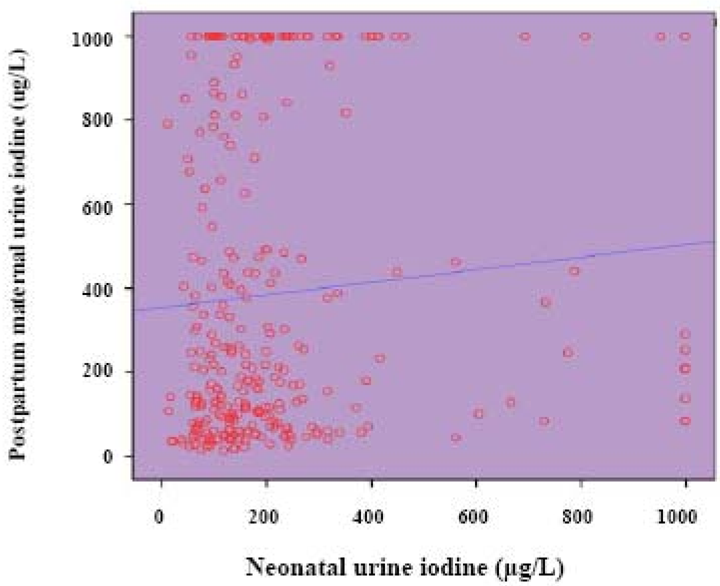

Figure 4. Correlation between maternal and neonatal urine iodine

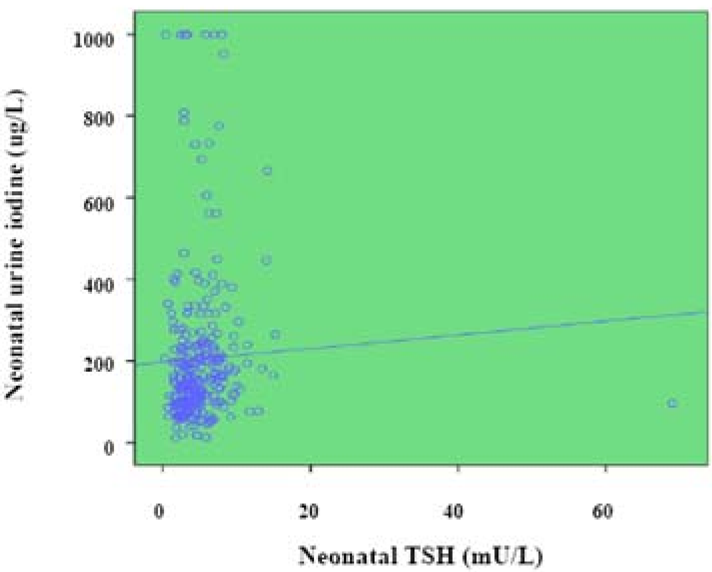

Figure 5. Correlation between neonatal urine iodine and TSH concentration

Discussion

Thailand is one of the countries in Southeast Asia where there is an endemic area of IDD. The National Control and Prevention of IDD Project of Ministry of Public Health established a strategy for IDD elimination that started in 2000. The concentration of maternal UI was measured by cyclical monitoring in 15 provinces annually (5-year cycle) by systematic random sampling. The data were collected from 300 samples per province, 4,500 samples per year [11]. From the survey in 2009, 43% of pregnant women had UI <100 μg/L and 59% had UI <150 μg/L. In northeast Thailand, where there was high prevalence of IDD, 47.9% of pregnant women had median UI <100 μg/L and 64.6% had median UI <150 μg/L. However, a previous survey in Khon Kaen province, northeast Thailand in 2007, 55.3% and 67.6% of pregnant women had median UI <100 and <150 μg/L, respectively. In addition, 20% of samples had a level <50 μg/L. Only 13.0% and 3% of maternal and neonatal urine iodine in our study had a level <50 μg/L (**Figures 1 and 2**). Moreover, the median maternal (208.4 μg/L) and neonatal UI (151.0 μg /L) level increased significantly. In children and non-pregnant women, median UI concentrations between 100 and 299 μg/L with <20% frequency of urine iodine in population <50 μg /L defined no iodine deficiency (1) and <3% frequency of neonatal TSH values >5 mU/L indicated iodine sufficiency in population [14]. Our results showed that most postpartum mothers (71.7%) and neonates (74%) had no iodine deficiency and only 3.0% of neonatal TSH values >5 mU/L. For population level, this means that lactating mothers had no iodine deficiency after salt iodization and drug contained iodine supplementation corresponded with the recent global study of iodine status, almost all countries showed decreasing iodine deficiency in population after salt iodization [13,14]. For individual levels, a small number of pregnant women failed to achieve the optimum UI level. Poor drug compliance may be a factor, some pregnant women believe that drug supplementation leads to large babies and difficult labor. As we know, UI excretion is widely variable within a single day as well as between days, and therefore a single UI measurement is not informative at an individual level. However, nutritional education and further assessment should be performed in mothers and neonates who had low iodine levels. For pregnancy, recommended mean daily iodine intakes of 220–250 μg were estimated to correspond to a median UI concentration of about 150 μg/L, and larger surveys from the iodine sufficient countries have reported a median UI in pregnant women ≥140 μg/L [14, 15].

Using current WHO criteria for iodine sufficiency in infant with median UI cut-off >100 μg/L. Twenty-six percent of neonates in our study had iodine deficiency in individual level. In iodine sufficient area, a median UI was 77 μg/L and increased within the range of 70–100 μg/L from days 1 through 4 which meant the current WHO criteria for iodine sufficiency in infancy may too high for the first week after birth [16].

By comparison with the previous studies in the north and the south of Thailand [17-19], no significant correlation between maternal UI and neonatal TSH levels was also observed in our study. Neonatal TSH level is depended on the time of blood sampling. For epidemiological studies, WHO state that heel-prick blood specimens should be collected 72 hours after birth, to avoid the surge of TSH levels. Most of our TSH specimens were collected with UI between 48–72 hours after birth and TSH levels were not adjusted for age at the time of sampling, which may affect our ability to detect a correlation between neonatal TSH level and maternal UI concentration. One study in Thailand showed that neonatal TSH screening using whole blood collected from a heal prick at 3 days of age was not sensitive enough to assess the iodine nutrition in neonates as there was no relation with the UI of paired-mothers [17]. By contrast with cord sera TSH, which had a significant relationship with paired maternal UI concentration [15]. In addition to IDD, there are other factors that make TSH rising including inactivating mutation of the TSH receptor gene [20], partial iodide organification defect by loss-of-function mutation in the thyroid peroxidase gene, etc. [21].

In conclusion, there is global improvement of iodine status and an increase of maternal and neonatal UI levels, and decreased risk of iodine deficiency in northeast Thailand after a national campaign of iodized salt coverage and oral iodine supplement drugs for all pregnant women.

Acknowledgements

This study was supported by grants from Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand (Grant Number HE531324). We wish to acknowledge the support assistance of the Khon Kaen University Publication Clinic, Research and Technology Transfer Affairs, for their assistance. The authors have no conflict of interest to declare.

References

1. Disorders ICfCoID, UNICEF, Organization WH. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. 3rd ed: World Health Organization; 2007.
2. Zoeller RT. Transplacental thyroxine and fetal brain development. J Clin Invest. 2003;111:954.
3. DeMaeyer E, Lowenstein FW, Thilly C, Organization WH. The control of endemic goitre: World Health Organization; 1979.
4. Sullivan KM, May W, Nordenberg D, Houston R, Maberly GF. Use of thyroid stimulating hormone testing in newborns to identify iodine deficiency. J Nutr. 1997; 127:55-8.
5. Rajatanavin R, Unachak K, Winichakoon P, Chailurkit LO, Vilasdechanon N, Tananchai P, et al. Neonatal thyrotropin profile as an index for severity of iodine deficiency and surveillance of iodine prophylactic program. Thyroid. 1997; 7:599-604.
6. Zimmermann MB. Iodine deficiency. Endocrinol Rev. 2009; 30:376-408.
7. Delange F. Iodine deficiency as a cause of brain damage. Postgrad Med J. 2001; 77:217-20.
8. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med. 1999; 341:549-55.
9. Pharoah P, Buttfield I, Hetzel B. Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. Lancet. 1971; 297:308-10.
10. Bleichrodt N, Born MP. A meta-analysis of research on iodine and its relationship to cognitive development. The damaged brain of iodine deficiency. New York: Cognizant Communication, 1994. p.195-200.
11. Bureau of Nutrition (BoN), Department of Health, Ministry of Public Health. Surveillance for urinary iodine concentration of pregnant women in Thailand 2006-2010. Bangkok: Department of Health, Ministry of Public Health.
12. Ohashi T, Yamaki M, Pandav CS, Karmarkar MG, Irie M. Simple microplate method for determination of urinary iodine. Clin Chem. 2000; 46:529-36.
13. Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. J Nutr. 2012; 142:744-50.
14. Zimmermann MB, Aeberli I, Torresani T, Burgi H. Increasing the iodine concentration in the Swiss iodized salt program markedly improved iodine status in pregnant women and children: a 5-y prospective national study. Am J Clin Nutr. 2005; 82:388-92.
15. Zimmermann MB. The impact of iodised salt or iodine supplements on iodine status during pregnancy, lactation and infancy. Public Health Nutr. 2007; 10: 1584-95.
16. Dorey CM, Zimmermann MB. Reference values for spot urinary iodine concentrations in iodine-sufficient newborns using a new pad collection method. Thyroid. 2008; 18:347-52.
17. Rajatanavin R. Iodine deficiency in pregnant women

and neonates in Thailand. Public Health Nutr. 2007; 10:1602-5.

18. Jaruratanasirikul S, Sangsupawanich P, Koranantakul O, Chanvitan P, Ruaengrairatanaroj P, Sriplung H, et al. Maternal iodine status and neonatal thyroid-stimulating hormone concentration: a community survey in Songkhla, southern Thailand. Public Health Nutr. 2009; 12:2279-84.

19. Jaruratanasirikul S, Chukamnerd J, Koranantakul O, Chanvitan P, Ruaengrairatanaroj P, Sriplung H. The relationship of maternal iodine status and neonatal thyrotropin concentration: a study in Southern Thailand. J Pediatr Endocrinol Metab. 2006; 19:727-32.

20. Alberti L, Proverbio MC, Costagliola S, Romoli R, Boldrighini B, Vigone MC, et al. Germline mutations of TSH receptor gene as a cause of nonautoimmune subclinical hypothyroidism. J Clin Endocrinol Metab. 2002; 87:2549-55.

21. Kotani T, Umeki K, Kawano J, Suganuma T, Hishinuma A, Leiri T, et al. Partial iodide organification defect caused by a novel mutation of the thyroid peroxidase gene in three siblings. Clin Endocrinology. 2003; 59: 198-206.