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Original Article

Neonatal iodine status survey by thyroid-stimulating hormone screening in Surabaya

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Abstract

Background Iodine deficiency disorders (IDD) are a significant public health problem globally. Iodine deficiency may cause subclinical hypothyroidism during pregnancy and early infancy. Neonatal thyroid screening of serum thyroid-stimulating hormone (TSH) to detect hypothyroidism may also be used to determine the prevalence of IDD in a population. Previous studies reported mild IDD status in different parts of Indonesia.

Objective To evaluate the iodine status of neonates born in Mitra Keluarga Surabaya Hospital (MKSH) by TSH screening over a 6-year period.

Methods This is a cross-sectional and hospital-based study conducted in MKSH from January 2005 to December 2010. Of the 5,619 infants born in MKSH during the study period, 3,349 (59.6%) healthy infants took part in this study. Blood specimens for TSH measurement were collected from subjects 2 to 6 days after birth, and sent to a reference laboraratory for evaluation. Using the neonatal TSH values, the iodine deficiency level of the group was determined according to the WHO/UNICEF/ International Council for the Control of IDD criteria.

Results A total of 3,349 newborn babies underwent neonatal TSH screening in MKSH. Subjects' mean TSH concentration was 5.14 mIU/L. A TSH concentration > 5mIU/L was found in 1270 (37.9%) subjects, 166 (27.6%) in 2005, 252 (44.0%) in 2006, 331 (47.1%) in 2007, 356 (57.7%) in 2008, 114 (20.7%) in 2009 and 51 (16.8%) in 2010. On the basis of the WHO/UNICEF/ International Council for the Control of Iodine Deficiency Disorder criteria, this frequency corresponded to a moderate level of IDD. Twenty-two neonates had TSH >20 mIU/L from which 2 infants were confirmed positive for hypothyroidism.

Conclusion A 6-year study of 3,349 newborns screened for TSH revealed that 37.9% of subjects had TSH concentration of more than 5mIU/L. This frequency indicates a moderate level of IDD in the study population. **[Paediatr Indones. 2012;52:289-93]**.

Keywords: *neonatal, TSH screening, iodine deficiency disorders, IDD*

Iodine deficiency disorders (IDD) are a significant public health problem, with an estimated one-third of the world's population currently at risk.[1] Among the population at risk, pregnant women have been found to be particularly vulnerable to IDD.[2,3] A compromised iodine status during pregnancy was shown to affect the thyroid function of the neonates as well.[2,4] A consequence of persistent iodine deficiency is subclinical hypothyroidism during pregnancy and early infancy (with a concomitant risk of minor brain damage and irreversible impairment of the neuropsychointellectual development of neonates).[5]

Neonatal thyroid screening can be used to assess early diagnosis of hypothyroidism in neonates. Screening by serum TSH, detects not only permanent sporadic congenital hypothyroidism, the incidence of which is about 1 per 4000 births, but also compensated or transient primary hypothyroidism, the incidence of which can be as high as 1 in 10 neonates and whose main cause is iodine deficiency.[6] The WHO reported that even moderate iodine deficiency can cause the loss of 10-15 points in intelligence quotient.[7] The WHO

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global database on iodine deficiency listed Indonesia as a nation with mild deficiency in 2004.[8] Data from maternal urinary iodine excretion of pregnant women in East Java 2010 also showed a median value that corresponded to mild iodine deficiency in the province with a wide distribution of data ranging from severe deficiency to adequate. Surabaya was found to have mild iodine deficiency.[9]

By conducting a hypothyroid screening, we aim to analyze neonatal TSH levels to determine the severity of neonatal iodine deficiency in MKSH. According to the WHO, UNICEF and the International Council for Control of Iodine Deficiency Disorders (ICCIDD), a frequency of neonatal TSH above 5 mU/L whole blood (or 10 mU/L serum) of less than 3% indicates an absence of iodine deficiency in the population. A frequency of 3%-19.9% indicates mild IDD, while frequencies of 20%-39.9% and above 40% indicate moderate and severe IDD, respectively. By knowing the severity of neonatal iodine deficiency, it is hoped that preventive measures can be taken to improve the situation in the future.

Methods

This was a cross-sectional and hospital-based study. Subjects were healthy, full-term infants born in MKSH from January 2005 to December 2010. All healthy newborns with parental consent had venous blood samples collected at least 48 hours after birth, as part of the routine congenital hypothyroidism screening program. From 2005 to 2010, there were 5,619 infants born in MKSH, of which 3,349 (59.7%) took part in our congenital hypothyroidism screening program. TSH was used to measure iodine status as it is determined mainly by the level of circulating thyroid hormone, which in turn corresponds with iodine intake.[10] Blood specimens collected 2 to 6 days after birth for the measurement of TSH, were taken directly from a venous puncture, put onto filter paper (Whatman S & S 903), and sent to the Hasan Sadikin Hospital, Bandung reference laboraratory. Subjects' TSH values were analyzed for iodine deficiency on the basis of WHO/UNICEF/ ICCIDD criteria. The criteria states that 3% or more of neonatal blood samples taken 3-4 days after birth with TSH concentration over 5 mIU/L is indicative of an iodine-deficient population. A frequency of 3%-19.9% indicates mild IDD, 20%-39.9% indicates moderate IDD and above 40% indicates severe IDD.[7] Patients with TSH concentration of 20 mIU/L and above were suspected of having hypothyroidism and were recalled to confirm the diagnosis. All disinfectants used for treating the umbilical cord prior to blood-sampling were alcohol-based, not iodine-based. Lab technicians were blinded to the patient's condition and TSH was measured by Delfia Neonatal TSH kit time-resolved fluoroimmunoassay. The percentage of neonatal TSH concentrations greater than 5 mIU/L for each year was calculated. Data was analyzed by SPSS version 13 software.

Results

Subjects' mean TSH concentration were 5.14 (SD 13.67) mIU/L. Of the 3,349 subjects, 651 (19.4%) blood samples were taken from neonates aged 2 days, 2,262 (67.5%) aged 3 days, 351 (10.5%) aged 4 days, 56 (1.7%) aged 5 days and 29 (0.9%) aged 6 days. In total, 2613 (78%) neonates had blood samples taken between the age of 3 and 4.

The overall mean TSH concentration from 2005 to 2010 was 5.14 mIU/L. The mean TSH concentration from 2005 to 2008 was 5.9 mIU/L. From 2009 to 2010 the mean TSH concentration dropped to 3.0 mIU/L. Of the 3349 participants in the study, 601 participated in 2005, 573 in 2006, 703 in 2007, 617 in 2008, 550 in 2009 and 305 in 2010 (**Figure 1**).

We found that 1270 subjects (37.9%) had TSH concentrations above 5mIU/L. There were 166 (27.6%) in 2005, 252 (44.0%) in 2006, 331 (47.1%) in 2007, 356 (57.7%) in 2008, 114 (20.7%) in 2009 and 51 (16.8%) in 2010 (**Figure 2**). Twenty-two neonates had TSH higher than 20 mIU/L, so the recall rate for this study was 0.7%. Only 2 subjects were confirmed positive for hypothyroidism.

Table 1. Subjects' characteristics

Characteristics	Newborns n=3,349
Mean newborn age at time of test, days (SD)	3 (0.7)
Mean maternal age, years (SD)	29.5 (4.2)
Mean birth weight, g (SD)	3215.4 (704.8)
Mean TSH concentration, mIU/L (SD)	5.14 (13.67)

Discussion

Our study included 59.7% of all the infants born in MKSH from 2005 to 2010, of which 37.9% had TSH concentration above 5mIU/L. On the basis of WHO/UNICEF/ICCIDD criteria, this population frequency was considered to be moderately iodine deficient. However, in 1996 Pardede LVH *et al*.[11] and a WHO nationwide map of goiter prevalence, categorized Indonesia to be mild for iodine deficiency.[8] In 2010, a study on maternal urinary iodine excretion of pregnant women in East Java also showed a median value that corresponded to mild iodine deficiency although data had a wide distribution ranging from severe deficiency to adequate. Surabaya was found to have mild iodine deficiency.[9] The discrepancy could be due to the different population and methods used to assess iodine deficiency.

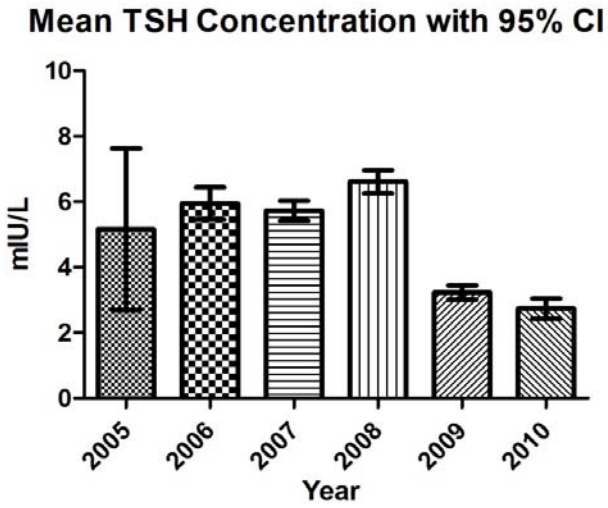

Figure 1. Mean TSH concentration with 95% CI (n=3349)

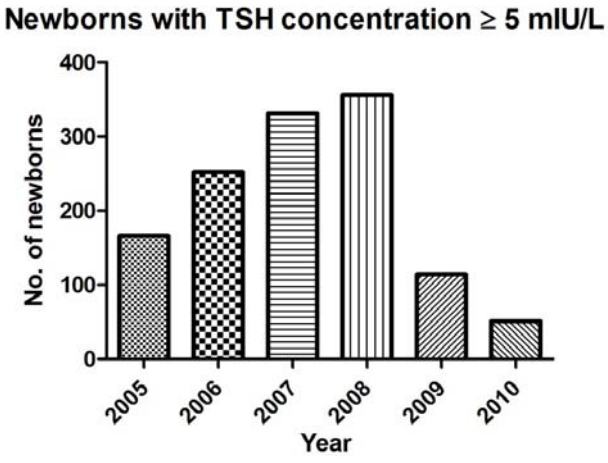

Figure 2. Yearly number of newborns with TSH concentration over 5 mIU/L

The main factor responsible for iodine deficiency is low dietary intake of iodine,[7,12] raising the question of whether our subjects' mothers were iodine deficient. According to an Australian study involving 824 newborns and 815 pregnant women, only 2.2% of newborns had TSH values above 5mIU/L even though urinary iodine excretion tests of the 815 pregnant women indicated iodine deficiency.[12] This seemingly conflicting data may have been due to the different levels of iodine deficiency severity in the pregnant women.

Another factor affecting newborn TSH concentrations may have been the use of iodine-based disinfectants. False-positive TSH levels were found significantly more frequently in infants treated with povidone-iodine, than in those treated with either alcohol or triple dye.[13,14] Since the disinfectants for umbilical cord care used in our study were alcohol-based, this factor was unlikely to influence our results.

According to the WHO/UNICEF/ICCIDD criteria for population iodine deficiency (3%-19.9% mild, 20%-39.9% moderate and ≥ 40% severe), the percentages > 5mIU/L TSH concentration indicated severe iodine-deficient status in the years 2006, 2007 and 2008, moderate in 2005 and 2009, and mild in 2010.[15] As a whole, there was an improvement in IDD status between year 2005 and 2010. IDD status worsened from 2005 to 2008 and drastically improved in 2009-2010. However, the number of infants screened in 2010 (n=305) was only about half that of previous years. The mean TSH concentration for the years 2005 to 2008 was 5.9 mIU/L, higher than the mean of years 2009 and 2010 (3.0 mIU/L). The reason for the rise and decline of TSH concentration ≥5 mIU/L was unclear. Despite the seemingly improved IDD status of the year 2009 and 2010, we cannot simply hope that 2011 will just follow suit with the trend. This is due in part, to the fact that the drastic improvement in year 2009 and 2010 themselves show how unpredictable IDD status can be.

Iodine deficiency is now accepted as the most common cause of preventable brain damage in the world.[1] Therefore, iodine deficiency prevention is important to avoid IDD. Although Indonesia has a program to handle iodine deficiency, *Penanggulangan Masalah Gangguan Akibat Kekurangan Yodium* (GAKY), Indonesia was classified as having mild iodine deficiency by the WHO. However, it should also be noted that this program is active mainly in government hospitals and health centers. Patients with middle to high socioeconomic status tend to visit private hospitals, such as the one in this study. The hospital does not accept payment from all government insurance agencies directed to the low income population and is not obligated to conform to nationwide health programs. Our results indicate that higher economic status did not lessen the risk of developing IDD. In fact, according to one Australian study, metropolitan populations had higher iodine deficiency than non-metropolitan populations.[16] Therefore, we can conclude that it is important to educate the population on sufficient dietary intake of iodine, regardless of their economic status.

Twenty-two neonates had TSH > 20 mIU/L, indicating potential hypothyroidism. These patients were recalled to undergo further examination, but only 2 were proven to have hypothyroidism. Although the recall rate (0.7%) was low compared to that of Iran (3.6%), it was similar to that of Thailand (0.66%), another Southeast Asian nation.[17-20] The prevalence of hypothyroidism observed was higher than the world population prevalence (2:3349 vs. 1:4000, respectively).[7] Nevertheless, our result may be affected by the relatively small sample size in this study. Although there were many false positives, TSH is considered to be one of the best screening modalities for hypothyroidism comparable to T4 and free T4.[21] It was only through screening that we were able to prevent two neonates from hypothyroidism, and subsequent mental retardation, growth and development disorders or even death.

According to the WHO/UNICEF/ICCIDD criteria, subjects' blood samples should be taken on the third or fourth day after birth. However, in reality this practice is not easily realized. Patients often request that the test be carried out on the second day together with other lab tests as they usually want to return home as soon as possible. A study in Australia on the analysis of neonatal TSH also relies on data obtained between 2-4 days after birth.[16] Guideline from International Atomic Energy Agency (IAEA) on Screening of Newborns for Congenital Hypothyroidism states that TSH testing should be carried out at least 24 hours after birth. Blood taken before 24 hours of age is not easily determined due to the biological variability in the timing and level of TSH surge which usually occur between 6 to 12 hours after birth.[21] Also, in infants of birth weight less than 2500g, prematurity and illness may temporarily elevate TSH, affecting screening results.[6]

In conclusion, we found that newborn subjects at MKSH from the year 2005 to 2010 were categorized as having IDD ranging from mild to severe. The average IDD status is moderate, higher than previously reported by the WHO[8], Pardede LVH *et al.*[11] as well as East Java Department of Health.[9] although there is a difference in population and methods used to assess iodine deficiency. We must remember that results from this study does not represent Surabaya as a whole; a city wide screening programme is required to ensure a proportional random sampling carried out to calculate the prevalence of IDD in Surabaya. Two neonates were found to have hypothyroidism from the TSH screening with a recall rate of 0.7%. Although there were many false positives, early diagnosis is very meaningful for the two neonates. Other than ensuring early diagnosis of neonates with hypothyroidism, TSH screening also aids in early diagnosis of neonates with IDD.

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