

URINARY IODIDE LEVELS IN TERM NEWBORNS AND THEIR MOTHERS - A PILOT STUDY

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Abstract. Although the Philippines is considered an iodine-deficient country, there are no documented iodine deficiency disorders (IDD) among newborns screened to be positive for congenital hypothyroidism. The objectives of this pilot study were: (1) to determine the levels of urinary iodide (UI) in normal term newborns and their mothers, and (2) to correlate the UI levels of newborns with that of their mothers. This study included 44 pairs of full term newborns and their mothers who delivered at two hospitals in Manila last July 2001. UI determination by the Rapid Urinary Iodide Test was done during the first 24 hours after delivery. Results showed that eighteen percent (8/44) of the neonates were iodine deficient (<10 µg/dl), 71% (31/44) had adequate UI levels (>10-30µg/dl) and 11% (5/44) had high UI levels (>30µg/dl). None of the mothers had deficient UI levels. Among the neonates who had deficient UI levels, 50% (4/8) of the mothers had adequate UI levels and the other half (4/8) had high levels. Among the neonates who had adequate UI levels, most mothers had high UI levels (22/31 or 71%) and the rest (9/31 or 29%) had adequate UI. All newborns with high UI levels had mothers with high UI levels. Screening for Congenital Hypothyroidism was negative in all the neonates who underwent newborn screening (39/44). In conclusion, most term neonates (82%) had adequate to high UI levels, and 18% had deficient UI levels despite adequate maternal levels. In case of low UI level, repeat determination is advised. If the level remains low, newborn screening using TSH is useful to rule out hypothyroidism. A bigger multicenter study to determine the incidence of IDD in neonates and infants is recommended.

INTRODUCTION

In 1996, the Philippines started its pilot newborn screening project. The incidence of congenital hypothyroidism is estimated to be 1:3800 live births (Philippine Newborn Screening Program, 2001). Although the Philippines is considered an iodine-deficient country (Sullivan *et al*, 1997; Paulino, 2000), there are no documented iodine deficiency disorders (IDD) among newborns screened to be positive for congenital hypothyroidism. We still need more data and studies on IDD, particularly in the newborns and among mothers in their reproductive age, since the inadequate dietary intake of iodine in the mothers can affect their newborns adversely. Urinary iodide levels can be used to document adequacy of iodine intake because iodide is mostly excreted in the urine. The objectives of this pilot study were: (1) to determine the levels of urinary iodide (UI) in normal term newborns and their mothers, and (2) to correlate the UI levels of newborns with that of their mothers.

MATERIALS AND METHODS

Normal term newborns delivered during the period from June to September, 2001 at two hospitals in Manila

were randomly selected. Inclusion criteria were: full term (37-42 weeks age of gestation); appropriate weight for gestational age (AGA); good Apgar scores (>7 at 1 minute and 9 at 5 minutes); absence of dysmorphic features and congenital anomalies involving the renal system; and absence of maternal thyroid disorders based on the medical history and physical examination. Excluded were those who had no parental consent, contaminated urine by meconium, inadequate urine specimen and absence of urine in the first 24 hours of life.

Informed consent was secured from the parents. Fresh urine voided within the first 24 hours of life was collected through urine bags. UI was determined using the Merck Rapid Urinary Iodide Test (Rendl *et al*, 1998), an easy, rapid test for the semiquantitative determination of iodide in urine samples. In this test, the interfering substances in the urine are eliminated using an extraction column containing activated charcoal. Detection is by means of the oxidation of tetramethylbenzidine with peracetic acid. This reaction is catalyzed by iodide and causes the sample solution to change color when urine iodine is at least 10 µg/dl. When the urine is deficient in iodide (<10 µg/dl), the

urine remains yellow. When the urine iodide is adequate and contains UI >10-30 µg/dl, the color is light green-blue, while dark blue to green color indicates high UI. The color of the chemical reaction was compared with the color categories of a pictogram. Urine iodine from mothers were determined using the same method. Data collected from mothers included demographic characteristics, illnesses and medications taken, weight gained during pregnancy, and a 3-day diet recall with emphasis on whether iodized salt was used in food preparation.

Prior to discharge, the newborn screening for congenital hypothyroidism was done. Babies with deficient UI levels were scheduled for follow-ups and a repeat UI determination was done.

Statistical analysis used was the chi square and fisher's exact test.

RESULTS

Forty-four pairs of babies and mothers were included in the study. The urine specimens of the newborns were collected as early as the first hour of life to as late as the 21st hour of life. The mean time of collection was the 10th hour of life.

Of the 44 babies, 64% (28/44) were males and 36% (16/44) were females. The age of gestation based on the Modified Ballard's Scoring was between 37 to 40 weeks with birth weights ranging from 2.5 to 3.8 kg. As to the mode of delivery, 61% (27/44) underwent spontaneous vaginal delivery and 39% (17/44) underwent Cesarean section. Povidone iodine was used to disinfect maternal skin during labor just prior to delivery.

Eighteen percent (8/44) of neonates were found to have deficient UI levels (<10 µg/dl), 71% (31/44) had adequate UI levels (>10-30µg/dl) and 11% (5/44) had high UI levels (>30µg/dl). Half of the neonates (22/44) were already on milk feeding when urine specimens were collected; ten were breastfed while twelve were fed with infant formula, consuming about 1 to 3 oz. of formula containing 1 to 9 µg iodine. The other half had no feeding yet when they voided the urine for collection during the early hours of life.

Maternal age ranged from 18 to 39 years old with a mean of 28 years. None of the mothers had deficient UI levels. All mothers had adequate to high UI levels. Thirty percent (13/44) mothers had adequate UI and 70% (31/44) had high UI. A 3-day diet recall was elicited from the mothers. Sixty-six percent (29/44) of the mothers did

not use iodized salt but had iodine-rich food intake; thirty-four percent (15/44) used iodized salt in food preparation. All mothers during pregnancy took multivitamins and mineral preparations containing 100 to 150 µg iodide per tablet. The average weight gain of the mothers during pregnancy was 12 kg (range: 9.5 to 14.5 kg).

Of the eight neonates who had deficient UI levels, fifty percent (4/8) of mothers had adequate UI levels while the other half (4/8) had high levels. Among the neonates who had adequate UI levels, 71% of mothers had high UI levels (22/31) and 29% (9/31) had adequate UI levels. Among the newborns with high UI levels, all their mothers (5/5) also had high UI levels. Table 1 summarizes the result.

Majority of the mothers had high UI levels (31/44 or 70%) and the rest (30%) had adequate levels. In spite of the high UI concentration in 31 mothers, 4 of their babies (13%) had deficient UI levels.

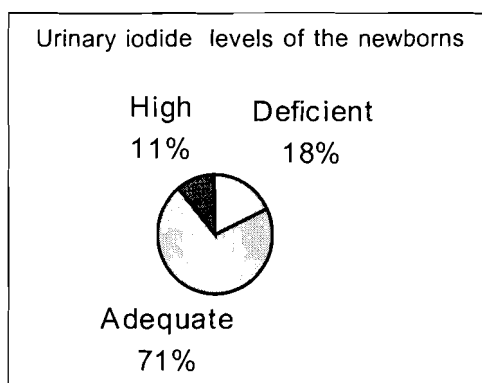


Fig 1. Urinary iodide levels of the newborns.

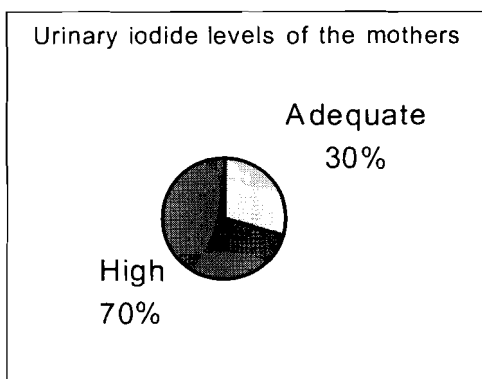


Fig 2. Urinary iodide levels of the mothers.

Table 1. UI levels of the neonates and their mothers.

Neonates (n = 44)		Mothers (n = 44)	
Deficient UI	8 (18%)	Adequate UI	4 (50%)
		High UI	4 (50%)
Adequate UI	31 (71%)	Adequate UI	9 (29%)
		High UI	22 (71%)
High UI	5 (11%)	High UI	5 (100%)
Total	44 (100%)		44

Thirty-nine neonates (89%) underwent newborn screening and all of them had negative results for hypothyroidism. The 8 neonates with deficient urine iodine had a TSH screening result not higher than 5 μ IU/ml. Repeat UI levels of these neonates on follow-up were adequate (>10 -30 μ g/dl). The feeding history as well as growth and development were assessed. The iodide content in the milk ranged from 70 to 100 μ g/day. The developmental milestones were appropriate for age.

There was no significant correlation between neonatal and maternal urinary iodide levels as well as between neonatal UI and mode of delivery. There was a significant correlation between maternal UI and mode of delivery.

DISCUSSION

The adequate to high urinary iodide levels in majority of the term AGA newborns may be explained by a significant transplacental passage of iodine from the mother to the growing fetus (Das and Isichei, 1994). All mothers who were included in the study took multivitamin and mineral preparations containing iodide during pregnancy, and they also had either intake of iodine rich food or iodized salt in their food preparation. The adequate iodide supplements in the mothers generally affected favorably the babies' iodide storage.

A study that demonstrated the rate of iodine deficiency in the neonates could be higher if the mothers had no iodine supplements. Polish mothers who received iodide had newborns with low concentration of iodine 15.4% while the rate of iodine deficiency was 3.7 times higher in those mothers who received no supplements (57.2%) (Urban *et al*, 2000). The low neonatal urinary iodide levels in 4 babies whose mothers had normal UI probably could be explained by the relatively lower iodine content of the neonate's thyroid and an accelerated

turnover rate of their intrathyroidal iodine reserves (Delange, 1998). A study indicated the existence of a postnatal temporarily negative iodine balance: the excretion of iodine prevailed over the intake and the newborn's thyroidal iodine, stored during pregnancy (Bakker *et al*, 1999). The prenatally acquired iodine stores might not be sufficient to completely compensate for the transient postnatal losses in the babies showing deficient urinary iodide levels. The computed iodine content of the milk consumed by some babies was small to significantly increase their UI levels during the early hours of life.

Among the newborns with high UI levels, all their mothers (5/5 or 100%) also had high UI levels. There was documented transplacental passage of iodine from the mother to the fetus, and positive correlation was found between neonatal total thyroxine and birth weight ($r=0.61$; $p<0.001$) and maternal urinary iodine concentration ($p<0.001$) (Ardawi *et al*, 2002). In this study, the correlation between the neonatal and maternal urinary iodide (UI) levels after the delivery was not significant (p value >0.05). The eight neonates having deficient iodide concentration in the urine voided during the first 24 hours had newborn screening done after 24 to 48 hours of life, and their TSH levels were normal (levels = 5 μ IU/ml). Iodine deficiency in these newborns was mild and did not cause hypothyroidism. On follow-up, the neonates who initially had deficient UI levels were assessed to have normal growth and development. The repeat UI levels were already normal (>10 -30 μ g/dl). The transient iodine deficiency in these newborns could possibly be compensated by the regular oral milk intake containing sufficient iodide.

With regards to the mode of delivery, there was significant correlation of the mode of delivery with the maternal urinary iodide level. In cesarean section, povidone iodine was applied to more skin areas and this possibly contributed more to the maternal iodine pool and increased the urinary iodide excretion. There have been reports documenting that the application of povidone iodine on mothers during delivery could have an effect on neonates. It was previously reported that the use of povidone iodine on mothers is associated with transient neonatal hyperthyrotropinemia (Koga *et al*, 1995; Vilain *et al*, 1994; Robuschi and Montermini, 1987). However, there was no significant correlation of the mode of delivery with the newborns in this study; the neonates delivered by cesarean section did not show significantly higher iodide excretion compared to those delivered vaginally and also did not show any hyperthyrotropinemia on newborn screening. A study showed that the cord blood thyroid hormone

concentrations in the newborns of iodine exposed mothers were not significantly different from those in control newborns although cord blood TSH concentrations in the neonates of mothers exposed to PVP-I during the last trimester of pregnancy were significantly higher than values in control neonates (Glinooer, 2000).

CONCLUSIONS

In this pilot study, eighty-two percent of the term AGA newborns had adequate to high urinary iodide levels while 18% had deficient UI levels in spite of adequate maternal levels. Iodine deficiency in these newborns was mild, transient and not causing hypothyroidism. Neonates with low UI level had normal TSH, and adequate UI levels on repeat determinations. All mothers having intake of iodine-rich food or iodized salt, and multivitamin and mineral preparations containing iodine during pregnancy also had adequate to high urinary iodine concentration. Although there was transplacental passage of iodine from the mother to the fetus, this study did not demonstrate any significant correlation between the neonatal and maternal urinary iodide levels. However, there was significant correlation between the maternal urinary iodide levels and the mode of delivery.

RECOMMENDATIONS

A bigger study to determine the incidence of IDD in neonates and infants is recommended. Other studies may include the investigation of IDD among neonates with congenital hypothyroidism and IDD in mothers with goiters. Using a method that can do quantitative, and not just semiquantitative, determination of iodide in urine samples may be considered if feasible.

REFERENCES

Ardawi MS, Nasrat HA, Mustafa BE. Urinary iodine excretion and maternal thyroid function. During pregnancy and postpartum. *Saudi Med J* 2002; 23: 413-22.

- Bakker B, Vulsma T, de Randamie J, Achterhuis AM, Wiedijk B, Oosting H, Glas C, de Vijlder JJ. A negative iodine balance is found in healthy neonates compared with neonates with thyroid agenesis. *J Endocrinol* 1999; 161:115-20.
- Das SC, Isichei UP. A study on transplacental transfer of thyroid hormones in pregnant Nigerian women of Jos-Plateau State. *West Afr J Med* 1994;13:138-41.
- Delange F. Screening for congenital hypothyroidism used as indicator of IDD control. In: Pinchera A, Mann K, Hostalek U, ed. *The Thyroid And Age*. Stuttgart: Schattauer 1998:121.
- Glinooer D. Thyroid dysfunction in the pregnant patients. *The Thyroid and Its Disease*. January 2000; 14:1.
- Koga Y, Sano H, Kikukawa Y, Ishigouoka T, Kawamura M. Effect on neonatal thyroid function of povidone-iodine used on mothers during perinatal period. *J Obstet Gynaecol* 1995; 21: 581-5.
- Paulino LS. Status of iodine deficiency disorders in the Philippines. *PTA News* 2000; 5:11-2.
- Philippine Newborn Screening Program Update as of July 2001.
- Rendl J, Bier D, Groh T, Reiners C. Rapid urinary iodide test. *J Clin Endocrinol Metab* 1998; 83:1007-12.
- Robuschi G, Montermini. Cord blood iodothyronine and thyrotropin concentrations in newborns of mothers exposed to povidone iodine in the last trimester. *J Endocrinol Invest* 1987;10:183-6.
- 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.
- Urban G, Wnek M, Bazowska G. Iodine supplementation during pregnancy and its influence on the newborn. *Ginekol Pol* 2000;71:690-4.
- Vilain E, Bompard Y, Clement K, Laplanche S, de Kermadec S, Aufrant C. Brief antiseptic application of iodine in neonatal intensive care units: effects on thyroid function. *Arch Pediatr* 1994;1:795-800.