

## Original Article

# Maternal iodine status and the thyroid function of pregnant mothers and their neonates in Jaffna District of Sri Lanka

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### ABSTRACT

**Introduction:** Iodine status of pregnant women and their newborns have not been studied in Jaffna District, Sri Lanka. This study was planned to assess the maternal iodine status and thyroid function at the third trimester of gestation and the thyrotrophin level of their neonate. **Methods:** Four hundred and seventy-seven pregnant women and their newborns were randomly selected among six Medical Officers of Health Divisions out of 12 in Jaffna District, Sri Lanka. Maternal thyroid stimulating hormone (TSH), free thyroxine (fT<sub>4</sub>), thyroglobulin (Tg), urinary iodine levels, and the neonatal thyrotrophin (nTSH) level were assessed. **Results:** In this study, mean age, weight, height, and gestational age of the mothers were 28.95 (±5.46) years, 63.02 (±11.56) kg, 154.39 (±6.00) cm, and 39.33 (±1.37) weeks, respectively. Maternal median urinary iodine concentration (UIC) was 140.0 µg/L (inter-quartile range 126.0–268.0 µg/L). Median values of the maternal serum TSH, fT<sub>4</sub>, and Tg were 1.9 mIU/L, 12.6 pmol/L, and 21.4 IU/L, respectively. Among the 477 newborns, 50.5% (n = 239) were males. Mean birth weight of newborn was 3.03 (±0.43) kg, while the mean length was 51.1 (±2.1) cm. Among the newborns, 18% (n = 86) had nTSH level >20 mIU/L and 37.7% (n = 180) within TSH level >5 mIU/L. nTSH level had positive but very weak correlations with maternal thyroid parameters, that is, UIC (r = 0.06, P = 0.13), fT<sub>4</sub> (r = 0.01, P = 0.05), TSH (r = 0.09, P = 0.05), and Tg (r = 0.12, P = 0.03). **Conclusion:** On the basis of the World Health Organization criteria, the iodine status of pregnant women was inadequate in this region and also nTSH levels indicate moderate iodine deficiency during pregnancy. Therefore, the continuous education on adequate iodine intake during pregnancy and monitoring of iodine status are useful.

**Key words:** Iodine status, maternal thyroglobulin, maternal thyrotrophin, neonatal thyrotrophin, pregnant mothers, urinary iodine concentration

## INTRODUCTION

Iodine is an essential element for the production of hormones, triiodothyronine (T<sub>3</sub>), and thyroxine (T<sub>4</sub>). Women need more iodine during pregnancy to maintain

normal metabolism as well as to meet the requirements of T<sub>4</sub> and iodide transfer to the fetus.<sup>[1]</sup> Iodine deficiency and hypothyroidism during pregnancy have long been known to be associated with neurological deficits and mental retardation; however, there is also evidence for an increased risk of adverse effects on obstetrical outcomes such as preeclampsia or placental abruption, and negative effects on the offspring such as preterm birth, fetal death, or low birth weight (BW).<sup>[2,3]</sup>

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It has been shown that in some countries iodine intake was sufficient among school-age children, but not with pregnant women.<sup>[4]</sup> Such findings justified the need for continuous monitoring of iodine nutrition status in these two vulnerable populations. Further, the status of maternal iodine nutrition and its effect on neonatal thyroid function has not yet been assessed at national level in Sri Lanka as well as in Northern Province. Further, no data are available on maternal iodine status and neonatal thyroid function in Sri Lanka. In addition, after the implementation of the Universal Salt Iodization Program (USI) in Sri Lanka there have not been any published data relating the iodine status between the mother-newborn pair. The special emphasis on iodine supplementation during pregnancy is not a routine practice in Sri Lanka. In such situation, an adequate dietary intake of iodine throughout the gestation has to be investigated. Therefore, this study was planned to assess the maternal iodine status and thyroid function at the third trimester and its influence on neonatal thyroid function.

## METHODS

### Ethical approval, subject selection, anthropometry measurements, and dietary assessment

Ethical approval of this study was obtained from the Ethical Review Committee of the Faculty of Medicine, University of Jaffna. Four hundred and seventy-seven pregnant mothers were randomly selected among six Medical Officers of Health (MOH) divisions out of 12 MOH divisions in the Jaffna District, Sri Lanka. Mothers were selected from their antenatal clinics for this study and followed-up until delivery of the newborn. Height of the mother was measured by using a portable stadiometer (IUCHI, Yamato Scientific, Japan) with a precision of  $\pm 0.1$  cm and readability up to 200 cm, and weight was measured using a portable beam balance (Bauman, Germany) with nondetachable weights with a precision of  $\pm 0.1$  kg and readability up to 100.0 kg. Both instruments were checked for zero error before commencing each anthropometric session. The weight of the newborn was measured by digital infant scale with the precision of 10 g without wearing nappy or even any light clothing. Dietary intake was assessed by 24 h recall on three nonconsecutive days. Pregnant mothers were questioned about the intake of iodine rich food items using standard cups and spoons through face-to-face interview.

### Blood and urine collection for analysis

Five milliliters of maternal blood was collected, and serum was separated for the analysis of thyroid profile such as thyroid stimulating hormone (TSH), free thyroxine ( $fT_4$ ), and thyroglobulin (Tg) using enzyme-linked immunosorbent assay (ELISA), and reagent kits were provided by MP Biochemicals, USA. A spot morning

urine sample from each mother was collected and assayed in duplicates for the determination of maternal urinary iodide concentration (UIC) using ammonium persulphate digestion method.<sup>[5]</sup>

### Neonatal blood spot thyroid stimulating hormone

Once the baby was delivered, a heel prick blood spot (by filter paper collection method) was collected from the baby prior to the discharge from the hospital or through the home visits within a week of delivery for the determination of neonatal TSH levels. The blood spot analyses carried out using the Immuchem™ Neonatal TSH-MW ELISA (bulk kit –20 plates) and radioimmunoassay (RIA) kits (500 tubes kit) were provided by MP Biochemicals, USA.

### Reference ranges

The reference range of maternal serum TSH concentration is 0.2–5.2 mIU/L and serum  $fT_4$  is 6.4–25.7 pmol/L, whereas maternal hypothyroidism is defined as serum TSH  $>5.2$  mIU/L.<sup>[6]</sup> The cut-off values for neonatal TSH were decided depending on the age of the newborn at the time of blood spot collection and as per the guidelines of International Atomic Energy Agency, neonatal serum TSH level of the blood spot was categorized  $>20$  mIU/L and  $<20$  mIU/L. Once a positive baby (neonatal TSH  $>20$  mIU/L) was found, a repeat serum test was performed to confirm the results. Parents were contacted immediately through the telephone to get a serum sample. Both serum TSH and free  $T_4$  were determined. Congenital hypothyroidism (CH) was confirmed if serum TSH  $>9.8$  mIU/L and  $fT_4 <10$  pmol/L.<sup>[6]</sup>

### Statistical analysis

Results of laboratory analysis were presented as mean ( $\pm$  standard deviation) or median with inter-quartile range (IQR). For variables exhibiting a skewed distribution (UIC and serum TSH concentration), the median was used as the measure of central tendency together with the IQR. Simple linear regression analysis was used to test the correlations between UIC and serum TSH or  $fT_4$  concentrations. A  $P < 0.05$  was considered as significant. Correlations between neonatal and maternal variables were performed using the Pearson correlation or Spearman's rank correlation tests. Statistical analyses were performed using the SPSS version 16 (SPSS, Chicago, IL, USA).

## RESULTS

### General characteristics of pregnant women

Demographic characteristics of the pregnant women, who were recruited for the study, are summarized in Table 1. Among the 477 pregnant women average age, weight, height, and gestational age were  $28.95 \pm 5.5$  years,

63.02 ± 11.56 kg, 154.39 ± 6.00 cm, and 39.33 ± 1.4 weeks, respectively. Main items in meals consumed by pregnant mothers were identified as rice, fish, chicken, cow's milk, eggs, potatoes, soy meat, fruits, and green leafy vegetables. Twelve percent of mothers (*n* = 57) reported that they avoided the consumption of fruits, and 13.6% (*n* = 65) avoided vegetables (green leaves) throughout the gestational period. Most of them ([81.6%] *n* = 389) consumed at least one fruit (200 g) per week and 58.7% (*n* = 280) consumed at least two spoons (150 g) of vegetables (green leafy) per week. The mean daily cow's milk consumption was 0.82 cup-205 ml (range 1–3 cups). The average intake of iodine rich food by the mothers at the third trimester is shown in Table 2.

### Maternal iodine status

Maternal median UIC in the spot urine sample was 140.0 µg/L (IQR 126.0–268.0 µg/L) with a range of 36.0–644.0 µg/L. There were 65.1% (*n* = 311) mothers who had UIC <150.0 µg/L, while 22.7% (*n* = 109) had the adequate level of 150–250 µg/L and 11.7% (*n* = 57) had

UIC >250.0 µg/L [Table 3]. Median values of the serum TSH, free T<sub>4</sub>, and Tg were 1.9 mIU/L, 12.6 pmol/L and 21.4 IU/L, respectively. The serum TSH level ranged from 0.20 to 16.40 mIU/L, while serum fT<sub>4</sub> and Tg levels ranged from 10.1 to 28.2 pmol/L and 0.8–86.9 IU/L, respectively. The sub-clinical hypothyroidism (SCH) (SCH is defined as elevated serum TSH with normal fT<sub>4</sub> level) was seen among 3.4% (*n* = 16) of pregnant women and none of them were found to be overt hypothyroid. There were negative correlations between mothers' TSH level with UIC (*r* = -0.05, *P* = 0.25) and fT<sub>4</sub> (*r* = -0.04, *P* = 0.43) levels but significantly associated only with Tg (*r* = -0.15, *P* = 0.002). Further, there was a significant positive correlation between UIC and Tg levels (*r* = -0.10, *P* = 0.05).

### Characteristics of the newborns

Newborns' characteristics and their thyroid statuses are given in Table 4. Among the 477 newborns, 50.5% (*n* = 239) were males and 68.1% (*n* = 325) are delivered by vaginal and the rest via cesarean section. Mean BW of the neonates was 3.03 ± 0.43 kg, while the mean length was 51.1 ± 2.1 cm. BW of males ranged from 1.7 to 5.0 kg and of females from 1.50 to 4.35 Kg. Length of the newborns ranged from 45.0 to 58.0 cm for males and from 44.0 to 57.0 cm for females. Mean neonatal TSH concentration was 9.80 ± 2.10 mIU/L and ranged from 1.00 to 53.46 mIU/L. Among the newborns, 18% (*n* = 86) were identified as positive (TSH >20 mIU/L) for CH screening and 37.7% (*n* = 180) with neonatal TSH level >5 mIU/L. However, none of them had serum TSH >9.8 mIU/L on serum analysis.

### Association between maternal and neonatal characteristics

Correlation between the maternal characteristics and indicators for iodine nutrition status and the newborns' anthropometries (BW and length) are given in Table 5. Even though BW and length of the newborns were higher in males (3.06 kg and 51.2 cm) than in females (3.00 kg and 50.9 cm), these values did not differ significantly between the male and female babies (*P* = 0.13, 0.23, respectively). Increasing maternal age had significantly correlated with the BW of the newborns (*r* = 0.137, *P* = 0.003). Educational attainment of mothers had statistically correlated with the BW of the newborns (*r* = 0.119, *P* = 0.009). With the increase in the period of gestation, low BW (LBW) decreased and normal BW (NBW) increased. The gestational age of mothers had significantly correlated with BW (*r* = 0.196, *P* = 0.001) and length (*r* = 0.128, *P* = 0.005) of the newborns. Neonatal TSH concentration had positive but very weak correlations with maternal thyroid parameters, that is, UIC (*r* = 0.06, *P* = 0.13), fT<sub>4</sub> (*r* = 0.01, *P* = 0.05), TSH (*r* = 0.09, *P* = 0.05), and Tg (*r* = 0.12, *P* = 0.03).

**Table 1: General information of the pregnant women<sup>a</sup>**

Information	Percentage (n)
Age (years)	
<19.9	1.5 (7)
20-29.9	52.0 (248)
30-39.9	44.0 (210)
≥40	2.5 (12)
Height (cm)	
<144.9	4.8 (23)
145-149.9	14.4 (69)
150-154.9	31.9 (152)
155-159.9	28.5 (136)
160-164.9	20.4 (97)
Weight (kg)	
Up to 50.0	13.4 (64)
50.1-60.0	35.4 (169)
60.1-70.0	28.9 (138)
Above 70.1	22.3 (106)
Educational attainment	
Nonformal	0.2 (1)
Grade 1-5	9.6 (46)
Grade 6-11	58.9 (281)
Grade 12 and 13	23.9 (114)
Degree or above	7.3 (35)

<sup>a</sup>Results given as percentage (*n*)

**Table 2: Average intake of iodine rich foods**

Food item	Mean amount/day	Range/day
Cow's milk	0.82 cup (205 mL)	1-3 cups
Meat (chicken)	0.42 spn (32 g)	1-3 spoons
Sea food (fish)	1.13 pcs (90 g)	1-5 pieces
Egg with yolk	0.45 egg (36 g)	1-4 eggs
Potatoes	0.67 spn (50 g)	1-6 spoons
Fruits (apple, mango, and banana)	0.46 fts (92 g)	1-3 fruits
Vegetables	0.65 spn (49 g)	1-6 spoons
Soy meat	0.51 spn (38 g)	1-2 spoons

Quantification (1 cup=250 mL; 1 spoon=75 g; 1 piece=80 g; average weight of a fruit=200 g). Source: Nuclear Medicine Unit, University of Jaffna, Jaffna

**Table 3: Association of maternal UIC and serum TSH with age and gestational period<sup>a</sup>**

Maternal demography factor	Percentage (n)					
	UIC (µg/L)			TSH (mIU/L)		
	<150	150-249	≥250	<0.2	0.2-5.2	>5.2
Age (years)						
<20	1.0 (5)	0.2 (1)	0.2 (1)	0.0 (0)	1.2 (6)	0.2 (1)
20-29.9	37.3 (178)	12.1 (58)	2.5 (12)	0.8 (4)	49.5 (236)	1.6 (8)
30-39.9	25.6 (122)	9.6 (46)	8.8 (42)	1.5 (7)	41.5 (198)	1.0 (5)
≥40	1.2 (6)	0.8 (4)	0.2 (1)	0.2 (1)	1.9 (9)	0.4 (2)
Gestational period (weeks)						
Preterm (<37 weeks)	1.7 (8)	0.4 (2)	0.4 (2)	0.4 (2)	1.5 (7)	0.6 (3)
Term (37-41 weeks)	40.9 (295)	19.9 (95)	13.2 (63)	1.3 (6)	91.8 (438)	1.9 (9)
Postterm (≥42 weeks)	1.7 (8)	0.4 (2)	0.4 (2)	0.6 (3)	1.0 (5)	0.8 (5)

<sup>a</sup>Results given as percentage (n). UIC: Urinary iodide concentration; TSH: Thyroid stimulating hormone

**Table 4: Newborns characteristics<sup>a</sup>**

Newborn's parameter	Percentage (n)		
	Male	Female	Over all
Number of newborns	50.5 (239)	49.5 (238)	100 (477)
Birth weight (kg), mean (range)	3.06 (1.70-5.00)	3.00 (1.50-4.35)	3.03 (1.50-5.00)
Length (cm), mean (range)	51.2 (45.0-58.0)	50.9 (44.0-57.0)	51.1 (44.0-58.0)
LBW, % (n)	5.0 (24)	6.3 (30)	11.3 (54)
NBW, % (n)	46.3 (221)	42.2 (201)	88.5 (422)
HBW, % (n)	0.2 (1)	0 (0)	0.2 (1)
Blood spot TSH			
<20.0 mIU/L	40.0 (191)	42.0 (200)	82.0 (391)
>20.0 mIU/L	10.0 (48)	8.0 (38)	18.0 (86)

<sup>a</sup>Results given as percentage (n). LBW: Low birth weight; NBW: Normal birth weight; HBW: Higher birth weight; TSH: Thyroid stimulating hormone

**Table 5: Correlation between the mothers and their newborns<sup>a</sup>**

Mother	Newborn	r	P <sup>b</sup>
Age	BW	0.137	0.003
Educational attainment	BW	0.119	0.009
Gestational age	BW	0.196	0.001
Gestational age	Length	0.128	0.005
UIC	TSH	0.074	0.141
ft <sub>4</sub>	TSH	0.012	0.045
Tg	TSH	0.122	0.032
TSH	TSH	0.086	0.045

<sup>a</sup>BW: Birth weight; UIC: Urinary iodine concentration; ft<sub>4</sub>: Free thyroxine; TSH: Thyroid stimulating hormone; Tg: Thyroglobulin. <sup>b</sup>P<0.05 considered as significant level

## DISCUSSION

In 1995, the Government of Sri Lanka launched USI Program as the mainstay of iodine deficiency control and achieved a satisfactory coverage after the initiation of this program.<sup>[7]</sup> Iodine sufficiency in a population is defined as median UIC of 100 µg/L or more in nonpregnant women and children and 150 µg/L or more in pregnant women.<sup>[1]</sup> This prime investigation showed that pregnant women and their newborns in the Northern Sri Lanka have iodine deficiency as assessed by maternal UIC (65.1% of pregnant

women had UIC <150 µg/L). Suboptimal iodine status has been reported in pregnant women from areas with only partial house-hold coverage with iodized salts such as Italy, Kuwait, and India.<sup>[8-11]</sup> Even though our study confirms those previous findings, countries with long-standing successful iodized salt programs have reported an optimal median UIC in pregnant women.<sup>[12]</sup>

As the salt is supposed to be an obligatory vehicle for iodine supplementation in Sri Lanka, proper iodization of the salt during its production and maintenance of the required iodine content until it is consumed is very important. Milk and other dairy products are important sources of iodine<sup>[13]</sup> and it has contributed approximately 55% and 70% of the dietary iodine intake in adults and children, respectively, in Norway.<sup>[14]</sup> In a recent study conducted among pregnant women, milk was the only variable influencing UIC in a multivariate analysis including the use of iodized salt, iodine supplementation, and different foods.<sup>[13]</sup> Milk seems to be the main dietary source of iodine; however, the median UIC in women with a high intake of milk (more than 2 cups/day) is shown below as the World Health Organization (WHO) recommendations.<sup>[1]</sup> Fish and shellfish are also known to be rich in iodine content; however, these foods do not contribute to the variability in iodine status in this Jaffna population. Further, despite the proximity to the sea, the population of the Jaffna region, particularly in the lower socioeconomic classes, had a low consumption of iodine rich food. Similar unexpected iodine deficiency has been observed in countries that have coastal areas.<sup>[15,16]</sup>

Maternal iodine nutrition and thyroid function can have a significant impact on fetal and newborns' TSH levels. However, data on the association of maternal UIC with neonatal TSH levels are conflicting.<sup>[17]</sup> A transient elevation of TSH was observed in some neonates born to Jaffna women who were supposed to consume high amount of iodine-rich food such as seafood (fish) and

cow's milk, especially at the third trimester of gestation. In the present study, there was no direct relationship between maternal iodine intake and neonatal TSH concentration on the third postnatal day (i.e., age of the newborn before 72 h), and this observation was consistent with the studies<sup>[18,19]</sup> carried out in iodine insufficient areas as well as in sufficient and mildly iodine-deficient areas in Australia.<sup>[17]</sup>

In this study, it has been observed that the consumption of fish and milk during gestation has a significant association with neonatal TSH concentration. The dietary iodine intake during gestation from these sources may have induced the elevated TSH in neonates. The utilization of neonatal TSH to assess iodine status may be an attractive method because it is assumed that the thyroid of the newborn is very sensitive to iodine status and even mild iodine deficiency during pregnancy. The best criteria for assessing the degree of iodine deficiency in pregnant women have not been established because of the lack of sufficient data for UIC in this group. Other potential indices of iodine deficiency, such as neonatal TSH, are not completely reliable due to many factors, including the timing of sample collection.<sup>[1,13-14,17,20]</sup> Although the present study showed that the newborns met the WHO criteria for iodine deficiency on blood spot TSH concentrations (iodine sufficiency is considered if <3% of the newborns have TSH >5mIU/L), it is now well recognized that the regulation of TSH secretion in the newborn does not follow the same feedback mechanisms observed when the thyroid-pituitary axis is fully developed.<sup>[21]</sup> Therefore, the cut-offs for defining the severity of iodine deficiency on the basis of newborn TSH concentrations originally proposed by the WHO have been questioned and are not considered in most of the recent recommendations.<sup>[13]</sup>

We found the prevalence of SCH to be 3.4%. In contrast, a study in Iran reported 4.15%.<sup>[22]</sup> About 2.0–2.5% of healthy nonpregnant women in the United States were considered as having SCH, but it would be anticipated that such percentages would be higher in the areas of iodine insufficiency.<sup>[23]</sup> Since the SCH a biochemical diagnosis, symptoms may be mild, nonspecific and mimic typical symptoms in pregnancy.

We observed a significant negative correlation between maternal TSH and Tg ( $r = -0.15$ ,  $P = 0.002$ ) toward the end of pregnancy. Although the measurement of thyroid antibodies does not give any indication of thyroid status, their presence does have important implications for the pregnancy as a rise in Tg toward the end of pregnancy is documented previously.<sup>[24,25]</sup> The percentage of women

having elevated Tg levels increased from 4.7% in the first trimester to 6.6% near term in a study done in Hong Kong.<sup>[26]</sup> Changes in thyroid function and thyroid antibodies during gestation must be viewed against the backdrop of the immune changes that occur during and immediately after pregnancy.<sup>[27]</sup> Although a uniform correlation between maternal or newborn serum thyroid auto-antibodies and sporadic CH is lacking, there are many reports relating maternal autoimmune thyroid disease to transient CH in newborn thyroid screening programs.<sup>[28]</sup> In studies conducted in Hong Kong<sup>[26]</sup> and Saudi Arabia,<sup>[29]</sup> maternal free T<sub>4</sub> and urinary iodine excretion values, respectively, have been found to be negatively correlated with neonatal TSH values. On the other hand, a significant positive correlation between serum Tg and nTSH was noticed in this study.

This study has indicated that the UIC of pregnant mothers at the third trimester does not reflect the other indicators of iodine status. However, the UIC has positively correlated with neonatal TSH level ( $r = 0.06$ ,  $P = 0.13$ ). Although the use of neonatal TSH concentration is attractive for monitoring iodine status, many issues need to be addressed before it can be recommended for this purpose, particularly to mildly iodine-deficient countries. On the other hand, iodine deficiency among pregnant women may be better detected by using maternal free T<sub>4</sub> as an indicator in the first trimester of gestation. Because the small decreases in serum free T<sub>4</sub> during pregnancy is an important risk factor for impaired psychomotor development in infants.<sup>[30]</sup>

Our findings suggest several ways to increase the iodine intake during pregnancy in this region. The iodized salt legislation recommends iodization of salt, that is, sold directly to the consumer but is legally binding. The legislation could be modified to recommend iodization of salt used for food processing too. Further, regular consumption of seafood products should be encouraged during pregnancy. Alternatively, targeted iodine supplementation of pregnant women may be preferable in this setting.

There are several limitations to our study design. The major limitation of this study is the possible variability in iodine content in each food group. The iodine content of foods varies with geographical location and season, as it depends on the iodine content of the soil. The iodine content of fish also varies across species,<sup>[31]</sup> and we were unable to classify fish intake based on iodine content. UIC was measured at the third trimester of gestation only, although it is known that an adequate iodine intake is mainly critical for the fetus in the first trimester of gestation.<sup>[21]</sup> However, chronic low iodine intake during

pregnancy becomes more severe with the progression of gestation to the final stages, when the intra-thyroidal iodine stores become more depleted.<sup>[32]</sup> Further, we did not evaluate/follow-up infants whether they are at risk of becoming short stature (cretinism) due to maternal iodine deficiency.

## CONCLUSION

On the basis of the WHO criteria, the iodine status of pregnant women was inadequate in this region and also nTSH levels indicate moderate iodine deficiency during pregnancy. Furthermore, maternal iodine nutrition and thyroid function can have a significant impact on fetal and newborns' TSH levels. Therefore, the continuous education on adequate iodine intake during pregnancy and monitoring of iodine status are useful. This study suggests that iodine supplementation through salt iodization program should be continued and monitored strictly with a close surveillance to maintain the iodine-replete status in the pregnant women and their neonates.

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## Conflicts of interest

There are no conflicts of interest.

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