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Neonatal thyroid status in an area of iodine sufficiency

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ABSTRACT. ***Background:*** **Iodine deficiency constitutes a public health problem in many countries worldwide. Fetal neurodevelopment is affected by maternal iodine intake. The aim of present study was to assess urinary iodine excretion (UIE) in the 3 trimesters of pregnancy and evaluate its association with newborn thyroid function in Tehran, an area of iodine sufficiency.** ***Methods:*** **Based on median urinary iodine in 3 trimesters, 138 pregnant women were divided into 2 groups with UIE<150 (group I) and UIE≥150 µg/l (group II). Cord blood samples of their newborns were evaluated for serum concentrations of TSH, T_3, T_4, free T_4 (FT_4), and thyroglobolin. Quartiles of UIE were also determined. Correlations between mothers' UIE and newborns' thyroid function in both groups were investigated.** ***Results:*** **Fifty-two pregnant women (38%) had median UIE<150 µg/l and 86 had (62%) UIE≥150 µg/l. Median UIE in groups I and II in the 1st, 2nd, and 3rd trimesters were 125 and 212 µg/l, 97 and 213 µg/l, 93 and 227 µg/l, respectively. No significant difference was seen in thyroid function of newborns in the 2 groups. Mean concentrations of T_4, T_3, FT_4, and TSH of newborn did not show significant difference in median UIE of mothers in various quartiles.** ***Conclusion:*** **This study shows that newborns, irrespective of mothers' UIE, in an area with a sustained iodine supplementation program, may not be at risk of alterations in thyroid functions.**
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INTRODUCTION

Iodine is an essential element for the production of thyroid hormones, T_4 and T_3. During pregnancy a woman needs more iodine to maintain normal metabolism as well as to meet the requirement of T_4 and iodine transfer to the fetus (1). Iodine has a significant role in the metabolism of many organs, particularly the brain. Neurodevelopment of fetus and breastfed newborns and infants is affected by maternal iodine intake (2, 3); therefore, in recent years, attention to the adequate iodine intake of pregnant and lactating women and their offspring has increased (4). The most common strategy for elimination of iodine deficiency is through universal salt iodization; despite effective control measures, iodine deficiency disorders (IDD) constitute significant public health problem in many countries worldwide (5). Many regions even in the most industrialized countries of the world are afflicted by iodine deficiency (6). While individual iodine intakes vary daily, urinary iodine excretion (UIE) is a reasonable population indicator of iodine status (7).

The newborn thyroid has limited iodine stores, and even mild deficiency will increase TSH secretion (8). Multiple factors other than maternal iodine status can influence measurements of TSH concentrations in newborns (9). Therefore, cutoffs originally proposed by the World Health Organization (WHO) (10) for defining severity of iodine deficiency on the basis of newborn TSH concentrations are not included in the latest recommendations (11, 12). While several studies have examined maternal UIE, newborn TSH levels, and their associations (13-26), only one has investigated UIE in 3 trimesters of pregnancy and its association with newborn's thyroid function (15). Since the Islamic republic of Iran has been declared IDD-free, we designed this study to assess UIE in the 3 trimesters of pregnancy and evaluate its association with thyroid function, among Tehranian newborns.

MATERIAL AND METHODS

This cross sectional study, performed in Tehran, an area of iodine sufficiency, included a total of 138 pregnant women referring to 2 mother-child health care centers in Tehran, the capital city of I.R. Iran consecutively from November 2005 to June 2006. The study was approved by the appropriate Human Research Committee of Shahid Beheshti University of Medical Sciences. Informed written consent was obtained from all subjects.

At initial presentation, before the end of the 1st trimester, 3 separate urine samples were obtained from each subject, and their median was considered as UIE in the 1st trimester. Mother's UIE was also measured one time in the 2nd and 3rd trimesters. Cord blood samples of all their newborns were evaluated for serum concentration of TSH, T_3, T_4, free T_4 (FT_4), T_3 resin uptake (T_3 uptake), and thyroglobulin (Tg). The median of 3 trimester UIE was calculated and pregnant women divided into 2 groups according to WHO recommendation (12): group I with median UIE<150 µg/l and group II with median UIE≥150 µg/l.

UIE was measured in random urine samples using a manual method based on Sandell-Kolthoff technique (26). Results were expressed as µg of iodine per liter of urine (µg/l). Serum total T_4, FT_4, and T_3 were measured by the radioimmunoassay method, TSH, Tg measurements were done by immunoenzymometric asaay using commercial kits [Izotop, Budapest, Hungray and Orgentec Diagnostic GmbH, Mainz, Germany, respectively, with gamma counter (Wallac Wizard, Wallac Oy, Turku, Finland)]. Intra and inter-assay coefficient of variations

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Table 1 - *Serum concentrations of TSH, T_4, free T_4 (FT_4), T_3, T_3 uptake and thyroglobulin (Tg) in cord blood of newborns of mothers with urinary iodine excretion <150 (group 1) and ≥150 µg/l (group 2).*

Group	T_4 (µg/dl)[a]	T_3 uptake (%)[b]	FT_4 (pmol/l)[b]	T_3 (ng/dl)[b]	TSH (mIU/l)[b]	Tg (ng/ml)[b]
Group 1 (no.=52)	10.8±2.5	26 (24-27)	15 (13-16)	65 (54-88)	7.3 (5.3-11.3)	23 (12-40)
Group 2 (no.=86)	10.8±2.4[a]	25 (24-27)	16 (14-17)	64 (48-80)	7.5 (5.5-10.3)	21 (14-32)

[a]Mean±SD; [b]median.

(CV) were 3.3% and 6.2% for T_4, 6.7% and 7.8% for T_3, 3.8% and 5.8% for FT_4, 3.9% and 7.1% for TSH and 2.3% and 2.3% for Tg, respectively. T_3 uptake was measured by enzyme immunoassay using Pishtazteb kit (Tehran, Iran). The intra and inter-assay CV were 2.5% and 3.3%, respectively. Tg was measured by immuno enzymometric assay using kit from Orgentec Diagnostica GmbH, Maniz, Germany. The intra- and interassay CV were 2.2 and 4.9%, respectively.

FT_4<11.69 pmol/l was considered abnormal (17). To define a cutoff for abnormal serum TSH concentration in cord blood, various values were found in literature from 13 to 30 mIU/l (17-19) therefore we compared TSH values >30, >20, and >13 mIU/l between the 2 groups.

Statistical analysis

The normality of UIE, in 3 trimesters and cord serum concentrations of T_4, T_3, FT_4, TSH, Tg, and T_3 uptake were checked using histograms and the Kolmogorov-Smirnov test. Since both methods showed non-normal distribution for all variables, with the exception of T_4, we employed non-parametric methods for the analysis of all variables and parametric method for T_4. To test differences in newborn thyroid function between the two groups, we used t test for T_4 and Mann-Witney test for other parameters. Analysis of variance and Kruskal Walis tests were used to evaluate any differences between newborn's T_4 and other newborn's thyroid parameters in quartiles of UIE, respectively. For detection of correlation between the newborn's thyroid function and mother's median and 3rd trimester UIE, Pearson test was employed; *p*-values <0.05 were considered significant.

RESULTS

Mean±SD age of pregnant women was 25.1±5.1 yr. Mean±SD gestational age was 11.9±3.6 weeks in the 1st trimester. All pregnancies were singleton and there was no twin pregnancy. There was no statistical difference in gestational age between 2 groups. In the 1st trimester, 43 (31%) women had median UIE<150 and 95 (69%) had median UIE≥150 µg/l; 1.9% of participants had UIE<50 µg/l, 9.9% between 50-99 µg/l, 19.4% between 100-149 µg/l, 36.3% between 150-250 µg/l, and 32.5% had UIE>250 µg/l. When median UIE of all 3 trimesters was considered, 52 (38%) pregnant women had median UIE<150 µg/l and 86 (62%) pregnant women had median UIE≥150 µg/l.

Median UIE in groups I and II in the 1st, 2nd, and 3rd trimesters were 125 (55-143) and 212 (150-488) µg/l, 97 (20-147) and 213 (155-400) µg/l and 93 (22-147) and 227(155-400) µg/l, respectively. Of all women sampled during 3 trimesters of pregnancy only 4 pregnant women had UIE<150 µg/l in all samples taken.

Table 1 shows serum concentrations of hormones in the cord blood of newborns in the 2 groups. No significant difference was seen in serum concentrations of T_4, FT_4, T_3, TSH, Tg, and T_3 uptake in newborns of mothers with UIE of <150 and ≥150 µg/l. There was no difference between UIE of mothers whose newborn had TSH<20 and newborns with TSH≥20 mIU/l. No significant correlation was found between mothers' UIE and newborns' serum TSH (Fig. 1) and Tg concentrations.

Serum concentration of thyroid hormones in cord blood according to quartiles of mothers' UIE has been shown in Table 2. No significant difference was seen in serum concentration of T_4, T_3 uptake, FT_4, T_3, TSH, and Tg in newborns of mothers with median UIE in various quartiles.

Table 3 shows the results of abnormal TSH and FT_4 in cord blood; no significant difference was found in number of abnormal tests between 2 groups. All 3 neonates with elevated TSH levels had transient hyperthyrotropinemia in cord blood.

DISCUSSION

The aim of this study was to obtain information on UIE during pregnancy and to evaluate the newborns' thyroid parameters in relation to iodine status of healthy pregnant Tehranian women living in an area of iodine sufficiency. The results showed no significant difference between thyroid functions of newborns of 2 groups of

Table 2 - *Serum concentrations of T_4, free T_4 (FT_4), T_3, TSH and thyroglobulin (Tg) cord blood of newborns according to quartiles of median maternal urinary iodine excretion (UIE) during the 3 trimesters.*

Quartiles	UIE (µg/l)[b]	T_4 (µg/dl)[a]	FT_4 (pmol/l)[b]	T_3 (ng/dl)[b]	TSH (mIU/l)[b]
1 (no.=34)	† 133	11.6±0.4	15 (14-16)	61 (45-87)	6.9 (4-10)
2 (no.=35)	134-174	10.5±0.5	14 (13-16)	66 (48-94)	6. 9 (4.9-8.9)
3 (no.=35)	175-241	11.0±0.4	15 (13-17)	65 (50-80)	7.2 (5.7-12.1)
4 (no.=34)	‡ 242	10.0±0.4	16 (14-17)	63 (50-81)	9.1 (6.1-12.2)

[a]Mean±SD; [b]median.

Table 3 - *Abnormal TSH and free T_4 (FT_4) concentrations in cord blood of newborns from mothers with UIE<150 (no.=52) and ≥150 µg/l (no.=86).*

Variable	Mothers' median UIE (µg/l)		p
	UIE<150	UIE≥150	
TSH>13 mIU/l	8 (15.4)	12 (14)	0.81
TSH>20 mIU/l	4 (7.7)	4 (4.7)	0.45
TSH>30 mIU/l	1 (1.9)	2 (2.3)	0.41
FT_4<11.69 pmol/l	2 (3.8)	5 (5.8)	0.92

*Number in parenthesis denote percentage.

pregnant women with median UIE≥150 µg/l and <150 µg/l. There was no significant correlation between mother's UIE and newborn thyroid function, which is compatible with other investigations in areas with mild to moderate iodine deficiency (8, 13, 14). Travers et al. reported results from a cross sectional study of 815 pregnant women and 824 newborns. The median UIC for pregnant women was 85 µg/dl, indicating mild iodine deficiency (8). UIE can vary from day to day and there is a wide intrapersonal variation in UIC values from <50 to >500 µg/l among pregnant women residing in iodine-replete areas, supporting the notion that casual UIC would not reflect iodine status of an individual; thus in epidemiologic studies the median UIC must be considered to determine the status of iodine nutrition (27). Although there was no statistically significant linear correlation between neonatal whole-blood TSH level and maternal UIC, mothers with a UIE<50 µg/l, were 2.6 times more likely to have a baby with a TSH level >5 mIU/l. The Mceldulf et al. study, conducted in an area with mild iodine deficiency, showed no predictable relationship between maternal UIC and neonatal TSH concentration (13). Nohr et al. found that iodine supplementation of the mother did not improve fetal thyroid function in areas with mild iodine deficiency (14). These data are in contrast with results of the Jaruratanasirikul et al., which demonstrated 32% of pregnant women had UIE<100 µg/l that was found to be associated with neonatal TSH concentration >5 mIU/l (21).

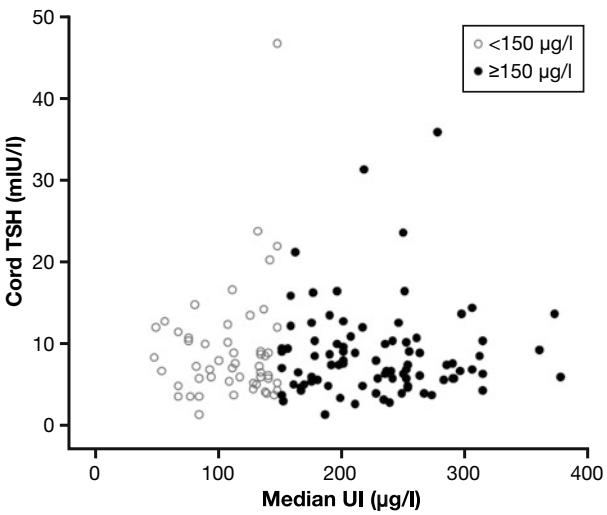

Fig. 1 - *Correlation between urinary iodine concentration of pregnant women and the cord serum concentration of TSH in cord blood; open circle: maternal median urinary iodine excretion (UIE) <150 and closed circle: maternal median UIE ≥150 µg/l.*

We showed that maternal UIE has no correlation with cord Tg, a marker of iodine deficiency, a finding which is in contrast with 2 other studies (28, 29); however, the median UI of pregnant women in those studies were 36 and 55 µg/l, respectively.

Our results are somewhat in contrast with the findings of studies suggesting that thyroid function of newborns is significantly correlated to maternal iodine intake. This is because all other studies have been done in areas of iodine deficiency and another reason may be the time of newborn's thyroid function assessment and definition of abnormal newborn's thyroid function. In addition, it should be considered that the transient TSH elevation observed in iodine-deficient areas might be induced by iodine excess from, e.g., the use of iodine-containing disinfectants in mothers. This is why some studies have recommended cord blood sampling, because cord blood is less influenced by pre-natal factors (17, 30, 31).

This study has a few limitations. The cross sectional design of the study limits cause and effect determination. In addition, we did not follow the newborn to determine effects of maternal iodine UIE levels on cognition and growth in the future.

The variation in UIE during pregnancy is of great interest. While 38% of pregnant women had median UI of 3 trimesters <150 µg/l, only 4 pregnant women had UIE<150 µg/l in all samples taken during pregnancy. This emphasizes that this indicator should not be used for the purpose of evaluation of iodine nutrition in individual pregnant woman. Therefore the cutoff median UI of 150 µg/l proposed by WHO technical consideration (12) remains the best indicator to use in population surveys to assess iodine nutrition of pregnant women.

In conclusion, this study confirms that in areas with well-established effective and sustained universal salt iodization program, the amount of iodine stored in the thyroid of a child at birth and its thyroid functions are normal.

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Conflict of interest

None declared.

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