EVALUATION OF URINARY IODINE LEVELS AND THYROID FUNCTION TESTS IN PREGNANT WOMEN AND THEIR INFANTS

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Abstract

Introduction. In this study we aimed to evaluate urinary iodine excretion and the serum levels of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4) and thyroglobulin (Tg) in pregnant women and their newborn infants.

Materials and Methods. This study was performed in Konya Faruk Sukan Children and Maternity Hospital, Konya Beyhekim State Hospital and Hospital of Selcuk University Medical Faculty. 180 pregnant women and their healthy infants born at 37-40 gestational weeks. Term infants included in this study were aged between 1-7 days, healthy. Midurination urine samples were taken into deiodinized plastic bottles and 2 mL of these samples were aliquoted to deiodinized eppendorf tubes.

Results. Median urinary iodine concentration (UIC) was 95.5 µg/L for pregnant women and 245 µg/L for their infants. Frequency of iodine deficiency was observed as 63.3% (n=114) (<150 µg/L) and 24.4% (n=44) (<100 µg/L) in mothers and their infants, respectively. UIC of the infants whose mothers used iodized salt was significantly higher than the one whose mothers used rocksalt (p=0.030).

Conclusions. It was stated in our study that UIC of pregnant women was lower than the target limit (<150 µg/L), suggested by World Health Organisation (WHO) and iodine deficiency in pregnant women is still a problem in our city located in the centre of Turkey. Iodine deficiency was observed in 24.4% of the infants and this prevalence suggests us that iodine deficiency is still an important health problem in infants.

Key words: urinary iodine, thyroid function tests, pregnancy, infants.

INTRODUCTION

Iodine is an essential element for the production of hormones, triiodothyronine (T3), and thyroxine (T4). Women need more iodine during pregnancy to maintain normal metabolism as well as to meet the requirements of T4 and iodide transfer to the fetus (1). Brain development may be irreversibly affected in iodine deficiency during intrauterine period

and postpartum first three months. Iodine deficiency and hypothyroidism during pregnancy have long been known to be associated with abortion, stillbirth, congenital abnormalities, increased rates of perinatal mortality, endemic cretinism in fetal period (2-4).

Iodine deficiency is still a serious health problem all over the world especially in the pregnant women and the children (5). Approximately 140 million people are at risk of iodine deficiency in Europe. 700 millions people among the world (13% of the world population) and 100 millions in Europe are affected from goiter. Mental retardation is seen in 1 million of this affected population in Europe and more than 11 million cases with cretinism exist among the world (6, 7).

Recommended daily intake in pregnancy and lactation is 250 µg (8). Suggested daily intake of iodine by UNICEF (United Nations International Children's Emergency Fund), ICCIDD (International Council for Control of Iodine Deficiency Disorders) and WHO (World Health Organization) for preschool children (0-59 months), school aged children (6-12 years), adolescents and adults (>12 years), and pregnant and lactating women are 90 µg, 120 µg, 150 µg, and 250 µg, respectively (8).

According to the results of epidemiological studies in Turkey, mild and intermediate iodine deficiency is still a problem in our country (4, 9, 10). Researches indicating the status of iodine intake in the term pregnant women and infants in our country are limited. Therefore we aimed to evaluate urinary iodine excretion and serum levels of TSH (Thyroid-Stimulating Hormone), fT3, fT4 and thyroglobulin in the term pregnant women and their newborn infants in Konya located in the centre of Turkey.

MATERIALS AND METHODS

Patient recruitment

This study was performed in Konya Faruk Sukan

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Children and Maternity Hospital, Konya Beyhekim State Hospital and Hospital of Selcuk University Medical Faculty between July and September 2011 after approval of the protocol by the ethics committee of Selcuk University Medical Faculty (November 25, 2010- 2010/34). A total of 180 pregnant women, aged between 16-40 years (at gestational weeks of 37 and over) who lived in the centre and districts of Konya and their newborn infants (n=180) were included in this study. Term infants included in this study are aged between 1-7 days, healthy and without any symptoms of asphyxia and abnormalities. Written informed consents were obtained from all the term pregnant women contributed in this study. A questionnaire was also performed for all the pregnant women in order to have information about education, health status, pregnancy period, number of births, drug and multivitamin use during pregnancy, topical iodine application, habit of salt intake and ingredients of salt used at home, smoking status and frequency of seafood intake of the participants.

Determination of urinary iodine levels

Urine samples were obtained from the women before delivery, in the third trimester and from the infants at 1-7 days after the birth as morning urine samples. Midurination urine samples were taken into deionized plastic bottles and 2 mL of these samples were put into aliquoted to deionized eppendorf tubes. All urine samples were stored at -80 °C until analysis, thawed before analysis, centrifuged at 800 g for 3 minutes and the supernatants were used for measurement of urinary iodine levels.

Determination of urinary iodine levels were performed with the colorimetric method based on seric-arsenide reaction described by Sandell-Kolthoff which was suggested by WHO and ICCIDD, and the results were estimated as µg/L. This method was linear up to 20 µg/L and intra and inter-assay CV values were 6.45%-9.89%, respectively.

Reference ranges

The classification of iodine deficiency in mothers was based upon urinary iodine excretion as suggested by WHO: <150 µg/L: deficient, 150-249 µg/L: sufficient, 250-499 µg/L: over intake, >500 µg/L: severe over intake. Grading of deficiency: 100-149 µg/L: mild iodine deficiency, 50-99 µg/L: moderate iodine deficiency, and <50 µg/L: severe iodine deficiency. Iodine status in infants was assumed as <100 µg/L: deficient, ≥100 µg/L: sufficient (8).

Reference ranges of TSH for pregnant women at third trimester and infants (cord blood) were defined as 0.3-3.00 mIU/L and 2.3-13.2 mIU/L, respectively (11-13). Analytical range for fT4 is 0.23-7.77 ng/dL. Reference ranges of fT4 for pregnant women at third trimester and infants (cord blood) were defined as 0.7-1.2 ng/dL and 1.7-4.0 ng/dL, respectively (12, 14). Analytical range for fT3 is 0.260-32.55 pg/mL. Reference ranges of fT3 for the pregnant women at third trimester and infants (cord blood) were defined as 2.0-3.3 pg/mL and 0.15-3.91 pg/mL, respectively (12, 14). Analytical range for thyroglobulin test is 0.1-1000 ng/mL. Reference ranges of thyroglobulin for pregnant women at third trimester and infants (cord blood) were defined as 1.4-69 ng/mL and 15-101 ng/mL (13, 14).

Analysis of thyroid function tests

Venous blood samples were obtained from the mothers after cleaning the antecubital area with 70% ethanol before labor and from the cords of the infants. Topical iodine application for umbilicus disinfection was not applied to any of the infants after the birth, following removal of placenta. TSH, fT4, fT3 and thyroglobulin levels were determined with electrochemiluminescent method on Hitachi Modular E170 (Roche Diagnostics, USA) using original Cobas reagents (Roche Diagnostics, USA). Detection range for TSH is 0.005-100 mIU/L.

Statistical analysis

SPSS (version 16.0) was used for statistical evaluation of the data. Descriptive statistics was performed, distribution pattern of the numeric data were tested with Shapiro Wilk test. Chi-square test was used for evaluation of the categorical parameters. Mann-Whitney U and Kruskal Wallis tests were used for comparison of medians. Pearson and Spearman correlation analyses were also performed for testing the relations between the parameters. p<0.05 was assigned as statistically significant.

RESULTS

Mean age, body height and weight of women were 25.68±5.04 years, 161±5.20 cm, and 75.53±10.43 kg, respectively. 5% of participant mothers were smokers and mean cigarettes were 5.66±4.55 number/day (min=1-max=15 number/day). Mean gravida was 2.20±1.29. 96.7% (n=174) of the pregnant women used various medications including iron-multivitamin supplements at least one month duration during

Table 1. Thyroid function tests of the pregnant and infants

	Pregnants				Infants			
	n=180				n=180			
	Mean	SD	Median	Min-Max	Mean	SD	Median	Min-Max
TSH (mIU/L)	3.11	2.12	2.59	0.50-19.93	8.80	6.29	6.92	1.00-50.07
fT4 (ng/dL)	1.03	0.17	1.03	0.69-1.58	1.32	0.17	1.32	0.81-1.90
fT3 (pg/mL)	2.68	0.50	2.68	0.66-4.17	1.58	0.46	1.57	0.63-3.36
Tg (ng/mL)	29.86	44.06	19.50	0.10-403.90	82.11	54.21	72.64	1.88-420

Table 2. The relation between iodine status and TSH levels of pregnant

Median TSH of pregnant IU/L)	p	
Iodine status of pregnant		
Deficiency (≤ 149 $\mu\text{g/L}$)	2.76	
Sufficient (150-249 $\mu\text{g/L}$)	1.56	
Overintake (>250 $\mu\text{g/L}$)	2.42	0.004**

**Kruskal-Wallis variance analysis

their pregnancies, while 3.3% (n=6) did not use any medications. Iodine supplements were not applied to none of the mothers. The percent of women eating iodized salt was 92.2% (n=166) and the percent of women eating rocksalt was 7.8% (n=14). Our results for iodized salt consumption rates were 92.8% in general, 94.9% in city center and 72.7% in districts or villages of Konya. 61.7% (n=111) of the term pregnant used lower than 8 gr iodized salt daily and 30.6% (n=55) of them used more than 8 gr iodized salt daily.

All of the pregnant women did not use iodine supplements during the pregnancy. None of the pregnant women were diagnosed with hypothyroidism before pregnancy or took thyroid hormone replacement. But, 38% (n=70) of women had TSH levels over 3 mIU/L based on the blood tests evaluated in our study.

Demographic characteristics of the infants were as follows: Mean gestational weeks: 39.67 ± 0.84 weeks mean birth weights: $3330.0 \pm 445.09\text{g}$, mean birth stature 50.12 ± 1.24 cm. Delivery types of the infants were 87.2% (n=157) as spontaneous vaginal, 12.8% (n=23) as cesarean section. 67.2% (n=121) of the infants were male, and 32.8% (n=59) were female.

Urinary iodine levels and thyroid function tests of the term pregnant women

Median urinary iodine levels of the term pregnant women were 95.50 $\mu\text{g/L}$. The frequency of iodine deficiency ($<150\mu\text{g/L}$) in the term pregnant women was 63.3% (n=114). When urinary iodine excretion levels were evaluated, 32.8% (n=59) were

presenting severe (0-49 $\mu\text{g/L}$), 18.9% (n=34) moderate (50-99 $\mu\text{g/L}$), and 11.7% (n=21) mild iodine deficiency (100- 149 $\mu\text{g/L}$). 9.4% of it (n=17) was sufficient (150-249 $\mu\text{g/L}$), 9.4% of it (n=17) was overintake (250-499 $\mu\text{g/L}$), and 17.8% of it (n=32) was severe overintake (>500 $\mu\text{g/L}$). Thyroid function tests of the participants were presented in Table 1.

Urinary iodine levels and thyroid function tests of the infants

Median urinary iodine levels of infants were 245.00 $\mu\text{g/L}$. 24.4 % (n=44) of infants' iodine status were deficient (<100 $\mu\text{g/L}$) and 75.6% were (n=134) sufficient (≥ 100 $\mu\text{g/L}$). Thyroid function tests of the infants were presented in Table 2.

Urinary iodine levels in infants whose mothers used iodized salt were significantly higher than the ones whose mothers used rocksalt (p=0.030).

When we categorized iodine status of the term pregnant women we have determined that TSH levels were the lowest in the term pregnant women with sufficient urinary iodine levels. Because all three median TSH values in iodine deficiency, sufficiency and excess group are within the normal range for the third trimester of pregnancy (p=0.004) (Table 2). Categorized iodine status of the term pregnant women did not reflect TSH levels of the infants (p>0.05).

Thyroglobulin levels in infants whose mothers used rocksalt were significantly higher than the ones whose mothers used iodized salt (p=0.007) (Table 3). The term pregnant women who used iodized salt in their diets presented lower thyroglobulin levels compared to the ones who used rocksalt, but this difference was not statistically significant (p=0.058). TSH levels were not significantly different in terms of salt used (p=0.085). Thyroglobulin concentrations were significantly lower in infants from nullipar women than in infants from the multipar ones (p=0.012), and it were also higher in infants with normal vaginal delivery than infants with cesarian section (p=0.008). Infants with deficient

Table 3. The relation between salt consumption of pregnant, delivery characteristics and iodine status of infants and thyroglobulin levels of infants

	Median thyroglobulin (ng/mL)	p
Characteristics of salt		
Rocksalt	105.22	0.007*
Iodized salt	72.32	
Parity		
Nullipar	62.82	0.012**
Primipar	76.78	
Multipar	89.12	
Labour		
Normal vaginal labour	77.06	0.008*
Cesarian section	58.20	
Iodine status of infants		
Sufficient (≥100 µg/L)	66.84	0.058*
Deficient (<100 µg/L)	89.44	

*Mann Whitney U test. **Kruskal-Wallis variance analysis.

iodine status had higher cord blood thyroglobulin concentrations than the infants with sufficient iodine status, but this difference was not statistically significant ($p=0.058$) (Table 3).

Thyroglobulin levels of the term pregnant women who stored iodized salt in proper saltcellars were significantly lower than the ones who did not ($p=0.032$). The term pregnant women from city centers presented significantly lower thyroglobulin concentrations than the term pregnant women from the villages and the districts ($p=0.009$) (Table 4).

Although median urinary iodine excretion of the infants were higher than the term pregnant women's urinary iodine excretion, the difference was not statistically significant ($p>0.05$).

Table 4. The relation between thyroglobulin status and the salt consumption and settlement of the pregnant

	Median thyroglobulin (ng/mL)	p
Characteristic of the salt used		
Rocky salt	42.02	0.058*
Iodized salt	19.10	
Saltcellar		
Improper	20.28	0.032*
Proper	11.97	
Settlement		
City center	18.72	0.009*
District or village	26.85	

*Mann Whitney U test.

DISCUSSION

Iodine deficiency is still a serious health problem in pregnant women and children all over the world. 31% (1909.9 million) of the world's population are assumed to be iodine deficient and the South Asia and Europe are mostly affected. Currently 70% of the individuals are suggested as using iodized salt (5, 8). This prime investigation showed that pregnant women and their newborns in the middle Anatolia have iodine deficiency as assessed by maternal urinary iodine concentration (UIC) (63.3% of pregnant women had UIC < 150 µg/L).

In Turkey Demographic and Health Survey study (TDHS) 2008 report rates of iodized salt consumption in our country are 85.3% in general, 89.9% in city centers, 71.5% in districts and 92.5% in west middle Anatolia covering Konya (15). Our results

Table 5. Urinary iodine excretion of pregnant and infants and rates of iodine deficiency in our country and other countries

		Year	n	Pregnant UIC(µg/L)			n	Infant UIC (µg/L)		
				<100 µg/L		<150 µg/L		<100 µg/L		<50 µg/L
				Median	%*	%*		Median	%*	%*
Turkey										
Bolu(16)	Şimsek et al. 2005	1999-2002	212	31.4	-	-	212	62.2	-	-
Duzce (16)	Şimsek et al. 2005	1999-2002	212	44.2	-	-	212	82.7	-	-
Zonguldak(16)	Şimsek et al. 2005	1999-2002	212	75.2	-	-	212	154.6	-	-
Kayseri(17)	Kurtoğlu et al. 2004	2004	70	30.2	90	-	70	23.8	-	63
Malatya(4)	Egri et al. 2009	2005	824	77.4	83.3	-	-	-	-	-
Istanbul(18)	Gültepe et al. 2005	2005	124	128.0	36.7	-	-	-	-	-
Adana(19)	Kut et al. 2010	2006	141	149.7	-	49.6	-	-	-	-
Kayseri(20)	Budak et al. 2009	2008	70	70.2	54.3	-	70	100.0	31.4	-
Outlanders										
Iran(21)	Ordookhani et al. 2007	2004-2005	48	107.0	-	79.1	48	271.0	-	-
India(22)	Chakraborty et al. 2006	2005	267	144.0	21.7	-	-	-	-	-
France(23)	Raverot et al 2012	2009	228	81.0	-	77	-	-	-	-
Swiss(24)	Andersson et al. 2010	2009	648	162.0	-	47	368	91.0	58	-
Spain(1)	A-Pedrerol et al. 2010	2010	600	104.0	-	72	-	-	-	-

*(<100 µg/L for pregnant before 2007, <150 µg/L for pregnant after 2007, <50 µg/L for infants before 2007, <100 µg/L after 2007 (2,8))

for salt consumption rates are similar with results of TDHS 2008. These rates were reported to be increased by time and differ in residences or cities. In our study we have determined that iodized salt consumption rate is significantly higher in the term pregnant women living in city centers ($p=0.001$). This result suggests that iodized salt consumption is still unsatisfactory in districts and villages, therefore educational programs are needed for consciousness to use iodized salt in these residences.

In Table 5 the results of the researches carried on iodine status of the term pregnant women and infants in Turkey and the other countries were presented. Median urinary iodine levels in other countries were higher than the levels of our study and the other studies in our country. These levels demonstrate that although consumption rate of iodized salt increased by time in our country, iodine deficiency is still a serious problem in the term pregnant women in our country. Therefore iodination of salts and educational programs for women in fertile period in order to inform about iodine enriched diets and iodine supplementation in cases diagnosed as iodine deficient should be continued.

The rates of iodine deficiency in infants are lower than the term pregnant women in national and international reports, and do not reflect the deficiency in the term pregnant women. Although the main reason for this was not clarified exactly, perinatal iodine exposure may cause this situation (16).

We did not find any significant relation between iodized salt consumption of the term pregnant women and urinary iodine levels ($p>0.05$). Similarly, urinary iodine excretion was not significantly affected by iodized salt consumption as reported by many other authors (1, 4, 19, 24). In our study urinary iodine concentrations did not differ between the groups with and without salt restriction ($p>0.05$). All of these results suggest that iodized salt consumption in the term pregnant women is important but not satisfactory alone.

Urinary iodine levels were significantly higher in infants of the term pregnant women who used iodized salt than the ones who used rocksalt ($p=0.030$). In literature review we did not meet any report evaluating the impact of salt quality on urinary iodine levels of infants, while there are some reports which demonstrated the effect of mother's iodine status on thyroid function of the mother (25), and the iodine status of the infant (21). There is a few number of surveys on infants dealing this issue, therefore further detailed studies are needed.

Raverot *et al.* found median Tg levels during pregnancy were higher than the non pregnant women (23). In our study we determined higher Tg levels in the infants whose mothers used rocksalt. TSH levels of the mothers and the infants were weakly positively correlated with their Tg concentrations. Tg levels elevate because of increased thyroid stimulus in order to achieve euthyroidism in iodine deficient residing areas (23).

According to WHO, when determining iodine sufficiency the prevalence of neonatal TSH elevation should be lower than 3% by measuring TSH in cord blood or in serum of 3 day old infants. If this rate was 20-49.9% a moderate iodine deficiency exists (5). In our study we have found a prevalence of 27.8%, and this supports that our city is an area with moderate iodine deficiency. But high median urinary iodine excretion in infants with high TSH levels suggests that this might be as a result of perinatal iodine exposure due to the use of povidone iodine for antisepsis during childbirth. Hypo or hyperthyroidism will occur due to sudden iodine intake in iodine deficient population. The risk of thyroid insufficiency is related with the degree of existing iodine deficiency and the speed of iodine intake (26). Iodine overload will occur especially in infants with exposure of iodine deficiency in fetal period. The observations suggest that Wolff-Chaikoff effect may occur in infants with iodine deficiency during intrauterine period (27). This probability can be eligible for the infants in our study. We suggest that the infants were exposed to iodine deficiency during fetal period because we have detected iodine deficiency in 63.3% of the term pregnant women in our study. Therefore further studies with reevaluation of iodine status in the term pregnant women and iodine deficiency and perinatal iodine exposure in infants and the results of these situations by obstetricians and pediatricians are needed.

In conclusion, urinary iodine excretion of the term pregnant women in Konya is lower than the target level of WHO (150 $\mu\text{g/L}$) and therefore iodine deficiency is still a significant problem in our city.

Conflict of interest

The authors have no relationship with any industry.

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