Original Investigation

Iodine deficiency in pregnant women at first trimester in Ankara

Koyuncu et al. Iodine deficiency

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Abstract
Objective: Iodine deficiency in pregnant woman in Ankara was shown in previous studies. We aimed to conduct a study in a tertiary center to investigate for the need for iodine replacement in our population.
Material and Methods: This was a single tertiary center, non-interventional, retrospective, cross-sectional study. Data were retrieved retrospectively from 440 women who had been in first trimester in gestational age. Maternal iodine status, TSH levels, T4 levels were examined. Urinary iodine concentration (UIC) was calculated based on Sandell-Kolthoff reaction which is a colorimetric method. We excluded patients with previous thyroid disease or current thyroid disease. Thyroid hormones and TSH were measured by chemiluminescence immunoassays.
Results: Iodine deficiency prevalence (UI <150 μg/L) was 84.7 % in first trimester of pregnancy in our population. The median UIC was 81.6 (1-450) μg/L, indicating iodine insufficiency. All the patients declared iodized salt use. None of the patients were taking iodine replacement. The mean TSH level was 1.53±1.27 mIU/l, (0.01 mIU/l-14.74 mIU/l) and mean T4 levels was 12.51±5.01 mIU/l, (7.09 mIU/l, -23.7 mIU/l). TSH levels of 56 patients were higher than 2.5 mIU/l. According to these results 12.72% of the patients had subclinical hypothyroidism based on serum TSH and Free T4 levels. Isolated hypothyroxinemia was present in one patient.
Conclusion: Our study demonstrated that pregnant women still suffer from iodine deficiency in Ankara despite of mandatory iodine salt use. Iodized salt use does not provide enough iodine supplement especially in pregnant women. Iodine supplementation is shown to enhance neurological development and psychomotor performance. We suggest that iodine should be a part of routine laboratory evaluation at the first prenatal visit for its importance in early pregnancy. Also, iodized salt use education should be provided to the women to eradicate iodine deficiency. Iodine supplements should be recommended to all pregnant women in addition to iodized salt. (J Turk Ger Gynecol Assoc 2018)
Keywords: Iodine deficiency, pregnancy

Introduction

Iodine deficiency is still a serious public health problem all over the world despite of th efforts (1). In previous studies iodine deficiency status was determined by calculating urinary iodine concentration (UIC) in school age children (2). If median results of urinary iodine levels were below 100 μg/L, it is concluded that iodine intake is insufficient in the whole population (3). WHO suggest classification for UIC; which is enough between 150-249 μg/L, insufficient if it is below 150 μg/L and excessive above 250 μg/L (3).
Iodine status is important in pregnancy because of its importance of maternal thyroid hormone production for fetal central system maturation (4). Severe iodine deficiency was found to be associated with mental retardation, decreased brain development and low intelligence (5,6). Physiological changes in pregnancy such as increased glomerular infiltration and developing fetal thyroid gland increases the need for iodine beginning at the early weeks of pregnancy. The WHO recommends 250 μg/L iodine intake for pregnant and lactating women (7).
Iodine deficiency may cause diffuse or nodular goiter, hypothyroidism and hyperthyroidism. Although there are approved treatment modalities for hypothyroidism and hyperthyroidism in pregnancy, treatment of subclinical hypothyroidism is still controversial. A recent meta-analysis showed that subclinical hypothyroidism is relevant to lower intelligence and motor scores in children (8). In some studies, subclinical hypothyroidism were reported to relate with increased risk for low birth weight, premature delivery, fetal distress and fetal growth

restriction (9,10). Subclinical hypotyhroidism should be treated with 50 μg/daily LT4 before conception or during gestation (11,12).

Iodine status can be assessed by measurement of urinary iodine concentration, thyroid size, thyroglobulin and neonatal serum TSH (13,14). UIC indicates current iodine nutrition on the other hand other methods reflect long term iodine status. Iodination of salt is the first choice for iodine replacement (15,16).

After recognizing iodine deficiency from the studies in Turkey, Ministry of Health oblige companies to iodinate table salt and sell it in proper storage since 1994. It is shown that after a one-decade mandatory iodine prophylaxis was enough to eradicate goiter among school children (16). Ankara was shown to be an iodine-sufficient region of Turkey (median UIC in SAC; 135 μg/L), after mandatory iodization of salt (16).

Here we aim to show the iodine status in pregnant women in Ankara and clarify the need for iodine replacement with iodine supplementation.

Material and Methods

The present study was carried out in a tertiary center, between January - July 2016. 460 women who applied hospital for the first visit of pregnancy were retrospectively analyzed. Mean age of the pregnant women was 27.8∓5.71 years. Median gestational age of the patients was 7 weeks (6- 10 weeks). Patients were evaluated for fasting blood and urine samples for routine first trimester visit. Thyroid-stimulating hormone (TSH), free triiodothyronine (T3) and free thyroxine (T4) levels were assessed from the serum. Immunochemiluminescent assays performed on an automated analyzer (Advia Centaur XP; Siemens) were used to measure levels of TSH, free T3 and free T4. The UIC was determined with a colorimetric method based on the Sandell–Kolthoff reaction as recommended by WHO and ICCIDD, using Fisher reagents (17). The analytical sensitivity was 2 μg/L. The coefficient of variation <5% for measurement range.

A single spot urine analysis was taken from the patients in the morning (between 09.00 and 12.00 hours) and stored in de-iodized I tubes at −40°C. UIC was measured using the spectrophotometric method described by Sandell & Kolthoff. The coefficient of variation in the range investigated was <5%. Normal serum T3 and T4 values for nonpregnant women were 3.99-6.71 pmol/L and 7-15.96 pmol/L respectively. Results showed inter- and intra-assay coefficients of variation <5% for measurement range. Ensuring the Quality of Iodine Procedures (EQUIP), Center for Disease Control programme, has been carried out in our laboratuary since 2000 four times in a year. Laboratory external control reports has shown a success rate of 85–90 %.

Patients were excluded if they were on thyroid medication or were known to have thyroid diseases like thyroiditis or hypo-hyperthyroidism. 20 patients were excluded due to these reasons, so study was concluded with 440 patients.

Data were analyzed using SPSS software (Statistical Package for the Social Sciences, version 15.0; (SD) or, if not normally distributed, as medians (ranges). Statistical analysis was performed using parametric (v2 - and Student's t-tests) or nonparametric (Fisher's exact and Mann–Whitney U-tests) tests, when appropriate. Values for P <0·05 were accepted as statistically significant. The study was approved by the Ethics committee of Ankara University School of Medicine (Approval No: 12-568-16).

Results

440 pregnant women whose ages were between 17 to 45 years (27.86 ± 5.71) were enrolled for this study before 12 weeks of gestation. Median weeks of gestational age was seven. We found that the median UIC was 81.6 μg/L (1–414 μg/L) in pregnant women, which was described as insufficient iodine intake according to the WHO criteria. UIC was below 150 μg/L in 373 women (86.7 %), 9 (2.04%) women had UIC above than 250 μg/L and only 58 women (13.24 %) had adequate iodine intake. UIC in the study group was shown in Table 1. UIC were below 50 μg/L in 149 patients (33. 6%). None of the patients had UIC levels higher than 500 μg/L. The prevalence of iodized salt consumption was 100 %. Of the 440 patients, 56 (12.72%) patient TSH levels were found to be higher than 2.5 mIU/l with normal FT4, diagnosed as subclinical hypothyroidism. One patient (0.22%) had isolated hypothyroxinemia, with low FT4 (<7 pmol/L) and normal TSH concentrations. Thyroid values were shown in Table 2. We couldn't find significance correlation between TSH and urinary iodine. (Spearman's correlation coefficient is -0.009 p= 0,874) Patients with subclinical hypothyroidism were treated with 50 mcg levothyroxine. Isolated hypothyroxinemia was treated with only iodine replacement. Also, patients with iodine deficiency were given iodine replacement.

Discussion

Iodine deficiency is still a public health problem in Turkey (18). Although mandatory iodine salt, studies showed mild to severe iodine deficiency in pregnant population (19). Urinary iodine concentration (UIC) level has been accepted as a good indicator for assessing iodine status (18). Although studies in school age children showed enough iodine intake after mandatory iodized salt, it does not precisely represent iodine status in pregnant women (20). In our study we found that iodine deficiency is still high in pregnant population. Median UIC levels were found to be 81.67 μg/L, and were below 50 in 33.6 % of patients in this study. And this area

was found to be iodine sufficient area in previous studies which used school age children urinary iodine status (19).
Iodine deficiency is known to have an adverse effect on fetal development (20). Iodine is the essential component of thyroxine and triiodothyronine. Proper iodine replacement is necessary for appropriate development of the fetus (3). Thyroid hormone is essential for normal maturation of the central nervous system (21). Fetus is completely depending on maternal T4 during the first trimester of pregnancy. The production of TSH by the fetal pituitary gland start from week 18-22 of gestation. The production of fetal thyroxine starts from week 22-24.
Severe iodine deficiency was found to be associated with fetal hypothyroidism, mental impairment and increased neonatal and infant mortality (22). Hynes et al showed that even mild iodine deficiency has long-term adverse impacts on fetal neurocognition and these adverse effects cannot be reversed by replacement in childhood (23). Rydbeck et al also showed that birth weight and length increased by 9.3 g (95% CI: 2.9, 16) and 0.042 cm (95% CI: 0.0066, 0.076), respectively, for each 0.1-μg/L increase in maternal UIC (24). Bath et al also conducted a study known as ALSPAC in 1040 pregnant woman in their first trimester (21). They compared children IQ scores at the age of 8 and reading ability at the age of 9, and they found that children whose mother had UIC less than 150 mg/g in pregnancy, had lower IQ scores and reading accuracy (21).
Oral E and et al showed that 90% of the pregnant women are lacking iodine in their pregnancy in Istanbul which is defined as iodine-sufficient city and salt iodization program was not an efficient for pregnant population (25). Kutlu et al assessed pregnant women who are in their second trimester in Ankara and they also find that 72.8% of the woman had iodine deficiency (19). Despite mandatory iodized salt use, iodine deficiency can be explained by inconvenient storage or consumption of iodized salt. Erdoğan et al showed that only 56.5% people consumed iodinised salt at home which is lower than WHO suggestion, 90%, to eradicate iodine deficiency (18). Anafaroğlu et al also showed that 64.9% of the patients used salt inappropriately in cooking process and only 25% of the patients used proper containers for iodized salt (26,27).
Limitations of this study includes patients' knowledge about iodized salt and their socioeconomic status. Besides this was a single center study in the capital city of Turkey which may not reflect status of the rural areas.
In this study we found iodine deficiency were not eradicated despite of mandatory iodized salt use similar with the literature. Iodine status should be assessed in pregnant women, and proper iodine replacement should be advised to the patients even before pregnancy. To be successful to eradicate iodine deficiency, from iodination to cook process, every step must be checked. One mistake in these steps result in inadequate iodine intake. Iodized salt use education may be given to the pregnant women as a part of pregnancy education class. Attention should be given while buying salt, in order to not to take incorrect salt types. Proper iodine replacement should be given to all pregnant woman in company with iodinised salt use.

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Table 1. Urinary iodine concentration in pregnant woman

Reference ranges for median UIC (μg/L)	Number of pregnant woman	TSH mean range (mIU/l)
<50	149 (33.8%)	1.47∓1.34

<100	286 (65%)	1.46∓1.21
< 150	373 (84.7%)	1.49∓1.33
150-249	58 (13.18%)	1.36∓0.80
250-499	9 (2.04%)	1.50∓1.12

Table 2. Thyroid values of study population

	* Normal range	Mean SD	Median (range).
T3 (pmol/L)	3.99-6.71	4.67∓0.60	4.7 (3.3-6.33)
T4 (pmol/L)	7-15.96	13.99∓2.68	13.95 (7.09-23.07)
TSH (mIU/l)	0,1-2,5	1.53∓1.27	1.37 (0.01-23.7)

*TSH normal ranges calculated from non-pregnant population.