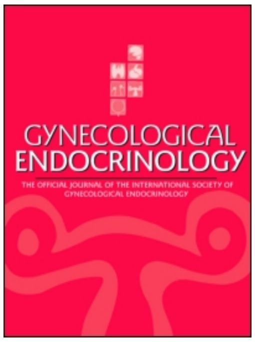

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ORIGINAL ARTICLE

Iodine status of pregnant women in a metropolitan city which proved to be an iodine-sufficient area. Is mandatory salt iodisation enough for pregnant women?

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Abstract

The objective of this study was to assess the iodine status of pregnant women in a metropolitan city which was stated as iodine sufficient area after salt iodination program. This multicenter, cross-sectional study was carried out on 3543 pregnant women. Age, gestational weeks, smoking, consumption of iodized salt, dietary salt restriction, history of stillbirth, abortus and congenital malformations were questioned. Spot urine samples were analyzed for urine iodine concentration (UIC). The outcomes were: (a) median UIC in three trimesters of pregnancy and (b) frequency of ID among pregnant women. The median UIC was 73 µg/L. The median UIC was 77 µg/L (1–324), 73 µg/L (1–600) and 70 µg/L (1–1650) in three trimesters of pregnancy, respectively (p: 0.14). UIC <50 µg/L was observed in 36.6% (n: 1295) and UIC<150 µg/L was observed in 90.7% (n: 3214) of pregnant women. Only 1% (n: 34) of the pregnant women had UIC levels higher than 500 µg/L. This study showed that more than 90% of the pregnant women in this iodine-sufficient city are facing some degree of iodine deficiency during their pregnancy. A salt iodization program might be satisfactory for the non-pregnant population, but it seems to be insufficient for the pregnant population.

Keywords

Iodine deficiency, iodine status, iodine-sufficient, pregnancy, salt iodination

History

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Introduction

Iodine deficiency (ID) is a matter of public health and has considerable consequences other than endemic goiter, otherwise known as iodine deficiency disorders (IDD). Neonatal hypothyroidism, growth retardation, and cretenism are the results of severe ID [1]. The most critical period for ID is the second trimester to three years period, when cerebral development is substantially completed [2].

Iodine requirement which is 150 µg/d increases to over 250 µg/d during pregnancy due to elevated thyroxin synthesis, iodine transfer to fetus, and increased renal clearance [3]. Neuronal migration and myelination of fetal brain requires iodine. Thus, insufficient intake of iodine during pregnancy may cause permanent fetal brain damage [4].On the other hand, the effect of mild–moderate ID on the long-term neuromotor development of fetus is not yet well established. Reanalysis of Avon Longitudinal Study of Parents and Children (ALSPAC) cohort confirmed that children of women with ID had lower scores for verbal IQ, reading accuracy than the children of iodine sufficient mothers [5]. Moreover, severe ID in pregnancy is also seen to be a risk factor for pregnancy outcome, such as stillbirth, miscarriage and preterm delivery [6,7].

Iodization of salt is the preferred method adopted in the ID eradication programs. The measurement of UIC is also an effective method for monitoring iodine status in a large population [8]. World Health Organization (WHO) recommends 250 µg/d iodine intake for pregnant and lactating women, whereas routine supplementation programs with iodized salt provides about 100–150 µg/d [9]. Thus, routine iodine containing supplements are much recommended in the United States and Europe, but current data indicates that it has not become much widespread yet [10,11].

Legislation for mandatory iodization of household salt in Turkey was passed in July 1999 and practically started in the year

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2000. Istanbul was shown to be an iodine-sufficient region of Turkey in the year 2007 (median UIC in SAC; 164 μg/L), seven years after mandatory iodization of salt. However, iodine status in SAC does not seem to reflect the actual iodine status in pregnant women. Wong et al. demonstrated that UIC of SAC and non-pregnant women also did not indicate the iodine status during pregnancy [12]. Number of studies investigating iodine status among pregnant women with large samples are not satisfactory [7,13,14].

Therefore, we aimed to investigate the iodine status of pregnant women in Istanbul, which was shown to be one of the iodine-sufficient regions of Turkey to identify if there is a need for extra iodine supplementation.

Methods

In this multicenter cross-sectional study, 3543 pregnant women were recruited from nine different obstetrics centers in Istanbul city between January 2014 and July 2014. Nine maternity units were chosen as they are located in distinct areas of the city and aimed to serve variable socioeconomic and educational backgrounds of women. This study was approved by Ethics Committee of Istanbul University School of Medicine. Informed consent was obtained from all the subjects. Inclusion criteria were pregnant women from all trimesters aged between 16 and 50 years and participants who have been residing in the same area for more than one month. Age, gestational age, smoking habits, consumption of iodized salt, dietary salt restriction, consanguineous marriage, history of stillbirth, abortus, congenital malformations, and smoking habits were questioned by the physicians. Exclusion criteria were: (a) pregnant women with a known history of hysterosalpingography and/or any imaging method using iodine containing contrast agents within six months, (b) patients with a current or past thyroid disease or using any medication related to thyroid disease, (c) patients who were taking multivitamins including iodine, and (d) patients who had urinary tract infections.

Spot urine samples were analyzed for urinary iodine concentration(UIC) in the Ankara University Medical School Iodine Laboratory, which is recognized by the Centers for Disease Control and Prevention (CDC) as a part of the external quality control program, i.e. QUICK. Urine samples were centrifuged and stored at −20 °C before the analysis. UIC was determined by using the catalytic spectro-photometric method of Sandell–Kolthoff.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 20.0 (IBM Corp, Armonk, NY). Categorical data were compared using the chi-square Fisher exact test. Group data with a normal distribution were compared using the Student *t* test or analysis of variance, and nonparametric data were compared using the Mann–Whitney *U* or Kruskal–Wallis tests. Values were expressed as mean ± standard deviation or median as appropriate. Pearson and Spearman correlation analysis was made for determining the correlation of parameters. Multivariate regression analysis with backward elimination method was used to investigate the independent association of variables with UIC. $p < 0.05$ was considered statistically significant.

Results

A total of 3543 pregnant women between 6 and 41 weeks of gestation were recruited for this study. The mean age of subjects was 29.3 ± 5.6 yrs. Demographic characteristics of the recruited pregnant women are summarized in Table 1. Among the pregnant women, 805 were in the first, 953 were in the second, and 1729 were in the third trimester (Figure 1). Gestational age was not available in 56 pregnant women and they were excluded from the statistical analysis. The median UIC of the 3487 pregnant women was 73 μg/L. The median UIC was 77 μg/L (1–324), 73 μg/L (1–600), and 70 μg/L (1–1650) in the women for the first, second and trimesters of pregnancy respectively ($p = 0.14$) (Figure 1). UIC level was not associated with the gestational age.

Table 1. Demographic characteristics of pregnant women.

Baseline characteristics	Number of patients (%)
Age (years)	29.3 ± 5.6
Gestational age (weeks)	25.4 ± 10.6
First trimester	805 (23.1%)
Second trimester	953 (27.3%)
Third trimester	1729 (49.6%)
Consanguineous marriage	495 (14%)
Primiparity	2020 (57%)
Multiparity	1523 (43%)
History of abortus	672 (18.9%)
History of congenital deformity	111 (3.1%)
History of stillbirth	672 (18.9%)
Consumption of iodized salt	2465 (69.6%)
Dietary salt restriction	124 (3.5%)

UIC below 50 μg/L was observed in 36.6% ($n = 1295$) and below 150 μg/L was observed in 90.7% ($n = 3214$) of pregnant women. Median UIC below 150 μg/L and below 50 μg/L in each trimester are given in Table 2. Only 1% ($n = 34$) of women had UIC levels higher than 500 μg/L. The prevalence of iodized salt consumption was 69.6%. The frequency of salt restriction was 3.5%. Mean age of pregnant women in salt intake restriction group was higher (30.2 ± 5.9 yrs) compared to salt intake not restricted group (29 ± 5.6 yrs) ($p < 0.01$).

UIC was not associated with the history of stillbirth, congenital anomalies, and spontaneous abortion ($p = 0.1$, $p = 0.9$ and $p = 0.4$, respectively). Multivariate regression analysis was performed using age as a confounding variable and history of stillbirth, congenital anomalies, abortion as independent variables. No significant relationship was identified between UIC and independent variables. On the other hand, multiparity was significantly associated with the stillbirth and spontaneous abortion ($p < 0.05$). Frequency of consanguineous marriage was found to be 14% ($n = 495$) in our study population. Consanguinity was positively associated with the congenital abnormality risk with a risk coefficient of 4.9. Smoking was not associated with the UIC levels.

Discussion

The Urinary iodine concentration (UIC) level has been accepted as a good indicator of the iodine status in pregnant women. In our study, the median urinary iodine levels declined following the trimesters. Although this study was conducted in a metropolitan city which was an iodine-sufficient area, unfortunately, the UIC level was found to be below 150 μg/L in 90.7% ($n = 3214$) of the participating pregnant women. Median UIC level < 150 μg/L in pregnancy indicates iodine insufficiency [15]. The median UIC level was 73 μg/L and consistent with ID. The UIC level of 36.6% of the pregnant population was below 50 μg/L, indicating severe ID.

Even though iodine supplementation programs are becoming widespread, ID still persists as a global public health issue [9]. Pregnant women are vulnerable to ID due to 20–50% increased iodine requirements, increased renal iodide clearance, and placental deiodination of thyroid hormones [1,16,17]. A previous screening for congenital hypothyroidism in Turkey showed that 37% of newborns with transient hypothyroidism and 82% of their mothers suffered from ID [18]. WHO and International

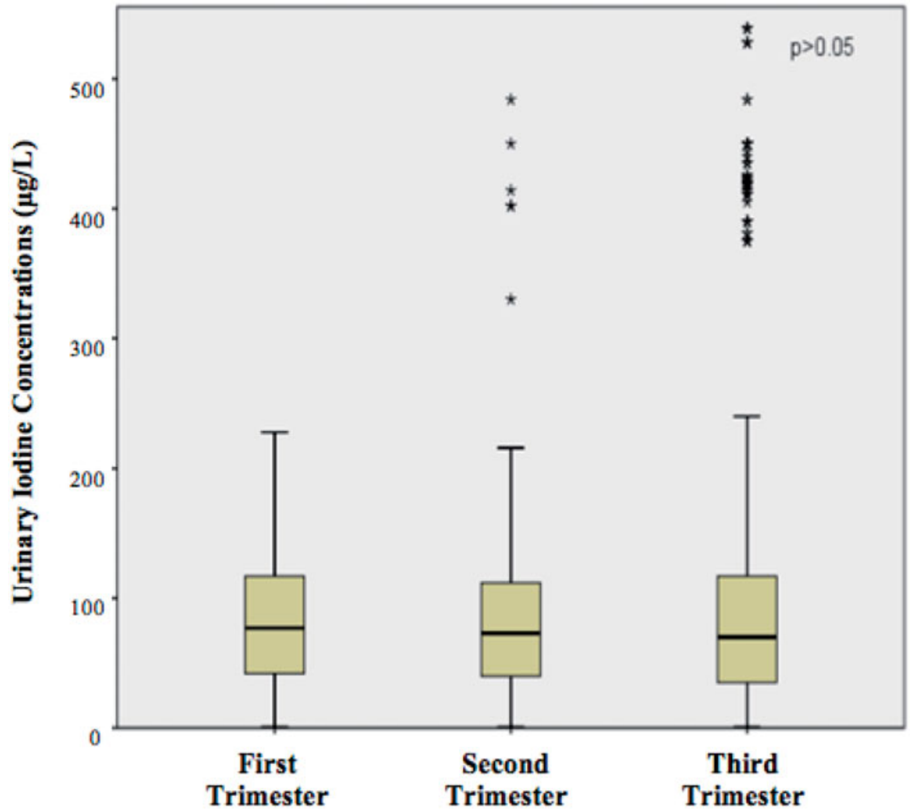

Figure 1. Distribution of median UIC in three trimesters of pregnancy.

Table 2. Median UIC of pregnant women in each trimester.

Trimester	Number of patients	Median UIC	Number of patients with median UIC ≤50 μg/L	Number of patients with median UIC ≤150 μg/L
1st	805	77 μg/L	262 (32.5%)	750 (93.2%)
2nd	953	73 μg/L	334 (35%)	894 (93.8%)
3rd	1729	70 μg/L	681 (39.4%)	1520 (87.9%)
Total	3487	73 μg/L	1277 (36.6%)	3164 (90.7%)

UIC: Urinary iodine concentration.

Council for Control of Iodine Deficiency Disorders (ICCIDD) recommends at least 250 μg/d iodine intake for pregnant or lactating women to meet the increased requirements [9].

Before mandatory iodization of salt, Turkey was a 'severe to moderately iodine deficient' country with median UIC level at 25.5 μg/L in school-age children (SAC) [19]. The latest national survey among SAC in Turkey was conducted in the year 2007 [20]. The median UIC levels were noted as 164 and 130 μg/L, in Istanbul and Turkey, respectively. Previous results have shown that UIC of SAC did not indicate the iodine status in pregnant women [12]. Wong et al. reported that when the median UIC in SAC or non-pregnant women indicated iodine intake was adequate, approximately half the time pregnant women had inadequate iodine intake [12]. Thus, it is clear that we need more broader studies addressing the iodine status of pregnant subpopulation.

Similar study from different region of Turkey also indicated mild–moderate ID in pregnant women [13]. Furthermore, many countries also reported high percentages of ID in pregnancy [21–26]. National Health and Nutrition Examination Survey (NHANES) data indicated mild ID in US pregnant women between 2007 and 2010 [21]. Recent reports from many European countries established mild to moderate ID among pregnant women [14,22–26].

WHO described adequate household salt intake as at least 90% of households consuming adequately iodized salt for elimination of ID [10]. Erdoğan et al. observed in Turkey that only 56.5% of the table salts contained iodine content higher than 15 ppm [19], which is mandatory according to the WHO/ICCIDD criteria [20,27]. In our study, iodized salt consumption was 69.6%. ID in our population might be partially due to the inadequate iodized salt consumption. However, the consumption of iodized salt may be inefficient to provide adequate iodine intake. According to the Turkish food codex 2012, fortification with 25–40 mg/kg KIO_3 is mandatory for table salt, but is not applicable for the salt used in food industry. Thus it is not a universal salt iodization program. Frequent fast food consumption may contribute to ID in the general population [28]. Usage of iodized salt by food industry may be a cheap and effective method for improving the iodine status. Also, iodization of dairy products and salt used in breads were found to have beneficial effects on iodine intake [22]. On the other hand, salt restriction is encouraged in many countries. The WHO recommends to decrease salt consumption lower than 5 g/d in order to prevent cardiovascular diseases, while consumption of 6–10 g iodized salt with 25–40 mg/kg KIO_3 provides only 94–152 µg elemental iodine intake [29]. This precaution triggers the need for alternative iodine supplementation strategies. The American Thyroid Association (ATA) recommends 150 µg iodine supplementation during pregnancy and lactation in addition to the use of iodized salt [10]. Iodine supplementation practices in addition to salt iodization seem to be safe as none would exceed 500 µg, which is the recommended upper limit of iodine intake for pregnant and lactating women [9].

The role of environmental factors, such as smoking also have important effects on the iodine status. Thiocyanate exposure through smoking has been suggested to increase the urinary iodine excretion [30]. We did not demonstrate an association between UIC, intermarriage, parity, and smoking habits of women. However, the smoking status was categorized as smokers and non-smokers, but the amount of consumption was disregarded in our study design. In further studies the relationship between amount of smoking and iodine status during pregnancy could be investigated.

An important finding of this study was that the median UIC was not significantly different between trimesters. Thus, ID beginning from the early gestational weeks indicates that iodine supplementation should be considered for all women planning pregnancy. We excluded the patients who were taking multivitamins because in our study population less than 10% of the participants were using multivitamins. In Turkey almost all of the commonly used multivitamins during pregnancy do not contain iodine. Thus, we believe our study population represents the real iodine status in Istanbul. Otherwise, if our participants were using iodine-containing multivitamins, we would need to perform sensitivity analysis.

Finally, our study had some limitations. Information on iodized salt storage and usage was arbitrary depending on the women declaration, which might lead to information bias. Our study aimed to investigate the iodine status of pregnant population and need for iodine supplementation.

This study showed that salt iodization alone does not solve the ID problem in pregnant women. Although the iodine status among school age children could be sufficient in a given area, pregnant women should receive 100–150 µg/d iodine supplements ideally, not only when pregnancy is planned but also throughout the pregnancy and lactation period.

Declaration of interest

There is no conflict of interest and this paper has not been funded by any organization or company.

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