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Is It Necessary to Recommend Iodine Supplement to Pregnant Women Living in Areas with Adequate Iodine Intake?

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Abstract

Background: Iodine need is increased during pregnancy and its deficiency can lead to complications in mother and fetus. The latest international guidelines have recommended a higher intake of iodine. Iran has implemented a national salt iodization program since 25 years ago, and the general population is iodine-sufficient. However, recent studies have shown that a significant proportion of pregnant women have urinary iodine concentration (UIC) below the recommended range of 150 - 250 μg/L. Based on the results of these studies, iodine supplement during pregnancy is widely used, but this practice is controversial.
Objectives: The aim of this study was to evaluate the necessity for iodine supplementation in pregnant women living in Shiraz, an iodine-replete area.
Methods: In this cross-sectional case-control study, UIC and thyroid-stimulating hormone of 174 pregnant women taking 150 μg/day iodine (group 1) were compared with 124 pregnant women not taking the supplement (group 2). The proportion of women with UIC below the recommended level in each group was also determined. UIC of the women in different trimesters in each group was also investigated and compared.
Results: Mean UIC in groups 1 and 2 was 175.71 $\pm$ 56.43 μg/L and 122.5 $\pm$ 44.37 μg/L and this difference was significant (P = 0.006). Also, 56% of women in group 2 and 24 % in group 1 had UIC below the recommended value (P < 0.01). Mean UIC in both groups decreased with advancing gestational age. In group 1, mean UIC remained in the recommended range, whereas in group 2, it decreased to less than 100 μg/L.
Conclusions: In areas covered by the national salt iodine implementation program, it is necessary to recommend iodine supplement to pregnant women to prevent iodine insufficiency.

Keywords: Pregnancy, Iodine, Supplement, Iran

1. Background

Iodine is an essential element for thyroid hormone synthesis. The daily requirement of iodine in a non-pregnant adult is 100 - 150 μg (1). Iodine need is increased during pregnancy for three reasons: (1) thyroxine-binding globulin is increased; thus, thyroid hormone production by mother is increased by 50% to maintain free thyroid hormones in the normal range; (2) iodine transfer to fetus for thyroid hormone production, especially in late pregnancy, and (3) increased iodine excretion by mother's kidneys (2, 3). Iodine deficiency during pregnancy can lead to neuropsychiatric disorders, neonatal hypothyroidism, abortion, and neonatal death (1, 2, 4, 5). The intelligence quotient of school children in areas with severe iodine deficiency is decreased by 12 scores compared with iodine-sufficient areas (1, 2).

In its latest recommendations, World Health Organization (WHO) has increased the daily iodine requirement of pregnant women to 220 - 250 μg and suggested that urinary iodine concentration (UIC) equal or more than 150 μg/L is an indication of sufficient iodine intake during pregnancy (6). Since most of the absorbed iodine is excreted in the urine, UIC is an accepted indicator of the recent iodine status of the population (7).

Iran has implemented the national salt iodization program since 1994 and the WHO has declared Iran as a country free of iodine deficiency disorders (8). Despite the sufficiency of iodine intake in the general population, some studies have shown insufficient iodine intake in pregnant women (8-11). In recent years, iodine supplementation for pregnant women as iodine tables has become a common practice in Iran, but this practice is controversial (12).

2. Objectives

The aim of this research was to evaluate the necessity for iodine supplementation in pregnant women living in Shiraz, an iodine-replete area.

3. Methods

This cross-sectional case-control study was conducted on pregnant women aged 18 to 45 years, referring for prenatal care to the obstetrics clinics of Shiraz University of Medical Sciences from July 2017 to March 2018 (10 months). Informed consent was obtained from each participant, and the study was approved by the Ethics Committee of Shiraz University of Medical Sciences. The sample size was calculated 55 cases for each group considering a 95% confidence interval, a significant level of 5%, and the prevalence of gestational iodine deficiency, as reported in previous studies (50%) (8, 9). Women taking iodine supplements were selected by consecutive random method, and for each selected case, the first woman not taking the supplement with age within ± one year and the same gestational trimester who referred during the study period was selected. Information regarding the use of iodized salt, daily iodine tablet containing 150 μg iodine as potassium iodides, and 500 μg folic acid (Iodofolic, Dorsa Pharmaceutical Company, Tehran, Iran), and systemic and thyroid diseases was collected. Gestational age was based on sonography data or calculated from the date of the last menstruation. Women with a history of thyroid and systemic diseases, as well as those unwilling to cooperate, were excluded.

Blood and 10 cc urine samples were taken and stored at -20°C temperature. Urine iodine was measured by the Sandell-Kolthoff method. Thyroid-stimulating hormone (TSH) was measured by the ELISA method. The intra-assay and inter-assay coefficient of variance was < 12% and within an acceptable range. Data were analyzed by SPSS 21. Chi-square and Fisher's test were used to compare proportions. A comparison of the means was done by the analysis of variance and *t*-test. Kolmogorov-Smirnov test was used to evaluate the normality of data. P values less than 0.05 were considered significant.

4. Results

Two hundred and ninety-eight pregnant women participated in this study. The mean age and gestational age were 29.0 ± 4.2 years and 21.2 ± 3.5 weeks, respectively. UIC had a mean of 158.6 ± 43.5 μg/L and median of 156.5 μg/L and the mean TSH was 2.13 ± 1.31 mU/L. All participants were taking iodized salt containing 40 μg/g iodine in the form of potassium iodate. One-handed seventy-four women were taking iodine tablets (group 1), and 124 women were not taking iodine supplements (group 2). The mean age of groups 1 and 2 was 28.8 ± 3.4 and 29.6 ± 4.2 years, respectively and the difference was not significant (P = 0.7). The mean gestational age in groups 1 and 2 were 20.9 ± 4.1 and 21.8 ± 4.8 weeks, respectively, and the difference was not significant (P = 0.10). UIC was significantly lower in group 2, but the mean TSH level was not statistically different between the groups (Table 1). Also, approximately a quarter of women in group 2 had UIC below 100 μg/L, which is categorized as iodine deficiency in the non-pregnant state, whereas more than half had UIC below the recommended value of 150 μg/L (Table 2). Five persons in group 1 had UIC above the recommended level of 250 μ/L, but this difference was not significant compared with group 2 (P = 0.16).

In group 1, the mean UIC in trimesters 1, 2, and 3 was 183.7 ± 40.2, 164.5 ± 38.2, and 154 ± 42 μg/L, respectively. Compared with the first trimester, the decrease in UIC in the second and third trimesters was statistically significant (P = 0.010 and P = 0.0003, respectively). In group 2, the mean UIC in the first, second, and third trimesters was 130.4 ± 42.3, 122 ± 38.2, and 90.5 ± 32.8 μg/L, respectively. The decrease from the first to third trimester was significant (P = 0.0001).

5. Discussion

The national salt iodization program has been implemented in Iran, since 25 years ago (8). In Fars province (the studied location), median UIC in school children has been above 100 μg/L since 2001 (13). Despite the iodine sufficiency of the general population, most studies have shown some degrees of iodine insufficiently in pregnant women in Iran (10). In the first national survey of iodine intake during pregnancy in 10 provinces, the median UIC was 87.3 μg/L, which was clearly less than the recommended level of 150 - 250 μg/L (14). In another study on pregnant women in 4 cities, the UIC was below the recommended level in 51% of women (9). Rostami et al. reported that between 66.9 and 98.6% of pregnant women in Urmia in North West Iran had UIC below 150 μg/L depending on the place of residence and trimester of the pregnancy (15). Iodine deficiency during pregnancy is also prevalent in other countries. A recent study in Italy showed that median UIC in the first trimester of pregnancy was 110.3 μg /L, and the authors concluded that pregnant women in their study were iodine-deficient despite the implementation of the national salt iodization program (16). In Turkey, a multi-central study has reported that median UIC in pregnant women was 73 μg /L, and 90.7% had UIC less than 150 μg/L. Also, UIC was

Table 1. Comparison of the Thyroid-Stimulating Hormone (TSH) and Urinary Iodine Concentration in Pregnant Women Taking and Those Not Taking an Iodine Supplement[a]

	Group 1 (Taking Iodine Supplement) (N = 174)	Group 2 (Not Taking Iodine Supplement) (N = 124)	P Value
Mean urinary iodine concentration, μg/L	175.71 ± 56.43	122.50 ± 44.37	0.006
TSH, mU/L	2.11 ± 1.3	2.47 ± 1.19	0.319

[a]Values are expressed as mean ± SD.

Table 2. Categorized Urinary Iodine Concentration in Pregnant Women Taking and Those Not Taking an Iodine Supplement[a]

	Urinary Iodine Concentration Category, μg/L			
	< 100	100 - 149	150 - 246	> 250
Women taking an iodine supplement	10 (6)	31 (18)	128 (73.5)	5 (3)
Women not taking an iodine supplement	30 (24)	40 (32)	54 (44)	0
P value for difference between two groups	0.0001	0.010	0.0002	0.16

[a]Values are expressed as No. (%).

less than 50 μg/L in 36.6% of the studies population. More than 90% of pregnant women in the mentioned study had some degrees of iodine deficiency, and it was concluded that the salt iodization program is not merely efficient for pregnant women (17). In our study, the median UIC in the whole study group was 156.5 μg/L, which is in an acceptable range; however, 56% of women who had not used iodine supplement had UIC below 150 μg/L, which is consistent with other studies in Iran (8, 9). This proportion in women taking iodine supplement was 24% i.e., iodine supplement partly decreased the percentage of women with iodine insufficiency to the half. Our data support the idea of recommending iodine supplement to pregnant women living in areas with iodine sufficiency. However, this issue is still controversial (12). The WHO/International Council for Control of Iodine Deficiency Disorders in 2007 stated that iodine supplement should not be recommended to pregnant women residing in areas, which had been iodine-sufficient for at least 2 years (6). Nonetheless, the American Thyroid Association recommends that all pregnant and breastfeeding women should receive at least a supplement of 150 μg/day iodine regardless of the iodine status of their place of residence (18). Despite the importance of preventing iodine deficiency during pregnancy and lactation, it is also important to prevent iodine excess. UIC of more than 250 μg/L is associated with a high risk of subclinical hypothyroidism, and UIC of over 500 μg/L is linked to a high risk of isolated hypothyroxinemia (19). High iodine intake can also increase the incidence of thyroid autoimmunity (20). In our study, only 3% of women taking iodine supplement had UIC of more than 250 μg/L and none had UIC above 500 μg/L.

Regarding UIC and gestational age, in both groups 1 and 2, there was a significant decrease in UIC with advancing gestational age. In group 1, the mean UIC in the third trimester remained in the recommended range of more than 150 μg/L; however, in group 2, it decreased to less than 100 μg/L. This finding is consistent with other studies (21, 22), and it is due to the transportation of iodine to the fetus for the synthesis of thyroid hormones in the final stages of pregnancy.

The main limitation of our study was its cross-sectional design, and the baseline data of our subjects were not available. The strength of this study was that we had two groups of case and control, and to the best of our knowledge, for the first time, we reported the effectiveness of domestically produced formulation of iodide (Iodofolic) in reducing iodine insufficiency during pregnancy.

5.1. Conclusions

In our study, a significant proportion of pregnant women who were using iodized salt but not taking the iodine supplement had UIC below the recommended value. The use of iodine supplement significantly decreased this proportion and prevented iodine deficiency during late pregnancy. Our study supports recommending iodine supplement to pregnant women living in areas covered with the national salt iodization program.

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Footnotes

Authors' Contribution: MB did study design, data collection, and preparing the manuscript. AS did study de-

sign, data collection, and preparing the manuscript. MS did study concept and design, data collection, preparing the manuscript, and the correspondence.

Conflict of Interests: The authors declare that they have no financial interest related to the materials in the manuscript.

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