

## Evaluation of Urinary Iodine Concentrations in Pregnant Women in Tehran

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### ABSTRACT

**BACKGROUND AND OBJECTIVE:** Congenital hypothyroidism due to iodine deficiency is the most common cause of preventable mental retardation in the world. The lowest level of iodine deficiency during pregnancy could result in disorders such as miscarriage, premature delivery, intrauterine fetal death, low birth IQ, mental retardation, hearing difficulty and speech impediments. This study aimed to evaluate urinary iodine concentrations during the first, second and third trimesters of pregnancy.

**METHODS:** This cross-sectional study was conducted on 354 pregnant women referring to prenatal care clinic of Akbar Abadi Hospital in Tehran. Demographic questionnaires were completed by an expert, and random urine samples were obtained to measure urinary iodine concentrations. In addition, venous blood samples were provided to determine the levels of thyroxine (T4) and thyroid stimulating hormone (TSH) during the first, second and third trimesters. Analysis of iodine status was based on the urinary iodine excretion in the patients. Urinary iodine deficiency was defined as concentrations of  $\leq 100$  micrograms/liter.

**FINDINGS:** In this study, 285 patients (80.5%) had urinary iodine levels of  $\leq 100$   $\mu\text{g/l}$  with a mean of  $62.35 \pm 67.7$   $\mu\text{g/l}$ . The mean urinary iodine concentrations during the first, second and third trimesters were  $65.83 \pm 72.4$ ,  $50.34 \pm 41.5$  and  $62.67 \pm 68.3$   $\mu\text{g/l}$ , respectively. No significant difference was observed in the mean of urinary iodine between the first and second trimesters, second and third trimesters, and first and third trimesters. Moreover, no significant differences were observed between patients with urinary iodine levels of  $< 100$   $\mu\text{g/l}$  and  $\geq 100$   $\mu\text{g/l}$  in terms of the mean of maternal age, age at pregnancy and TSH level.

**CONCLUSION:** According to the results of this study, despite the consumption of iodized salt, urinary iodine concentrations were below the standard limits in the studied pregnant women. It could be inferred that use of iodized salt may not be a proper solution for iodine deficiency in pregnant women. Therefore, it is recommended that iodine supplements be used before and during pregnancy, and iodine content of salt be increased as well.

**KEY WORDS:** Iodine deficiency, Pregnancy, Urinary iodine.

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## Introduction

Iodine deficiency is the preventable, most common cause of mental retardation among children across the world; iodine deficiency could also lead to hypothyroxinemia among pregnant women. However, since the levels of thyroxine (T4) and thyroid stimulating hormone (TSH) remain normal, this disorder might be occasionally disregarded. The lowest level of hypothyroxinemia during pregnancy is believed to increase the risk of neurological disorders and cause fetal cortical brain damage (1).

Maternal thyroid hormones are essential to the normal development of the fetus; therefore, it is vital for the mother to provide the fetus with sufficient thyroid hormones during the early stages of life (2). In case of severe iodine deficiency, the serum levels and synthesis of *triiodothyronine* (T3) and T4 are insufficient (3, 4). This evident hypothyroxinemia could cause irreversible damages to the central nervous system of the fetus while resulting in abnormalities such as mental retardation, hearing difficulty, speech impediments and movement disorders. The severity of neurological damages mainly depends on the time of iodine deficiency during the development of the fetus.

If iodine deficiency occurs within the early months of pregnancy, the neurological damages to the fetus will be drastically severe (1). In cases of low or moderate iodine deficiency, the synthesis and secretion of T4 decreases, T3 levels remain within the normal range, and TSH levels do not increase. Consequently, since clinical or subclinical hypothyroidism is diagnosed through the increase of TSH levels, women with hypothyroxinemia may not be identified.

Under such circumstances, the mother is considered as "euthyroid", while the available amount of T4 may not suffice the normal growth and development of the fetus. According to the literature, the lowest levels of iodine deficiency during pregnancy could increase the risk of neurological growth-retardation (4, 5). Iodine is an essential nutrient and the main component of thyroid hormones, which could only be obtained through diet and is reabsorbed through the gastrointestinal tract in the form of iodide, which is an inorganic anion.

The dietary iodine status of a population is determined by the measurement of urinary iodine concentrations, and random urine samples are used for the assessment and monitoring of the urinary iodine in large scales. According to the World Health Organization (WHO), the mean concentration of urinary iodine in a population that consumes sufficient

amounts of this substance is about 100 µg/l, and concentrations of <50 µg/l of urinary iodine should not be present in more than 20% of the population (6). Furthermore, the desirable urinary iodine concentration for pregnant women has been estimated between 150-249 µg/l (7). The efficacy of dietary iodine has not been thoroughly investigated in previous studies conducted in Iran (8-10), and a recent study in Tehran indicated that the intake of iodine was considerably lower than the recommended dose in the population of this capital city (11, 12). In addition, the amount of iodine in the consumed salt has reported to be insufficient for pregnant women (13). Given the importance of adequate levels of iodine in the dietary plans of pregnant women, assessment of the levels of this substance seems necessary in the field of medicine. This study aimed to offer a proper screening program for the determination of urinary iodine concentrations during pregnancy, as well as evaluate the levels of urinary iodine in pregnant women living in Tehran.

## Methods

This cross-sectional study was conducted on 364 pregnant women referring to the prenatal care clinic of Akbar Abadi Hospital in Tehran, and the study design was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran.

Exclusion criteria of this study were as follows: 1) history of thyroid diseases, thyroid hormone therapy or use of anti-thyroid medications and 2) history of abnormal pregnancies, such as multiple births. The sample size was determined based on the prevalence of iodine deficiency in Iran (12). The pregnant women selected for the study were examined by trained researchers, and informed consent was obtained from the subjects prior to participation.

In addition, demographic data including age, family history of thyroid disorders, pregnancy trimester and use of oral nutritional supplements (e.g. multivitamins) were recorded in separate forms. Following that, urine and blood samples were obtained for urinary iodine measurement, and T4 and TSH laboratory tests, respectively. In this study, T4 and TSH tests were performed via radioimmunoassay (RIA) and immunoradiometric assay (IRMA) methods, using the Immunotech Kit (manufactured in the Czech Republic). Inter- and intra-assay coefficients of variations of T4 and TSH were 5.6 and 5, respectively, and 5.7 and 3,

respectively. Considering the T4 changes during pregnancy, free thyroxine index (FTI) values were examined via  $T3RU/100T4 \times$  method. Moreover, urinary iodine concentrations were evaluated using the acid digestion method of Sandell-Kolthoff reaction, and inter- and intra-assay coefficients of variations were 9.6 and 10.4, respectively with a sensitivity of 2 mg/liter. Collected laboratory data were recorded in forms, and the results were classified into two groups of data description and hypothesis testing. Average central index and standard deviation were used to describe data, and normal distribution of quantitative variables was measured using one-sample Kolmogorov-Smirnov test. All the variables were observed to have a non-normal distribution.

Regarding the non-normal distribution of the variables, Mann-Whitney U test was used to compare the two groups of patients with urinary iodine levels of  $<100 \mu\text{g/l}$  and  $\geq 100 \mu\text{g/l}$ . Furthermore, Chi-square test was used for the assessment of qualitative data, and Kruskal-Wallis test was used for the comparison of the mean of the three trimesters. A P value of  $<0.05$  was considered significant.

## Results

In total, 364 pregnant women were enrolled in this study, 10 of whom were excluded due to the loss of urine samples. Out of the remaining 354 patients, 6.59% were in the first trimester, 2.29% were in the second trimester, and 91.12% were in the third trimester of pregnancy. The studied subjects were within the age range of 16-43 years (mean:  $35.5 \pm 8.26$ ). Approximately 47.7% of the subjects were in their first pregnancy, while 32.8% were in the second pregnancy, and others had had between 3-6 pregnancies.

Among the subjects of the present study, 285 patients (80.5%) had urinary iodine concentrations of  $<100 \mu\text{g/l}$  (i.e. iodine deficiency). If calculated based on the new criteria of measurement (i.e.  $150 \mu\text{g/l}$ ) (14), the rate of iodine deficiency among the studied patients would increase to 88.5%, which comprised of the majority of the participants.

In this study, the mean urinary iodine concentrations of the patients was  $62.35 \pm 67.7 \mu\text{g/l}$ ; the mean of urinary iodine levels during the first, second and third trimesters was  $65.83 \pm 72.4$ ,  $50.34 \pm 41.5$  and  $62.67 \pm 68.3 \mu\text{g/l}$ , respectively. No significant difference was observed in the mean of urinary iodine levels between the first and second trimesters ( $p=0.468$ ),

second and third trimesters ( $p=0.442$ ), and the first and third trimesters ( $p=0.839$ ).

The mean age of the pregnant women with urinary iodine concentrations of  $<100 \mu\text{g/l}$  was  $27 \pm 5.2$  years, while it was  $26 \pm 4.8$  years in those with urinary iodine levels of  $\geq 100 \mu\text{g/l}$  (Table 1). In addition, the mean gestational age in patients with urinary iodine concentrations of  $<100 \mu\text{g/l}$  was  $34 \pm 7.4$  weeks, while it was  $34 \pm 8.1$  weeks in women with urinary iodine levels of  $\geq 100 \mu\text{g/l}$ .

No significant difference was observed in the mean of maternal age ( $p=0.152$ ) and gestational age ( $p=0.701$ ) between the subjects with urinary iodine concentrations of  $<100$  and  $\geq 100 \mu\text{g/l}$  (Table 1). In patients with urinary iodine concentrations of  $<100 \mu\text{g/l}$ , 144 cases (49.6%) had a TSH level of  $<4$ , and 6 cases (2.05%) had a TSH level of  $>4$ .

As for patients with urinary iodine concentrations of  $\geq 100 \mu\text{g/l}$ , 30 cases (10.27%) had a TSH level of  $<4$ , and the TSH level was  $>4$  in one patient (0.34%); no significant difference was observed between the two groups in terms of TSH levels. Among the pregnant women participating in this study, 258 cases (72.9%) used multivitamins, out of whom 204 cases (71.5%) had urinary iodine levels of  $<100 \mu\text{g/l}$ .

**Table 1. Association of Urinary Iodine with Maternal age, Age at pregnancy and Thyroid function**

Variables	Levels	$<100 \mu\text{g/L}$ Mean $\pm$ SD	$\geq 100 \mu\text{g/L}$ Mean $\pm$ SD	P-value
Mean age of pregnant women		$27 \pm 5.2$	$26 \pm 4.8$	0.152
Mean gestational age (weeks)		$34 \pm 7.4$	$34 \pm 8.1$	0.701
Mean TSH		$2.27 \pm 1$	$2.35 \pm 1$	0.661
Mean TFI		$2.43 \pm 0.06$	$2.46 \pm 0.06$	0.679

The mean of TSH in women with urinary iodine concentrations of  $<100 \mu\text{g/l}$  was  $2.27 \pm 1$ , and it was  $2.35 \pm 1$  in women with urinary iodine levels of  $\geq 100 \mu\text{g/l}$ ; no significant difference was observed in the mean of TSH between the two study groups (Table 1). Moreover, only one patient had an FTI of 4.2 with the urinary iodine levels of  $<100 \mu\text{g/l}$ , and FTI was less than 3.9 in the other subjects.

Overall, the mean of FTI was  $2.43 \pm 0.06$  in patients with urinary iodine levels of  $<100 \mu\text{g/l}$ , while it was  $2.46 \pm 0.06$  in women with urinary iodine concentrations

of  $\geq 100$   $\mu\text{g/l}$ ; no statistically significant difference was observed between the two groups in this regard ( $p=0.679$ ). Furthermore, none of the subjects in the present study had FTI levels of less than 1.4 (table 1). Distribution of thyroid disease history in patients with urinary iodine levels of  $<100$  and  $\geq 100$   $\mu\text{g/l}$  constituted of only one subject in each group. Moreover, 258 patients (72.9%) used multivitamins, out of which 204 cases (71.5%) had urinary iodine concentrations of  $<100$   $\mu\text{g/l}$ .

## Discussion

In the present study, 80.5% of the pregnant women had urinary iodine levels of  $<100$   $\mu\text{g/l}$ , with the mean of  $62.35 \pm 67.7$   $\mu\text{g/l}$ . Considering the desirable level of iodine during pregnancy, 88.5% of the participants in the current had iodine deficiency. Similar to our study, Elahi et al. reported the mean of urinary iodine concentrations to be 67  $\mu\text{g/l}$  among their subjects (15). In another study conducted by Ruiz et al. in Spain, the mean urinary iodine concentration was reported to be 92  $\mu\text{g/l}$ , which is significantly different from the findings of the current study, and is indicative of a high intake of iodine among those patients (16).

In another study conducted by Alvarez-Pedrerol et al. in Spain, the mean of iodine concentrations was reported to be 104 and 113  $\mu\text{g/l}$ , which is higher than the observed iodine levels in our patients (17). These values are reported to be higher than the findings of the current study in the majority of the studies in this regard.

On the other hand, the mean of urinary iodine levels in women during the first, second and third trimesters was  $65.83 \pm 72.4$ ,  $50.34 \pm 41.5$  and  $62.67 \pm 68.3$   $\mu\text{g/l}$ , respectively; however, this differences was not considered to be significant.

Since the majority of participants were in the third trimester of pregnancy, and due to the lack of coordination between the number of samples during the three trimesters of pregnancy, the differences in the mean of urinary iodine levels in this study were not considered as statistically significant. This finding is inconsistent with the results obtained in a study conducted by Chakraborty in India (18).

According to the results of that study, the mean of iodine concentration during the first, second and third trimesters of pregnancy was 137.5, 135 and 160  $\mu\text{g/l}$ , respectively, which was indicative of a significant difference between the second and third trimesters in the studied pregnant women. Furthermore, TSH levels of

$>4$  were observed in 2.4% of the patients, while other subjects had TSH levels of  $<4$ .

According to the further results of that study, out of the patients with urinary iodine concentrations of  $<100$   $\mu\text{g/l}$ , 144 cases (49.60%) had a TSH level of  $<4$ , while 6 cases (2.05%) had a TSH level of  $>4$ . As for the patients with urinary iodine levels of  $\geq 100$   $\mu\text{g/l}$ , 30 cases (10.27%) had a TSH level of  $<4$ , and only one patient (0.34%) had a TSH level of  $>4$ ; however, no statistically significant difference was observed in TSH levels between the two groups.

In addition, the mean of TSH levels in women with urinary iodine concentrations of  $<100$  and  $\geq 100$   $\mu\text{g/l}$  was  $2.27 \pm 1$  and  $2.35 \pm 1$ , respectively, and no significant difference was observed in the mean of TSH between the two study groups. In fact, no association was found between TSH levels and urinary iodine concentrations. In another study, Krzyczkowska-Sendrakowska et al. reported the mean of urinary iodine levels in pregnant women to be 34.99  $\mu\text{g/l}$ , the mean TSH level to be 2.3 and the mean T4 to be 11.6 (19). On the other hand, Chakraborty et al. (2006) in the state of West Bengal, India concluded that 78.4% of the studied pregnant women had urinary iodine levels of  $>100$   $\mu\text{g/l}$ , (mean: 144  $\mu\text{g/l}$ ) and TSH levels of 1.4 (18).

The results of the aforementioned studies indicate that in low iodine concentrations, TSH levels tend to be higher; nevertheless, the findings of the current study revealed no significant differences in this regard. This could be due to the high levels of TSH in our study; furthermore, lack of communication could be the result of normal FTI values in the participants of this study. The mean of FTI in pregnant women with urinary iodine levels of  $<100$   $\mu\text{g/l}$  was  $2.43 \pm 0.06$ , while it was  $2.46 \pm 0.06$  in those with urinary iodine concentrations of  $>100$   $\mu\text{g/l}$ ; however, no significant difference was observed between the two groups in this regard. Furthermore, no significant difference was observed in the mean of FTI between the first and third trimesters since the majority of the subjects were in the third trimester of their pregnancies.

Another study was performed in Bangladesh in 2009 in order to assess the levels of iodine in pregnant women during different trimesters of pregnancy; the control group consisted of non-pregnant women, and serum levels of TSH, FT3 and FT4 were measured. Comparison of the two study groups was indicative of a significant difference between the mean of urinary iodine with the levels of TSH and FT4 (20). In another study, Alvarez-Pedrerol et al. reported that women who

used multivitamins were exposed to a lower risk of insufficient urinary iodine concentrations (17). In the present study, 71.5% of the patients with urinary iodine levels of  $<100 \mu\text{g/l}$  used multivitamin supplements; however, since the available pregnancy supplements in Iran do not contain adequate iodine, these supplements cannot compensate for iodine deficiency in pregnant women. The findings of the current study are mostly compatible with the results obtained by Elahi et al. (16), while relatively similar to the findings of Egri in Turkey (21) and Marchioni in Italy (7).

In the study conducted by Egri, out of 824 studied pregnant women, 83.3% had urinary iodine levels of  $<100 \mu\text{g/l}$ , and the mean of urinary iodine concentrations was reported to be  $77.4 \mu\text{g/l}$  among the participants. This finding is close to the mean of urinary iodine levels obtained in the current study, and is indicative of severe iodine deficiency among pregnant women. Although the results of the present study report a lower level of urinary iodine compared to other similar studies, iodine deficiency during pregnancy is still a prevalent disorder across the world, which is mainly due to the fact that T4 and TSH levels remain normal in this condition.

While mild hypothyroxinemia during pregnancy could increase the risk of neurological disorders in the fetus and cause damage to the fetal cortical brain tissues, severe maternal hypothyroxinemia could lead to irreversible damages to the central nervous system and

cause abnormalities such as mental retardation, hearing difficulty, speech impediments and movement disorders. In addition to the maternal thyroid hormones, the fetus is dependent on the iodine supplements of the mother during pregnancy and lactation; consequently, mild to moderate iodine deficiency during pregnancy could increase the risk of neurological growth-retardation in the newborn (5).

According to the results of the present study, the intake of iodine is insufficient among pregnant women; despite the consumption of iodized salt, urinary iodine concentrations are lower than the standard limits among pregnant women. Therefore, health authorities need to pay more attention to the rate of iodine deficiency during pregnancy, and use of iodine supplements in the dietary plans of pregnant women is recommended in addition to the consumption of iodized salt.

One of the limitations of the current study was that the majority of the subjects were in the third trimester of pregnancy, and there was the lack of suitable proportion between the number of samples and different trimesters of pregnancy.

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