

Inadequate iodine nutrition of pregnant women in an area of iodine sufficiency

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Received: 9 November 2015 / Accepted: 28 January 2016
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Abstract

Purpose I. R. Iran has been considered iodine replete since 2000, but iodine nutrition of vulnerable subjects is not clear. The main goal of this study was assessment of iodine nutrition and thyroid function in pregnant Iranian women.

Methods A total of 1072 pregnant women from ten provinces in the different parts of the country were recruited from November to March 2014. Median urinary iodine concentration (UIC) as the measure of iodine status and serum free T4 (FT4), thyrotropin (TSH), thyroglobulin (Tg), anti-thyroglobulin and anti-thyroid peroxidase antibodies (TgAb and TPOAb) were measured.

Results Mean \pm SD age of the cohort was 27.0 ± 7.2 years and gestational age was 20.7 ± 10.0 weeks. The median UIC for pregnant women was $87.3 \mu\text{g/L}$, being 92.1 , 86.0 and $76.8 \mu\text{g/L}$, in three trimesters of pregnancy, respectively. Median UIC of <100 , $100\text{--}149$, $150\text{--}249$, $250\text{--}499$ and $\geq 500 \mu\text{g/L}$ was found in 58.4, 19.8, 16.2, 5.13 and 0.46 % of subjects, respectively. Median (IQR) values in the first, second, and third trimesters were 1.7 (0.9–2.8), 2.1 (1.5–2.9), and 2.1 (1.4–2.8) mIU/L for TSH, and 16.4 (12.21–21.13), 14.34 (12.16–19.69), and 14/07

(12.02–18.64) pmol/L for FT4, respectively. The frequency of elevated serum TSH was 9.0 % (6.6 % subclinical, 2.4 % overt hypothyroidism). The frequency of low serum TSH was 0.6 %. The frequency of positive TPOAb was 7.6 %.

Conclusions Results of this study have clarified that despite iodine sufficiency of school children in Iran, pregnant women have moderate iodine deficiency and need iodine supplementation.

Keywords Iodine · Pregnancy · Iodine deficiency · UIC · Thyroid function

Introduction

Iodine is the major component of thyroid hormones which are vital for neurocognitive development of the fetus and newborn [1, 2]. Inadequate levels of thyroid hormones during pregnancy may contribute to obstetric complications for the mother and the fetus [3]. Pregnant women are vulnerable to iodine deficiency as the effects of in utero deficiency on the developing fetus may have life-long consequences

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for the offspring. Severe iodine deficiency during pregnancy is well known to cause cretinism and severe mental retardation [4–7]. Bath et al. have recently found mild-to-moderate iodine deficiency in a large UK cohort of pregnant women and the children of those that had low iodine status in early pregnancy were more likely to have significantly lower IQ and reading scores [8].

The fundamental changes in thyroid function during normal pregnancy and lactation include increased thyroid hormone production, increased renal iodine excretion and iodine secretion into breast milk, and iodine requirement for the fetus [9]. Therefore, a woman needs more iodine during pregnancy and lactation to maintain normal metabolism as well as for the transfer of thyroxine and iodine to the fetus and neonate. Though it is vital that pregnant women meet their iodine requirements, this is not always achieved even in developed countries such as the USA [10]. Ideally, women should have adequate intra-thyroidal iodine stores before conception, which should be ensured by universal salt iodization (UIC) programs, but the American Thyroid Association (ATA) has recommended 150 µg iodine daily as dietary supplement for all pregnant women [11]. The most recent recommendation has been endorsed by World Health Organization (WHO) [12], UNICEF [13] and Iodine Global Network (IGN) formerly ICCIDD [14]. According to recent guidelines of both the ATA [15], and the Endocrine Society [16], daily intake of 250 µg iodine has been advised for all pregnant and breastfeeding women, not only in iodine-deficient areas, but also in iodine-sufficient regions.

Iodine deficiency has been aggressively addressed in I. R. Iran by the production and consumption of iodized salt since 1970 and three national surveys have shown iodized salt consumption by >95 % of the population and an adequate UIC of 232, 190, and 140 µg/L among schoolchildren in 1996, 2001, and 2006, respectively [17–19]. In our latest national survey in 2014, the median UIC of 18,000 schoolchildren was 161 µg/L, which indicates sustainability of iodine sufficiency in I. R. Iran (unpublished data). However, pregnant as well as lactating women and their newborns (up to early infancy) are among the populations the most vulnerable to the detrimental effects of iodine deficiency. Therefore, the aim of this study was to assess iodine intake and the prevalence of thyroid dysfunction in a national representative sample of pregnant women in Iran.

Materials and methods

Study population

This is an observational, cross-sectional study. A total of 1200 pregnant women attending antenatal care clinics in the mother and child health care centers in 10 provinces,

randomly selected from 31 provinces of the country, included women aged 20–40 years who had lived in the city for more than 5 years with pre-gestational regular menses and were pregnant with a singleton pregnancy and in the first, second and third trimester of their pregnancy (400 pregnant women in each trimester) were consecutively recruited from November to March 2014. Excluded were smokers and those women with a history of thyroid disease or any other chronic diseases, and subjects on any medical regimen before pregnancy that may affect thyroid function, such as glucocorticoids, dopamine, or antiepileptic drugs. All women were asked to complete the study questionnaire at their first visit and written informed consent was obtained. The study was approved by the human research committee of the Research Institute for Endocrine Sciences. Of these 1200 women, 128 subjects were excluded, because of inadequate urine samples for measurement of urinary iodine concentration, and finally 338, 389 and 295 pregnant women recruited at the first, second and third trimester, respectively.

Procedures

Trained midwives explained the rationale of the study to the pregnant women and collected demographic data (including age, parity and gestational age) and medical history (including thyroid medications and history of previous thyroid disorders). Gestational age was calculated from the first day of the last normal menstrual period and gestational ages <12, 12–23.9, and >24 weeks comprised the first, second, and third trimesters of pregnancy.

Laboratory measurements

Urinary iodine concentration (UIC) was measured in random urine samples using a manual method based on the Sandell–Kolthoff technique [20] and the results were expressed as microgram of iodine per liter of urine (µg/L). The urine samples were not dipstick tested for other assays. The analytical sensitivity for iodine was 1.39 µg/L and the intra-assay and interassay coefficients of variation were 4.4 and 3.9 %, respectively.

Venous blood samples were collected from pregnant women, using anticoagulant-free tubes and after centrifugation the serum samples were stored at –80 °C until analyses. Serum FT4, TSH, and thyroglobulin (Tg) were measured by the electrochemiluminescence immunoassay (ECLIA) method, using Roche Diagnostics kits and the Roche/Hitachi Cobas e-411 analyzer (GmbH, Mannheim, Germany). Anti-thyroid peroxidase (TPOAb) and anti-thyroglobulin (TgAb) antibodies were determined by immunoenzymometric assay (IEMA) using commercial kit (Monobind, Costa Mesa, CA, USA). All tests performing

by enzyme-linked immunosorbent assays were done by a Sunrise ELISA reader (Tecan Co. Salzburg, Austria). Lyophilized quality control material (Lyphochek Immunoassay Plus Control, Bio-Rad Laboratories, Irvine, CA, USA) in three different concentrations was used to check accuracy of assays; also a pooled serum was prepared, aliquoted and stored at -80° and assayed in all runs for monitoring precision of measurements. The intra assay coefficients of variation (CV) of serum FT4, TSH, TPOAb, TgAb, and Tg were 1.49–4.18 %, 2.1–3.3 %, 2.40–6.1 %, 1.3–4.7 % and 1.9–5.0 %, respectively. The interassay CV values for above mentioned parameters were 4.65–7.99 %, 1.30–7.85 %, 2.2–6.7 %, and 3.8–5.8 %, respectively.

We applied our local trimester-specific reference ranges of TSH and FT4 definitions and diagnostic criterion for thyroid disorders

T4 made by our laboratory based on Guideline 22 of the National Academy of Clinical Biochemistry [21]. A total of 466 Iranian pregnant women, who had the same ethnicity of Persians, in the first trimester of pregnancy attending antenatal care clinics in the mother and child health care centers of two general hospitals of Tehran were consecutively recruited from November 2004 to November 2006. Only women with singleton pregnancies were enrolled. Inclusion criteria required documentation that thyroid-related measurements were available in all of the three trimesters. Of 466 women who were referred in the first trimester, 147 subjects were excluded because of pre-existing thyroid disorders or nodules; those taking medications affecting thyroid function and those not available in all trimesters or lost to follow-up (referring elsewhere for delivery, nonviable pregnancy) were excluded, and 219 healthy pregnant women were selected. A further 20 subjects were excluded due to laboratory results of positive serum thyroid peroxidase antibodies (TPOAb > 40 IU/mL), low urinary iodine level ($< 150 \mu\text{g/dL}$ in two out of three sample measurements in the first trimester) (34 subjects), and enlarged thyroid gland (thyroid volume greater than 30 mL) by ultrasonography (nine subjects). None had overt hypo- (TSH > 4.5 mIU/L and T4 < 5.5) or hyperthyroidism (TSH < 0.1 mIU/L and T4 > 14.5) or subclinical hypothyroidism (TSH > 10 mIU/L). Those with subclinical hyperthyroidism (serum TSH levels under 0.1 mIU/L and normal T4) were not excluded due to normal TSH suppression at pregnancy. Finally, 152 healthy iodine-sufficient women with viable, singleton pregnancies comprised the cohort study. Reference intervals in the first, second, and third trimesters were as follows: TSH 0.2–3.9, 0.5–4.1, and 0.6–4.1 mIU/L, respectively [22]. Subclinical hypothyroidism was defined as TSH between 3.9 and 10 mIU/L in the first and between 4.1 and 10

mIU/L in both the second and third trimester, with normal FT4 in all trimesters of pregnancy. Overt hypothyroidism was defined as TSH > 10 mIU/L or TSH > 3.9 mIU/L and FT4 < 12.5 pmol/L in the first, TSH > 4.1 mIU/L and FT4 < 12.8 pmol/L in the second, and TSH > 4.1 mIU/L and FT4 < 12.0 pmol/L in the third trimesters of pregnancy. The reference of TPOAb 0–35 IU/ml, and TgAb 0–115 IU/ml was provided by the manufacturer. According to UIC values, pregnant women were divided into five groups: UIC $< 100 \mu\text{g/L}$, UIC 100–149 $\mu\text{g/L}$, UIC 150–249 $\mu\text{g/L}$, UIC 250–499 $\mu\text{g/L}$, and UIC $\geq 500 \mu\text{g/L}$, but for defining nutritional status, they stratified in two groups with UIC < 150 and UIC $\geq 150 \mu\text{g/L}$.

Statistical analysis

The Kolmogorov–Smirnov method was used to test data distribution normality. Normally distributed values are reported as mean \pm SD, or if not so, were reported as median and interquartile range (IQR). Repeated measure test was used to compare FT4 between three trimesters and the Friedman test was used for TSH comparison. McNemar, *s* test was applied for comparison of prevalence of hypothyroidism based on two different cut points of TSH; *P* values < 0.05 denoted statistical significance. One-way ANOVA with post hoc Scheffe correction was used to test differences of serum Tg between groups of participants. Linear regression was used between UIC and thyroid function parameters. Mann–Whitney test was used to compare differences in continuous variables between trimesters. The statistical software SPSS version 20 was used for data analysis.

Results

A total of 1072 participants were recruited in this study. Table 1 shows demographic and biochemical parameters in participating women.

Urinary iodine concentration (UIC)

In total cohorts, the median (IQR) of UIC was 87.3 (46.5–139.1) $\mu\text{g/L}$, it was 92.1 (48.8–145.5), 86.0 (46.2–137.5), and 76.8 (42.8–132.8) $\mu\text{g/L}$ in the first, second, and third trimesters, respectively. 838 (78.2 %) of women had UIC $< 150 \mu\text{g/L}$ and 234 (21.8) had UIC $< 150 \mu\text{g/L}$. According to WHO criteria, 19.8 % of all pregnant women had mild (UIC = 100–150 $\mu\text{g/L}$) and 58.4 % had moderate (UIC = 50–100 $\mu\text{g/L}$) iodine deficiency. Table 2 shows the percent of frequency distribution of median UIC by trimester of pregnancy. The mean, median, 10th and 90th percentiles of UIC in the study population are depicted in Table 3.

Table 1 Demographic and biochemical parameters of thyroid function by trimester in 1072 pregnant Iranian women

Variable	First trimester (<i>n</i> = 388)	Second trimester (<i>n</i> = 389)	Third trimester (<i>n</i> = 295)	All (<i>n</i> = 1072)
Age (years) ^b	27.2 ± 6.9	26.8 ± 7.6	27.4 ± 6.8	27.1 ± 7.2
Gestational age (weeks) ^b	9.9 ± 2.4	21.4 ± 4.1	33.9 ± 2.6	20.7 ± 10.0
TSH (mIU/L) ^a	1.7 (0.9–2.8)	2.1 (1.5–2.9)	2.1 (1.4–2.8)	2.0 (1.3–2.8)
FT4 (pmol/L) ^a	16.4 (12.21–21.13)	14.34 (12.16–19.69)	14.07 (12.02–18.64)	15.92 (12.14–21.56)
Tg (µg/L) ^a	12.1 (5.6–20.3)	12.4 (5.2–20.9)	13.1 (6.9–24.8)	12.4 (5.9–21.7)
UIC (µg/L) ^a	92.1 (48.8–145.4)	86.0 (46.2–137.5)	76.8 (42.8–132.8)	87.3 (46.5–139.1)
TPOAb+ (%) ^a	44.0 (11.3)	24.0 (6.2)	14.0 (4.7) [†]	82.0 (7.6)

[†] *P* < 0.004

^a Values are given as median (IQR)

^b Values are given as mean ± SD

Table 2 Percent of frequency distribution of median UIC by trimester of pregnancy in study population

Trimester of pregnancy	Urine iodine concentration (µg/L)				
	<100	100–149.9	150–249.9	250–499.9	≥500
First (<i>n</i> = 388)	201 (32.20) ^a	94 (44.34)	72 (41.40)	20 (36.40)	1 (20.0)
Second (<i>n</i> = 389)	245 (39.10)	62 (29.24)	57 (32.80)	23 (41.80)	2 (40.0)
Third (<i>n</i> = 295)	180 (28.70)	56 (26.42)	45 (25.90)	12 (21.80)	2 (40.0)
All (<i>n</i> = 1072)	626 (58.40)	212 (19.78)	174 (16.23)	55 (5.13)	5 (0.46)

^a Number of women (%)

Table 3 Mean, median, 10th and 90th percentiles of urinary iodine concentration (UIC) during the three trimester of pregnancy in the study population

UIC (µg/L)	First trimester	Second trimester	Third trimester	All
Mean ± SD	110.6 ± 81.1	106.4 ± 86.9	100.1 ± 81.2*	106.2 ± 83.3
Median (IQR)	92.1 (48.8–145.5)	86.0 (46.2–137.5)	80.0 (45.0–136.0)	87.3 (46.5–139.1)
Range (min–max)	15.0–636.0	17.0–703.0	17.0–666.0	15.0–703.0
10th percentile	30.2	29.0	32.0	28.8
90th percentile	301.7	311.6	299.5	313.5

* No significant difference between trimesters

Thyroid tests results

The median (IQR) of serum TSH concentration was 1.70 (0.90–2.80), 2.10 (1.50–2.90) and 2.10 (1.40–2.80) mIU/L in the first, second, and third trimester, respectively, (*p* < 0.001). The median (IQR) of FT4 was 16.40 (12.21–21.13), 14.34 (12.16–19.69), and 14.07 (12.02–18.64) pmol/L in the first, second and third trimester, respectively (NS). TPOAb was positive in 82 subjects (7.6 %) of whom 44 (4.0 %), 24 (2.3 %), and 14 (1.3 %) subjects who were in their first, second, and third trimesters, respectively. Table 4 depicts serum concentrations of TSH, FT4, Tg and positive TPOAb in different UIC groups.

Prevalence of thyroid dysfunction

Considering our local trimester-specific reference range for TSH (0.2–3.9 mIU/L in the first and 0.3–4.1 mIU/L

in the second and third trimesters) 0.6 % (seven subjects) had low TSH and the frequency of elevated serum TSH was 9.0 % (96 subjects). 97.9 % of subjects with elevated TSH had subclinical hypothyroidism, but when the ATA recommended trimester-specific reference ranges were used, 33.9 % (359 subjects) had TSH >2.5 mIU/L in the first, while 10.6 % (114 subjects) had TSH >3.0 mIU/L in the second and third trimesters (Fig. 1). In total cohorts, there was significant difference in the prevalence of subclinical hypothyroidism based on two different cut points (*p* = 0.001). Overt hypothyroidism was detected in 6, 5, and 7 women in the first, second and third trimesters of pregnancy. No body had isolated hypothyroxinemia. In the total population, the frequency of positive TPOAb was 7.6 %. Median serum Tg was not significantly different in women with UIC ≥ 150 µg/L and those with UIC < 150 µg/L. Table 5 depicts prevalence of thyroid disorders in different UIC groups.

Table 4 Median (IQR) of serum concentration of thyroid parameters in different UIC groups

UIC groups				
UIC (µg/L)	n	TSH (mIU/L)	FT4 (pmol/L)	Tg (µg/L)
<100	626	1.9 (1.3–2.9)	15.9 (12.4–22.8)	12.9 (5.8–22.9)
100–149	212	1.8 (1.3–2.7)	16.7 (12.24–21.30)	11.1 (4.7–20.1)
150–250	174	2.1 (1.4–3.1)	15.20 (11.81–21.42)	11.7 (6.8–20.4)
250–500	55	1.9 (1.2–3.1)	14.59 (8.6–21.08)	13.2 (8.9–18.9)
≥500	5	2.1 (1.1–2.9)	15.06 (12.11–21.98)	9.8 (6.6–22.3)

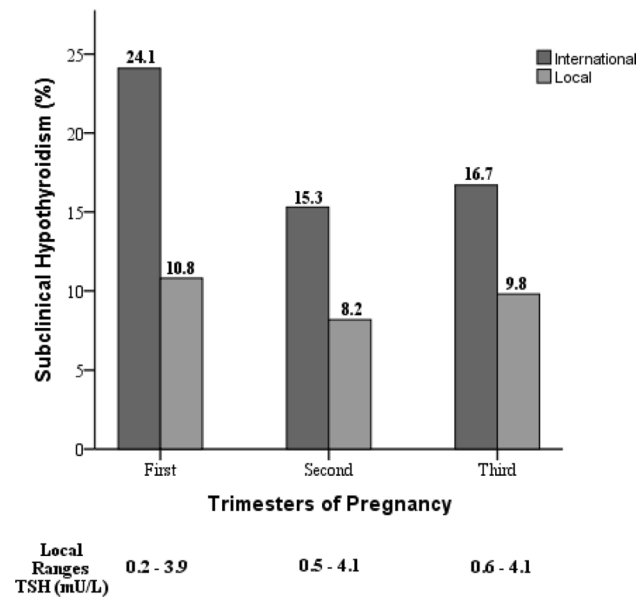


Fig. 1 Local versus ATA recommended TSH reference ranges in an iodine-sufficient region

Discussion

The median UIC of subjects in this study indicates moderate iodine deficiency among pregnant women in Iran, a country considered as iodine sufficient based on school-aged children UIC for one decade. The overall prevalence of thyroid dysfunction in pregnant women in this study was 9.6 %. Mean FT4 was not significantly different in three

trimesters of pregnancy ($P = 0.20$). TPOAb was positive in 7.6 % of women and nobody had increased in Tg levels. There are currently no validated thresholds for serum Tg values in pregnancy with regard to identifying population iodine status.

Inadequate levels of thyroid hormone during pregnancy may contribute to obstetric complications for the mother and neurodevelopmental deficits in the fetus [4, 5]. This topic received increased attention during last few decades and in 2012, the Endocrine Society guideline recommended: “As long as possible before pregnancy and during pregnancy and breastfeeding, women should increase their daily iodine intake to 250 µg on average by daily oral iodine supplement of 150–200 µg/days irrespective of historical iodine nutrition status” [16]. As a component of thyroid hormones, iodine is essential for regulation of metabolic processes in most cells, besides playing a vital role in the development of most organs, in particular the brain for adequate thyroid hormone synthesis throughout life, therefore assuring adequate iodine nutrition, especially during pregnancy is essential. Many physicians who encounter pregnant women do not have sufficient information about management of thyroid disorders and providing iodine support during pregnancy and lactation [23]. There are a few well conducted studies on iodine nutrition in pregnancy, based on median UIC [24–28]. Different studies have shown that median UIC in children cannot be used to define normal iodine nutrition in pregnancy and it is suggested that even in an iodine-sufficient area, an additional iodine supply might be necessary during pregnancy and lactation. The Yozen Fuse et al. study [29] in Japan, which is regarded as an iodine-sufficient or even excessive country, a substantial percentage of pregnant and lactating women had UICs below 100 µg/L and could be at risk for iodine deficiency if there is a restriction of iodine-rich foods. In the present study conducted in an area with iodine sufficiency, it was shown that despite a legislated national program of iodization of all household salts and the consumption of iodized salt by more than 95 % of the population, with sustained adequate median UIC among schoolchildren in all provinces of Iran during the years after national salt iodization, the median UIC of pregnant women was 87.3 µg/L, indicating moderate iodine deficiency. Only

Table 5 Prevalence of thyroid dysfunction according to iodine status

UIC (µg/L)	n	Overt hypothyroidism n (%)	Subclinical hypothyroidism n (%)	Subclinical hyperthyroidism n (%)	Overt hyperthyroidism n (%)
<100	626	11 (1.80)	51 (8.20)	4 (0.64)	1 (0.15)
100–149	212	2 (0.95)	10 (4.70)	1 (0.47)	0 (0.00)
150–250	174	4 (2.30)	13 (7.47)	1 (0.57)	0 (0.00)
250–500	55	1 (1.80)	3 (5.45)	0 (0.00)	0 (0.00)
≥500	5	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

21.8 % of subjects had UIC > 150 µg/L. In our previous study, we found variations of urinary iodine concentration (UIC) during a 4-week period among pregnant and non-pregnant women in Tehran, capital city of Iran. There was a wide intrapersonal variation in UIC values among pregnant and non-pregnant women residing in an iodine-replete area, supporting the notion that causal UIC would not reflect the iodine status of the individual [30]. Similar findings have been demonstrated in Ireland [31], Switzerland [32], Tasmania (Australia) [33], and Japan [34], whereas studies from Spain [35], France [36], and Hong Kong [37] have shown that with the progression of pregnancy, the median UIC was increased; however, a statistically significant change was observed only in Hong Kong study.

Based on trimester-specific reference ranges of thyroid parameters derived from our local study, the overall prevalence of thyroid dysfunction in Iranian pregnant women in present study was 9.5 %. According to recently published guidelines [15, 16] which recommend normal TSH value less than 2.5 mIU/L in the first trimester and 3.0 mIU/L in the second and third trimesters, in our study 395 subjects (66.8 %) had elevated TSH which was significantly higher than those using our local reference range ($p < 0.001$) (Fig. 1). In the present study, the frequency of positive TPOAb was 7.6 %. Pregnant women diagnosed with thyroid autoimmunity early in pregnancy should be monitored for further changes in serum TSH during the subsequent trimesters, since these women are considered to be at higher risks of early miscarriage and also of developing hypothyroidism later. There is no universal consensus regarding to prescribe levothyroxine in euthyroid women with autoimmune thyroid disease, but a few studies have addressed this issue [38].

In this study, we have found mild-to-moderate iodine deficiency among a pregnant population by measuring UIC, yet this deficiency was not reflected by other indicators (FT4 and TSH), supporting the notion that thyroid function is not considered to be a valid marker for mild-to-moderate iodine deficiency in adult. Study by Moleti and his co-worker has shown that the neuro-intellectual outcomes in children appear to be more dependent on their mothers' nutritional iodine status than on maternal thyroid function. These results support the growing body of evidence that prenatal, mild-to-moderate iodine deficiency adversely affects cognitive development later in life, with a seemingly greater impact on verbal abilities [39].

The causal UIC reflects iodine intake over a short time period and the variation is huge, which affects the reliability of studies of iodine nutrition and UIC should not be used for the purpose of individual diagnosis and treatment. Also, some studies have confirmed that if the spot urine samples are randomly collected from a sufficient number of individuals, the median UIC obtained would be a reliable indicator of iodine status of that population and there

would be no need for cumbersome and less feasible methods of measurement of iodine and/or creatinine in 24 h urine samples. The number of spot urine samples required to estimate iodine status in a population with a 95 % confidence interval within precision range of 10 and 5 % should be approximately 125 and 500, respectively [40]. A study by Antonin Korenek et al. of 168 pregnant women of the Czech Republic shows that although all participants had sufficient UIC measured as the amount of iodine in urine over 24 h during the first trimester of pregnancy, 14 subjects had elevated TSH levels signaling subclinical or incipiently clinical hypothyroidism [41]. A similar study by Raverot et al. from Lyon has shown that healthy pregnant French women are iodine deficient, and overall 11 % of them had abnormal TSH or positive TPOAb [42]. These data raise the question of what is the most appropriate indicator for assessing iodine status during pregnancy. Maternal free T4 during pregnancy is an important risk factor for impaired psychomotor development in infants and in an individual pregnant women. The best surrogate for measuring iodine sufficiency is maternal thyroid function. It seems that TSH and freeT4 may be better indicators for iodine deficiency in the first trimester, but this would require the development of method-specific and trimester-specific reference intervals for free T4 estimates in pregnancy. On the other hand, most experts would disagree with this concept.

Our study highlights the need for ongoing surveillance of the iodine status in various communities and supports the call to raise awareness of the need for pregnant women to increase their iodine intake. Many controlled iodine supplementation trials in pregnancy have been conducted in different countries which have shown no adverse effects of 50–300 µg daily iodine supplementation in moderately iodine-deficient women. These studies suggest that in areas of mild-to-moderate iodine deficiency, the maternal thyroid is able to adapt to meet the increased thyroid hormone requirements of pregnancy. Whether or not mild-to-moderate maternal iodine deficiency produces more subtle changes in cognitive and/or neurologic function in the offspring is uncertain. Mild maternal iodine deficiency may be associated with low child IQ even in the absence of TSH elevations or low FT4 [8]. Other studies using different measures of impaired maternal thyroid function also have reported developmental impairment in the offspring of affected mothers, even if maternal hypothyroidism is mild and asymptomatic [8, 43]. In a meta-analysis of 37 studies ($n = 12,292$ children), it was shown that the children of mothers supplemented by oral iodine either before or during pregnancy had higher scores of Intelligence Quotient (IQ) compared to children whose mothers were living in severely iodine-deficient areas [44]. The most recent NHANES survey (2005–2008) conducted in

the USA indicated that 35.3 % of pregnant women had UIC less than 100 µg/L [45]. Regarding concerns about mild iodine deficiency in at least some pregnant women, the ATA recommends that all women need 150–200 µg iodine daily as dietary supplements during pregnancy and lactation [11]. WHO has also advocated daily iodine supplementation or annual iodized oil supplements for pregnant women in region where only less than 30 % of households use iodized salt. In Iran, the main source of iodine supply is iodized salt for household use and it is mandated to be fortified in the country. As the universal salt iodization may not be adequate during pregnancy, we strongly recommend supplementation of 150 µg of iodine during pregnancy, and if possible for months before conception.

Acknowledgments The authors wish to thank the participants for their cooperation in this study. The authors also wish to acknowledge Ms. Niloofer Shiva for critical editing of English grammar and syntax of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they do not have any commercial associations which might create a conflict of interest in connection with this manuscript.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent No informed consent.

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