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پروپوزال نویسی
Evaluation of Accessibility of Iodinated Salt and Nutritional Iodine Status during Pregnancy

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Abstract
Background: To assess accessibility of iodinated salt and urinary iodine concentrations (UIC) during pregnancy. This cross-sectional study was carried out between October and December, 2009 in Urmia County, West Azerbaijan (WA), Iran.

Methods: Data on demographic characteristics and iodinated salt accessibility were gathered through a questionnaire at 1st trimester. Household salt samples and urine samples (1st and 3rd trimesters) were analyzed for iodine content. Pregnant women (n=490) at 1st trimester were interviewed. Of these, 490 subjects (12 prenatal care centers) were enrolled.

Results: All participants declared that they were exclusive users of iodinated salt. Segregation of the household salt samples according to iodine content (0, 8, 15 and 30 ppm) revealed that the respective distributions were 3.3%, 1.4%, 23.7% and 71.6%. Median UIC levels at 1st and 3rd trimesters were 73.5 µg/L and 114µg/L respectively. Accordingly, 86% and 70% of participants exhibited UIC < 150 µg/L.

Conclusion: Median UIC during pregnancy in WA is markedly lower than those previously reported for regions with adequate iodine status in the country. Thus, extra iodine is needed to maintain adequate iodine store during gestation. In addition, this preliminary study reveals that a significant proportion (28%) of the household salt samples had low iodine content (≤ 15 ppm) although a level (>20 and <40 ppm) is mandatory in Iran. Further studies are deemed necessary to elucidate the cause(s) for manifestation iodine deficiency among pregnant women despite 20 years after iodine fortification strategy.

Keyword: Urinary iodine excretion, Pregnancy, Iodine, Salt iodination

Introduction

Iodine is a micro-nutrient and hence it is scarcely found in food products of many regions through the world (1-3). Lots of efforts have been undertaken worldwide to eliminate Iodine Deficiency and its related Disorders (IDDs) over the four past decades (1-2). There are nearly 38 million newborns at risk of lifelong consequences of iodine deficiency annually, which are predominately born in developing countries (4-8).

The Iranian Universal Salt Iodination (USI) program was commenced in 1994. The country was subsequently declared free of iodine deficiency in 2000 (9). Azizi et al. (10) have reported that median Urinary Iodine Concentration (UIC) in pregnant women residing in four cities with more than adequate access ranged from 186 to 338 µg/L. They have also reported that median UICs in 1st and 2nd trimesters were similar but marginally higher than 3rd trimester. It was found that median
UIC fell from 193 µg/L at 1st trimester to 141 µg/L at 3rd trimester (11). Urmia County is the capital of West Azerbaijani (WA) and is located in northwest of Iran. The 2nd Iranian National Survey performed in 1996 has reported that the values for median UIC and total goiter prevalence (TGP) by palpation for school-aged children in WA were 150 µg/L and 45%, respectively (12). The corresponding values from 3rd Iranian National Survey conducted in 2004 were 140 µg/L and 7.1% (13). To the best of knowledge, no information is available on iodinated salt accessibility and/or nutrition iodine status in pregnancy in WA Province. Considering the impact of iodine status on the well-being of the fetus particularly in a mild-moderate deficient area, this study was undertaken to address iodinated salt accessibility and nutritional iodine status during pregnancy in Urmia County.

**Materials and Methods**

Pregnant women (n=1078) attending prenatal care units in Urmia County were interviewed between October, 2009 and December, 2009. Exclusion criteria were no history of thyroid dysfunction and/or abortion. Sample size calculation (n=394) was based on the prevalence of iodine deficiency in WA Province according to 3rd National Iranian Survey (13). To enhance the statistic power of the study, sample size was increased to 490 subjects. The studied population was allocated to five districts comprising 12 prenatal care centers. Sample size in each prenatal care was calculated according to annual live birth rate employing Population Proportionate Sampling Approach. Data on demographic characteristics and iodinated salt accessibility were gathered through a Food Frequency Questioner (FFQ) at 1st trimester. A table salt sample was also obtained from each participant during the 1st visit. A second UIC sample was collected at 3rd trimester. Fasting urine samples were collected at 1st and 3rd trimester. The samples were kept at -20°C until UIC testing. This investigation was approved by the ethical committee at Urmia University of Medical Science, Iran.

UIC was assessed by the Sandell-Koltoff reaction method A (14). Coefficient of variation of the assay was 8%.

Iodine content in the table salt samples was monitored using Field Test for Iodated Salt (Peyman Tashikhis, Tehran, Iran) (15). Descriptive and analytical statistics were performed using the STATA/SE 10.0 for windows. UIC values are presented as medians because the data were not normally distributed. Mann-Whitney U test was used to evaluate the impact of geographical on UIC whilst Wilcoxon signed-rank test was employed to examine the differences in UIC at 1st - and 3rd trimester. P-value <0.05 was considered significant.

**Results**

Mean age of the participants was 25.01 yrs ± 5.42 yrs. Sample size at the 1st trimester was 490 subjects. The sample size fell to 394 cases at 3rd trimester due to unavailability, relocations, abortion, or unwillingness to continue the study. Percentage of miss to follow up was 20% (n=96) at 3rd trimester. Based on FFQ interview, all participants had stated that they only consumed iodinated salt as specified by product disclaimer. Quality analysis of the household salt samples, the other hand, revealed that 95% of the obtained samples had an iodine content ≥ 15 ppm. Subdivision of the obtained household salt samples according to iodine content (i.e. 0 ppm, 8 ppm, 15 ppm and 30 ppm) revealed that the respective frequencies were as follows: 3.3%, 1.4%, 23.7% and 71.6% (Fig. 1). Mean and median UIC for the studied population, as a whole, at 1st trimester were 80.8±55.7 µg/L and 73.5µg/L, respectively. Accordingly, the corresponding figures at 3rd trimester were 109.7±64.1 µg/L and 114µg/L. The differences between median UIC at 1st – and 3rd trimester, however, failed to reach statistical significance. By contrast, pair-wise comparison of UIC values at 1st - and 3rd trimester revealed that the differences were statistically significant (P<0.05). Median UIC in pregnancy expressed as the average median UIC at 1st –and 3rd trimester was 93.7µg/L.
When UIC levels at 1st trimester divided according to WHO criteria (i.e. severe iodine deficiency: < 50 µg/L; mild iodine deficiency: 50-99 µg/L; moderate iodine deficiency: 100-149 µg/L; adequate iodine status: 150-199 µg/L and more than adequate iodine status: ≥ 200 µg/L) it was found the distributions were 33%, 35%, 18.5%, 10.4 and 3.1%, respectively (Table 1). The respective frequencies for UIC at 3rd trimester were as follows: 21.1%, 22.3%, 26.6%, 21.7% and 8.3% (Table1).

![Fig.1: Distribution of household salt samples when segregated according to iodine content](image)

**Table 1:** Distributions of urinary iodine concentrations (UIC) in gestation segregated according to WHO criteria for the evaluation of nutritional iodine status in school-age children

<table>
<thead>
<tr>
<th></th>
<th>Sever iodine deficiency (&lt; 50 µg/L)</th>
<th>Mild iodine deficiency (50-99 µg/L)</th>
<th>Adequate iodine intake (100-149 µg/L)</th>
<th>Optimal iodine intake (150-199 µg/L)</th>
<th>More than optimal iodine intake (&gt;200 µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UIC 1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>33.3%</td>
<td>34.9%</td>
<td>18.4%</td>
<td>10.4%</td>
<td>3.1%</td>
</tr>
<tr>
<td>UIC 3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>21.1%</td>
<td>22.3%</td>
<td>26.6%</td>
<td>21.7%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

**Discussion**

The main indicators of the sustainable elimination of IDDs in schoolchildren as recommended by WHO are: a) accessibility of iodinated salt; b) assurance of proper of iodine content (i.e. >20ppm but <40ppm) by more than 90% of households; and c) a median UIC < 100 µg/L in 20% of the population (16). In this investigation, all participants had declared that they solely consumed iodinated salt as specified by product disclaimer. Quality analysis of iodine content demonstrated that 3.3% of the samples were virtually iodine free. Secondly, we report that a high percentage (28.4%) of the obtained samples exhibited an iodine content ≤ 15 ppm. Taken together, our data demonstrate that iodine content in the provided samples is lower than the range >20ppm and <40ppm recommended by WHO. These findings urge for improved procedures to monitor iodinate salt production as well as distribution network by the Health Authority in WA Province.

The WHO has recommended a UIC range between 150 and 249 µg/L during pregnancy, as an indicator of iodine sufficiency (8, 16-17). The current investigation reveals that overall median UIC in pregnancy was 93.7 µg/L which is markedly lower than the reference value (140 µg/L) for school-aged in WA Province (13). Azizi et al. have reported that 84% of the pregnant women residing a region with more than adequate iodine status exhibited an UIC ≥200 µg/L. The respective percentage for pregnant women living in areas with adequate iodine status (i.e. UIC was ranging from 186 to 212 µg/L) was 51% (10). In this study, the proportions of subjects with sever iodine efficient (<50 µg/L) at 1<sup>st</sup> – and 3<sup>rd</sup> trimester were 33% and 21.1%, respectively. Our data analysis has revealed that 86.5% and 70% of the participants at 1<sup>st</sup> - and 3<sup>rd</sup> trimester did not meet the recommended WHO criteria for adequacy of nutritional iodine status during pregnancy (i.e. UIC>150 µg/L). Considering that the median
UIC for school-age children in WA province, the marked decline (34%) in overall median UIC during gestation appears to represent depletion of total body iodine stores due to fetal development and/or inadequate dietary iodine compensation (17). This investigation suggests that the current strategy for elimination of ID in WA Province does not fulfilling the especial requirement for iodine in pregnant women and extra iodine is need to maintain adequate iodine store during pregnancy.

A number of studies have been undertaken to examine the impact of gestation stage on UIC compared to with reference values from non-pregnant population and/or with those from school-aged children. However, some have reported an increased in median UIC with advancing gestation while other has shown a decline or no even changes (18-21). Aziz (10) has, however, examined inter-trimester variations in UIC among pregnant women in Tehran, a region with adequate iodine status. It was found that median UIC at 1st – and 2nd trimester were slightly (10.6% and 12.3%) higher compared to reference to school-aged children. The observed elevation in UIC at both 1st – and 2nd –trimester possibly reflects the enhanced iodine clearance which is expected to occur during early stages of gestation (18). On the other hand, Aniy et al. (11) found no differences between median UIC at 1st –trimester and that of reference value for school-aged children. They, however, reported steady decline in median UIC at both 2nd – and 3rd –trimester (21% and 27%, respectively). On the other hand, the drop in UIC at 2nd – and 3rd –trimester may indicate depletion of total body iodine stores due to inadequate dietary iodine compensation (18).

Our data shows that median UIC at 1st – and 3rd –trimester were 48% and 18% lower than that of the reference value for school-aged children in WA. The observed pattern seems to be similar to that reported for pregnant women living in area with mild iodine deficiency (21). The exact mechanism(s) behind the rise in UIC at 3rd – trimester in area with moderate to borderline adequate iodine intake is unclear. One likely explanation is enhanced thyroidal iodine extraction in borderline iodine deficiency (18). Taken together these findings indicate that iodine homeostasis in pregnancy is governed by different mechanism depending on thyroid physiology and/or whole body iodine pool. Further studies are required to address the impact of gestation stage on UIC.

Finally, it worth declaring that limitations of the present investigation study are: 1) lost to follow up in flat- and mountainous regions were 33% and 44%, respectively. These figures are considerable higher than the 20% recommended for follow up trials; and 2) sample size at entrance was small to allow a firm conclusion on dietary status in the mountain district. Therefore, greater measures should be taken to minimize lost to follow up in future investigation.

In conclusion, this investigation has demonstrated that median UIC during pregnancy in north-west of Iran is markedly lower than those previously reported for regions with adequate iodine status in the country. Thus, current strategy for elimination of ID in WA Province does not fulfill the especial requirement for iodine in pregnancy and additional extra sources of iodine are needed to maintain adequate iodine store in pregnancy. In addition, this preliminary study has also revealed that a significant proportion (28%) of the household salt samples had low iodine content (≤ 15 ppm) although a level (>20 and <40 ppm) is mandatory in Iran. Further studies are deemed necessary to elucidate the cause(s) for manifestation iodine deficiency among pregnant women despite 20 years after iodine fortification strategy.

**Ethical considerations**

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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References
