Abstract

Aim: The study aimed to assess the iodine status and maternal thyroid function in the pregnant women in Sivas that is a city in central Turkey. Material and Method: One hundred-ninety-three pregnant women in their second trimester who attended the hospital for routine antenatal care were included this study. Morning spot urine samples were collected in deiodized test tubes from the study population. Urine iodine levels were determined by colorimetric modified Sandell-Kolthoff reaction. Serum free triiodothyronine (fT3), free thyroxine (fT4) and thyrotropin (TSH) levels were measured by electrochemiluminescence immunoassays. Results: Median urine iodine levels were lower in Şarkışla, Suşehri Gürün, Divriği and Kangal than Sivas Center. Median urine iodine deficiency levels of pregnant women living in Şarkışla, Suşehri Gürün, Divriği, and Kangal indicated mild iodine deficiency. Discussion: Iodine deficiency is a significant problem in Sivas. Therefore, there is need for a policy such as iodine prophylaxis for pregnant women living in Sivas to eliminate this problem.

Keywords

Urine Iodine; Sivas; Pregnant Women

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Introduction
Trace elements are defined as chemicals present in minimal quantities [1]. Some of these elements including iodine, iron, and selenium are also entitled to micronutrients [2]. Iodine is an essential component of the thyroid hormones. Therefore, various metabolic and neurologic disorders have been associated with iodine deficiency (ID). ID is a threat throughout the lifecycle. The effects of inadequate iodine intake change according to the stage of lifecycle [3].

According to the World Health Organization (WHO), about 2 billion people are at risk for ID. It has also been indicated that 780 billion people are affected by ID related disorders. ID remains an important problem in Turkey whereas the presence of mandatory salt iodization [4,5]. Physiologic changes such as increase thyroxine-binding globulin (TBG), increased human chorionic gonadotropin level and increased renal filtration has been described in pregnant women. These changes affect the thyroid hormone balance. Thus, optimal iodine uptake is crucial for pregnant to cope with these changes [6]. Since the majority of iodine absorbed by the body is excreted in the urine the measurement of urinary iodine level is a reliable indicator of recent dietary iodine intake and therefore of iodine status [7]. The optimal urine iodine levels (UIL) change according to different target groups. WHO used the levels (< 150), (150-249), (250-499) and (> 500) µg/L to define insufficient, adequate, above requirement and excessive iodine levels for pregnant women, respectively [6].

The study aimed to assess the iodine status and maternal thyroid function in the pregnant women in Sivas that is a city in central Turkey. For this purpose, we examined thyroid function and urine iodine status of pregnant women in their second trimester. This is the first study to define the status of iodine status in Sivas. This study provides an exciting opportunity to advance our knowledge regarding the iodine status in Sivas.

Material and Method
This study was performed with the collaboration of Cumhuriyet University Department of Biochemistry and Department of Obstetrics and Gynecology and Sivas Numune Hospital Department of Obstetrics and Gynecology between 2015 and 2016. One Hundred-ninety-three pregnant women in their second trimester who attended the hospital for routine antenatal care were included this study. We excluded pregnant women with any acute or chronic disease, multiple pregnancies, those receiving any pharmacological agent. Samples were obtained from the city centre of Sivas and the distinct including Şarkışla, Kangal, Suşehri, Gürün, and Divriği. The study protocol was approved by the Cumhuriyet University (Approval number:2015-12/05).

Morning spot urine samples were collected in de-iodized test tubes. Urine samples were stored at ~ 80 °C until analysis. Urine iodine levels were determined by colorimetric modified Sandell-Kolthoff reaction as recommended by literature [8]. Morning fasting blood samples were collected from all participants into red top tubes (Becton Dickinson, UK). The serum sample tubes were allowed to clot before centrifugation. Analysis were performed immediately after centrifugation at 4°C for 15 minutes at 3500 rpm. Serum-free triiodothyronine (fT3), free thyroxine (fT4) and thyrotropin (TSH) levels were measured by electrochemiluminescence immunoassay using Roche Cobas e601 analyzer (Mannheim, Germany). TSH levels were determined using third generation immunometric assay. The intra and inter coefficient of variation of and reference intervals for pregnant women in the second trimester were given in Table 1.

Results
The range of gestation week was 5th-13th in all locations. Median gestation weeks were 8 weeks 2 day, 8 weeks, 8 weeks 4 day, 10 weeks, 7 weeks 2 day and 8 weeks in Sivas Centre, Şarkışla, Suşehri Gürün, Divriği, and Kangal, respectively. Median ID levels of pregnant women living in Şarkışla, Suşehri Gürün, Divriği, and Kangal indicated inadequate iodine intake. The clinical information, urinary iodine and thyroid function parameter levels in the study population were given in Table 2. Respectively 20.75%, 78.75%, 86.36%, 94.12%, 61.54% and 75.68% of participants had insufficient iodine intake in Sivas Centre, Şarkışla, Suşehri Gürün, Divriği, and Kangal. The distributions of pregnant women according to median iodine status were given in Figure 1. Deficiency is defined as either severe (median UI < 20 µg/L), moderate (20–49 µg/L), or mild (50–150 µg/L) [11]. The numbers of pregnant women grouped according to deficiency grade were given in Table 3.

Discussion
ID is a worldwide health problem. Although the application of mandatory salt iodization in several countries are performed, the insufficiency of iodine intake during pregnancy is still a problem. In a report published by WHO the proportion of insufficient iodine intake of school-age children is 52.4% in Europe [12,13]. ID during pregnancy is an important risk factor

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Concentration</th>
<th>Interassay CV (%)</th>
<th>Intraassay CV (%)</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>fT3 (pg/mL)</td>
<td>1.86</td>
<td>2.1</td>
<td>2.8</td>
<td>1.78–5.29**</td>
</tr>
<tr>
<td></td>
<td>2.51</td>
<td>2.2</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.7</td>
<td>1.5</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>fT4 (ng/dL)</td>
<td>0.68</td>
<td>1.6</td>
<td>3.5</td>
<td>0.76 – 1.23**</td>
</tr>
<tr>
<td></td>
<td>1.64</td>
<td>1.7</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.95</td>
<td>2.9</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>TSH (mIU/mL)</td>
<td>0.001</td>
<td>3.0</td>
<td>7.2</td>
<td>0.31 – 4.17**</td>
</tr>
<tr>
<td></td>
<td>0.002</td>
<td>2.7</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.102</td>
<td>1.1</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

Interassay and intraassay values obtained from kit insert (fT3 [lot no:22700101], fT4 [lot no:22515005] and TSH [lot no:25580201]). *This value was defined for pregnant women in the second trimester [9]. These values were defined for pregnant women in the second trimester [10].

Table 1. References and CV values of fT3, fT4, and TSH

<table>
<thead>
<tr>
<th>Location</th>
<th>MA (years)</th>
<th>MW (kg)</th>
<th>Median UIL (1st-3rd quartile)</th>
<th>TSH (mIU/mL)</th>
<th>FT4 (ng/dL)</th>
<th>FT3 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sivas Centre</td>
<td>28 ± 6</td>
<td>67 ± 14</td>
<td>260.1 (167.2 – 367.1)</td>
<td>1.75 ± 1.01</td>
<td>1.30 ± 0.15</td>
<td>3.49 ± 0.41</td>
</tr>
<tr>
<td>Şarkışla</td>
<td>28 ± 7</td>
<td>66 ± 10</td>
<td>75.93 (28.84 – 176.8)</td>
<td>2.06 ± 1.05</td>
<td>1.24 ± 0.15</td>
<td>3.36 ± 0.61</td>
</tr>
<tr>
<td>Suşehri</td>
<td>27 ± 6</td>
<td>66 ± 14</td>
<td>55.63 (24.77 – 96.29)</td>
<td>1.95 ± 1.54</td>
<td>1.19 ± 0.15</td>
<td>3.21 ± 0.29</td>
</tr>
<tr>
<td>Gürün (n: 44)</td>
<td>28 ± 6</td>
<td>62 ± 10</td>
<td>42.14 (31.31 – 75.57)</td>
<td>1.86 ± 0.19</td>
<td>1.19 ± 0.19</td>
<td>3.46 ± 0.46</td>
</tr>
<tr>
<td>Divriği (n: 15)</td>
<td>27 ± 5</td>
<td>59 ± 16</td>
<td>55.32 (23.31 – 243.7)</td>
<td>1.43 ± 0.88</td>
<td>1.19 ± 0.17</td>
<td>3.24 ± 0.41</td>
</tr>
<tr>
<td>Kangal (n: 37)</td>
<td>26 ± 6</td>
<td>61 ± 9</td>
<td>84.99 (57.43 – 144.3)</td>
<td>2.17 ± 1.4</td>
<td>1.30 ± 0.36</td>
<td>3.35 ±0.58</td>
</tr>
</tbody>
</table>
have been observed in 75% of all populations living in a Western part of Anatolia, Turkey [21]. Our finding is in accordance with the previous studies. There is trimester-specific reference for TSH. For the second trimester 0.2-3.0 mIU/L values are used to define lower and upper limit of serum TSH values. American thyroid association recommended the measurement of total T4 and the calculation of FT4 index [10]. The number of pregnant women who had TSH level > 3.0 mIU/L were 4, 3, 4, 2 and 6 in Sivas Centre, Şarkışla, Suşehri, Gürün, and Kangal, respectively. None of the pregnant women's TSH levels were >3.0 mIU/L in Divriği. In our study, we observed a concordance between the numbers of pregnant women who had an ID and abnormal TSH levels in all regions. Therefore, evaluating the urinary iodine level is important to define iodine intake status of pregnant women because serum TSH level does not indicate low iodine status. The main limitation of our study is the low number of individuals in some regions. Thus, further studies that include higher sample numbers should be performed to solidify these results.

Conclusion
Our results indicated that ID is a significant problem in Sivas. Therefore, there is a need policy such as iodine prophylaxis for women living in Sivas to eliminate this problem. Finally, these are only preliminary findings, and further investigations with larger samples are warranted.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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