ing pregnancy and, thus, the need for screening for the disease. This also appears to be inferred from various randomized studies where women in the control group having clinical hypothyroidism according to current criteria were known but were not treated, without this causing any ethical conflict.5,10 Regarding the problems derived from screening: after a comprehensive analysis of the literature, the authors still could not give a clear recommendation about which action should be taken when subclinical hypothyroidism is diagnosed in pregnancy, stating that the potential treatment should be based on a clinical assessment which is not defined. When population screening for a disease with a low prevalence is recommended, the impact of such screening on a more prevalent condition diagnosed with the same test should be considered. This is even more important in the setting of the emotional burden associated with an otherwise physiological process such as pregnancy. It, therefore, appears inadequate to promote a diagnostic strategy that causes uncertainty about adequate action in most detected cases. In this regard, the authors advocate training programs ‘mainly aimed at therapeutic abstinence in situations of unproven pathological value’. However, in view of the uncertainty and the disparity of the available criteria concerning the convenience and benefit of treatment of subclinical hypothyroidism in pregnancy, it is difficult to believe that such a training program would convey a coherent and consistent message.

Based on the foregoing, I think that the promotion of a universal strategy of screening for clinical hypothyroidism in pregnancy has no adequate scientific basis. In addition, because of the existing uncertainty, the impact of consen sus documents issued by scientific societies on healthcare professionals and the general population, and the evidence that any medical action, however trivial it may seem, may have unwanted consequences.11 I do not think it appropriate to make ethical judgments about the adequate course of action when faced with a clinical question for which no satisfactory answer is available.

Conflict of interest

The author states that he has no conflict of interest.

Thyrotropin reference values in the first trimester of pregnancy

Valores de referencia de tirotropina en el primer trimestre del embarazo

Sir,

A recent consensus document1 and the clinical guidelines of the Spanish Society of Endocrinology and Nutrition2 recommend that each center should establish its own normal reference value for each trimester of pregnancy in their population using adequate laboratory techniques, but as stated by the American Thyroid Association (ATA),3 in the absence of such values, it is recommended that a value of 2.5 mcU/mL be used as the cut-off point for thyroid releasing hormone (TSH) in the first trimester of pregnancy.

In Spain, normal TSH levels adequate for the first trimester of pregnancy have only been reported in four populations: Aragon, with reference values ranging from 0.41 to 2.63 mcU/L;4 Catalonia, 0.12–4.75 mcU/mL;5 Cartagena, 0.13–3.71 mcU/mL;6 and Jaén, 0.23–4.18 mcU/mL.7 A simple calculation of the non-weighted mean of these populations would give an upper limit close to 4 mcU/mL, very far from that proposed by the ATA (Table 1).

References

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Table 1  Thyroid releasing hormone levels in the first trimester of pregnancy in women with negative anti-thyroid peroxidase antibodies.

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>2.5th p</th>
<th>97.5th p</th>
<th>Gestational weeks</th>
<th>Method</th>
<th>Laboratory</th>
<th>No.</th>
<th>Normal values</th>
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<tr>
<td>Bocos-Terraz et al.</td>
<td>1.0</td>
<td>0.41</td>
<td>2.63</td>
<td>&lt;14</td>
<td>IMA</td>
<td>Abbot Architect</td>
<td>481</td>
<td>&lt;4.94</td>
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<tr>
<td>Vila et al.</td>
<td>1.36</td>
<td>0.12</td>
<td>4.75</td>
<td>9</td>
<td>IMA</td>
<td>Advia-Bayer</td>
<td>178</td>
<td>0.4–4.0</td>
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<tr>
<td>García de Guadalupe</td>
<td>1.44</td>
<td>0.13</td>
<td>3.71</td>
<td>11–13</td>
<td>IMA</td>
<td>Roche</td>
<td>400</td>
<td>0.27–4.2</td>
</tr>
<tr>
<td>Romualdo et al.</td>
<td>1.52</td>
<td>0.23 (p3)</td>
<td>4.18 (p97)</td>
<td>7–10</td>
<td>IMA</td>
<td>Beckman</td>
<td>305</td>
<td>0.26–5.6</td>
</tr>
<tr>
<td>Santiago et al.</td>
<td>1.76</td>
<td>0.17</td>
<td>4.15</td>
<td>6–12</td>
<td>IMA</td>
<td>Roche</td>
<td>264</td>
<td>0.45–5</td>
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<td>Oviedo (current)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>

IMA: Immunometric assay; 2.5th p: 2.5th percentile; 97.5th p: 97.5th percentile.
TSH data in mIU/mL.

At our center, plasma TSH and anti-thyroid peroxidase antibody (anti-TPO Ab) levels were measured in 309 women in the first trimester of pregnancy (6–12 weeks) using a chemiluminescence immunosassay from Roche Diagnostics. Thirty-nine women (11.7%) had positive anti-TPO Ab (>35 U/mL). In this group, the 2.5th and 97.5th percentiles were 0.45 and 7.89 mIU/mL respectively. Excluding these women with positive anti-TPO and those with TSH levels higher than 5 mIU/mL, the 2.5th and 97.5th percentiles of TSH in the remaining 264 women were 0.17 and 4.15 mIU/mL respectively, which are considered the reference levels in our population using this test method.

Using these normal reference values for thyroid function screening performed at our health area during 2010 and 2011 on 4461 women in their first trimester of pregnancy, the prevalence of hypothyroidism with elevated TSH (>4.17 mIU/mL) was 7.2%, higher than that found in other populations. If we had not had our own reference values and had used instead the level recommended by the ATA of 2.5 mIU/mL, the result would have been a prevalence of 28.2%, a very high rate, and the number of false diagnoses would therefore have been totally unacceptable.

Based on the foregoing, and before any universal or selective screening program is considered, we believe that each center should have its own reference values appropriate for its method and population as an indispensable precondition for adequate thyroid function assessment in pregnancy. In Spain, the use of the cut-off values recommended by scientific societies from other countries could lead to overdiagnosis, with significant healthcare and financial implications.

References


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