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.[6,10] *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 abstention 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 consensus 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.

References

1. Vila L, Velasco I, González S, Morales F, Sánchez E, Lailla JM, et al. Detección de la disfunción tiroidea en la población gestante: está justificado el cribado universal. Endocrinol Nutr. 2012;59:547–60.
2. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011;21:1081–125.
3. Blatt AJ, Nakamoto JM, Kaufman HW. National status of testing for hypothyroidism during pregnancy and postpartum. J Clin Endocrinol Metab. 2012;97:777–84.
4. Menéndez E, Sánchez V, Avello N, Aller J, Bellido V, Boix P. Cribaje poblacional de la función tiroidea en mujeres embarazadas del área sanitaria de Oviedo. Endocrinol Nutr. 2011;58:120–1.
5. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol. 2005;105:239–45.
6. Lazarus JH, Bestwick JP, Channon S, Paradice R, Maina A, Rees R, et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med. 2012;366:493–501.
7. Vissenberg R, van den Boogaard E, van Wely M, van der Post JA, Fliers E, Bisschop PH, et al. Treatment of thyroid disorders before conception and in early pregnancy: a systematic review. Hum Reprod Update. 2012;18:360–73.
8. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid. 2002;12:63–8.
9. Männistö T, Vääräsmäki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al. Perinatal outcome of children born to mothers with thyroid dysfunction or antibodies: a prospective population-based cohort study. J Clin Endocrinol Metab. 2009;94:772–9.
10. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. J Clin Endocrinol Metab. 2010;95:1699–707.
11. Gray JA, Patnick J, Blanks RG. Maximising benefit and minimising harm of screening. BMJ. 2008;336:480–3.

Gabriel Giménez-Pérez

Unitat d'Endocrinologia, Hospital General de Granollers, Granollers, Barcelona, Spain
E-mail address: 26082ggp@comb.cat

Thyrotropin reference values in the first trimester of pregnancy☆

Valores de referencia de tirotropina en el primer trimestre del embarazo

Sir,

A recent consensus document[1] and the clinical guidelines of the Spanish Society of Endocrinology and Nutrition[2] 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).

☆ Please cite this article as: Aller Granda J, Rabal Artal A. Valores de referencia de tirotropina en el primer trimestre del embarazo. Endocrinol Nutr. 2013;60:405–406.

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

	Median	2.5th p	97.5th p	Gestational weeks	Method	Laboratory	No.	Normal values
Bocos-Terraz et al.[4]	1.0	0.41	2.63	<14	IMA	Abbot Architect	481	<4.94
Vila et al.[5]	1.36	0.12	4.75	9	IMA	Advia-Bayer	178	0.4–4.0
García de Guadiana Romualdo et al.[6]	1.44	0.13	3.71	11–13	IMA	Roche	400	0.27–4.2
Santiago et al.[7]	1.52	0.23 (p3)	4.18 (p97)	7–10	IMA	Beckman	305	0.26–5.6
Oviedo (current)	1.76	0.17	4.15	6–12	IMA	Roche	264	0.45–5

IMA: Immunometric assay; 2.5th p: 2.5th percentile; 97.5th p: 97.5th percentile.
TSH data in mcIU/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 immunoassay 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 mcIU/mL respectively. Excluding these women with positive anti-TPO and those with TSH levels higher than 5 mcIU/mL, the 2.5th and 97.5th percentiles of TSH in the remaining 264 women were 0.17 and 4.15 mcIU/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 mcIU/mL) was 7.2%, higher than that found in other populations.[8] If we had not had our own reference values and had used instead the level recommended by the ATA of 2.5 mcIU/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

1. Vila L, Velasco I, González S, Morales F, Sánchez E, Lailla JM, et al. Detection of thyroid dysfunction in pregnant women: universal screening is justified. Endocrinol Nutr. 2012;59:547–60.
2. Galofré Ferrater JC, Corrales Hernández JJ, Pérez Corral B, Cantón Blanco A, Alonso Pedrol N, Pérez Pérez A, et al. Clinical guideline for the diagnosis and treatment of subclinical thyroid dysfunction in pregnancy. Working Group on Subclinical Thyroid Dysfunction of the Spanish Endocrinology Society. Endocrinol Nutr. 2009;56:85–91.
3. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011;21:1081–125.
4. Bocos-Terraz JP, Izquierdo-Alvarez S, Bancalero-Flores JL, Alvarez-Lahuerta R, Aznar-Sauca A, Real-López E, et al. Thyroid hormones according to gestational age in pregnant Spanish women. BMC Res Notes. 2009;2:237.
5. Vila L, Serra-Prat M, Palomera E, Casamitjana R, de Castro A, Legaz G, et al. Reference values for thyroid function tests in pregnant women living in Catalonia, Spain. Thyroid. 2010;20:221–5.
6. García de Guadiana Romualdo L, González Morales M, Martín-Ondarza González MC, Martín García E, Martínez Uriarte J, Blázquez Abellán A, et al. Evaluation of thyroid function during pregnancy: first-trimester reference intervals for thyroid-stimulating hormone and free thyroxine. Endocrinol Nutr. 2010;57:290–5.
7. Santiago P, Berrio M, Olmedo P, Velasco I, Sánchez B, García E, et al. Reference values for thyroid hormones in the population of pregnant women in Jaen (Spain). Endocrinol Nutr. 2011;58:62–7.
8. Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, et al. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol. 2008;112:85–92.

Javier Aller Granda*, Antonio Rabal Artal

Servicio de Endocrinología y Nutrición, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain

*Corresponding author.
E-mail address: javierallergranda@gmail.com
(J. Aller Granda).