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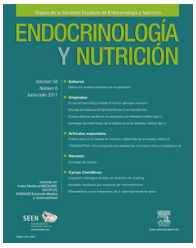

LETTERS TO THE EDITOR

Some considerations about the consensus document ''Detection of thyroid dysfunction in pregnant women: Universal screening is justified''☆

Algunas consideraciones sobre el documento de consenso «Detección de la disfunción tiroidea en la población gestante: está justificado el cribado universal»

Sir,

A consensus document on the detection of thyroid dysfunction in pregnant women endorsed by the Spanish Society of Endocrinology and Nutrition and the Spanish Society of Gynecology and Obstetrics has recently been published.[1] First of all, I would like to express my most sincere thanks to the authors for their comprehensive and rigorous review of the literature, their synthesis of and reflection on it, and their preparation of a list of recommendations intended to unify the criteria for thyroid dysfunction screening during pregnancy based on the available evidence. There are, however, some aspects of the abovementioned document which, in my view, should be reconsidered. These relate to the first and most distinctive recommendation made, namely the justification of universal thyroid dysfunction screening to detect and treat previously unknown cases of clinical hypothyroidism.

As far as I can judge, the authors base their recommendation, amongst other considerations, on the prevalence of clinical hypothyroidism in pregnancy and the availability of a reliable screening test and effective treatment. *Regarding prevalence*: the authors estimate a prevalence of unknown clinical hypothyroidism in pregnancy of 0.3–0.5% or higher based on studies[2–5] that did not exclude women with known hypothyroidism and which are therefore not valid for establishing such a prevalence. A higher prevalence is also suggested, quoting the Blatt et al. article[3] (with an errata in the year of publication), which according to the authors found a 2.5% prevalence of hypothyroidism. However, this percentage was based on women with TSH levels higher than 2.5 mIU/L (15.5%), and the actual prevalence of clinical hypothyroidism in all pregnant women in this study was 0.37%. An abstract of a poster presented at a meeting[4] is also discussed, but a detailed analysis is not possible based on the data provided. It would have been more informative to have used the data reported by Lazarus et al.,[6] who stated that among the 10,924 women with no known thyroid disease screened at approximately week 14 of pregnancy, 25 (0.23%) had elevated TSH together with FT4 levels lower than the 2.5th percentile. There is therefore no reason for suggesting a higher prevalence of unknown clinical hypothyroidism in pregnancy. *Regarding the screening test*: the authors recommend that the diagnosis of clinical hypothyroidism be made ''as in the non-pregnant population, and the availability of reference values for the pregnant population is indispensable''. This apparently obvious statement has some limitations when one intends to establish a screening strategy for clinical hypothyroidism during pregnancy. According to the reflections of the authors themselves, it does not appear that the measurement of FT4 in pregnancy is a ''reliable, acceptable, and safe'' test because, as they state, ''there could be no absolute FT4 value that may define hypothyroxinemia with these techniques''. Thus, situations which may be considered striking, to say the least, may occur in the diagnosis of clinical hypothyroidism in pregnancy, because a woman in her first trimester of pregnancy with a TSH level of 2.3 mIU/L and a FT4 level below the reference value would have isolated hypothyroxinemia, which ''may not be considered to be a pathological condition with any certainty'', while a woman with a TSH level of 2.7 mIU/L and the same FT4 value would have clinical hyperthyroidism ''unquestionably related to poorer intellectual or neurocognitive outcomes, increased fetal death, and other complications''. *Regarding effective treatment*: the need for the treatment of clinical hypothyroidism in the setting of pregnancy is considered to be sufficiently proven, and we will not challenge this statement. However, the evidence on which this statement is based is poor and inconsistent.[7] The most emblematic study of the effect of the treatment of clinical hypothyroidism on perinatal outcome is probably the one conducted by Abalovich et al.,[8] in which perinatal outcomes in a retrospective series were clearly better in patients with adequately treated clinical hypothyroidism (TSH 33.4 ± 8.8 mIU/L). If, by contrast, the current criteria for clinical hypothyroidism in pregnancy are used, the condition does not appear to be associated with poorer perinatal outcomes.[9] It is, therefore, possible that the application of current criteria for abnormal TSH levels in pregnancy invalidates the benefit expected from treatment of all cases of clinical hypothyroidism dur-

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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.

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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).

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