

UNIVERSAL SCREENING FOR THYROID DISORDERS IN PREGNANCY

Wang W, Teng W, Shan Z, Wang S, Li J, Zhu L, Zhou J, Mao J, Yu X, Li J, Chen Y, Xue H, Fan C, Wang H, Zhang H, Li C, Zhou W, Gao B, Shang T, Zhou J, Ding B, Ma Y, Wu Y, Xu H, Liu W. The prevalence of thyroid disorders during pregnancy in China: the benefits of universal screening in the first trimester of pregnancy. *Eur J Endocrinol*. November 8, 2010 [Epub ahead of print].

SUMMARY

BACKGROUND

Maternal and perinatal morbidities are well-documented complications of pregnancy in mothers with thyroid dysfunction, both clinical and subclinical, and in euthyroid mothers diagnosed with chronic thyroiditis. Impaired fetal brain development and decreased intelligence quotient have been demonstrated in children of such mothers, and also in those mothers diagnosed with hypothyroxinemia (1,2). The vast majority of affected women are asymptomatic; therefore, in view of the potential pregnancy and progeny complications, it has been suggested that every woman be screened for thyroid dysfunction before or very early after conception. The prevalence of overt or clinical hypothyroidism in pregnancy is reported to be about 0.3%, subclinical hypothyroidism between 2% and 4%, euthyroid thyroiditis between 5% and 20%, isolated hypothyroxinemia early in pregnancy between 0.8% and 1%, and clinical hyperthyroidism <1% (3). Universal screening is a very controversial topic, the most powerful argument against it is the lack of a randomized, clinical trial showing a beneficial effect of thyroid therapy on pregnancy outcome.

METHODS

In a 4-year period, Wang et al. recruited 2899 pregnant women before 12 weeks' gestation from 10 antenatal clinics in Shenyang, China, from iodine-adequate areas. Blood samples were obtained from all women after overnight fasting for serum thyrotropin (TSH), free thyroxine (FT₄), (FT₃), thyroid peroxidase antibodies (TPOAb) and urinary iodine excretion. Gestational age was assessed by patient last normal menstrual period and confirmed by ultrasonography. All participants answered a questionnaire that gathered information about reproductive age, personal and family history of thyroid disorders, personal history

of type 1 diabetes or other autoimmune disease and history of therapeutic or neck irradiation. Any woman with a positive answer was identified as being at high risk for thyroid disease during pregnancy. First trimester-specific reference intervals for this population were previously published by the authors. The first trimester-specific reference ranges were: TSH, 0.13 to 3.93 mIU/L; FT₄, 12.0 to 23.34 pM, and TPOAb <50 IU/ml.

RESULTS

The mean (±SD) age of the 2899 women was 27.61±3.55 years and the median gestational age was 6 weeks (range, 4 to 12). The median urinary iodine was 177 µg/L. A little over half of the women were nulliparous; the authors classified 367 of the 2899 women (12.7%) as a high-risk group according to *The Endocrine Society Clinical Practice Guidelines*. The vast majority of the 367 women were included in the high-risk group because of a personal or family history of thyroid disease or a previous miscarriage.

Of the 2899 women with thyroid tests recorded, 294 had thyroid dysfunction, a prevalence of 10.2%; 28 (1.0%) had clinical hyperthyroidism; 217 (7.5%) hypothyroidism (8 of them diagnosed with clinical hypothyroidism); and 26 (0.9%) hypothyroxinemia. High titers of TPOAb were present in 279 (9.6%) of the 2899 women, 196 of whom were euthyroid. Of the 217 hypothyroid women, only 72 had TPOAb detected (33.2%), whereas in the hyperthyroid group, 7 of 28 (25%) were TPOAb-positive.

The prevalence of thyroid dysfunction in the 367 women in the high-risk group was significantly higher than in the non-high-risk group (15.0 vs. 9.4%, $P = 0.001$). However, of the 217 women with elevated serum TSH, 38 were in the high-risk group and 171 (78.8%) in the low-risk group. Of the 8 women with clinical hypothyroidism, 6 were in the

non-high-risk group. Of the 28 patients with clinical hyperthyroidism, only 7 were in the high-risk group.

There was no difference in the prevalence of hypothyroxinemia between the high-risk and the non-high-risk groups (0.9% vs. 0.9%, $P = 0.928$).

COMMENTARY ●●●●●●●●●●●●●●

The controversy about universal versus selective screening for thyroid disease and/or thyroid dysfunction in pregnancy continues. Several studies in the past decade showed that women with untreated hypothyroidism had adverse pregnancy outcomes and adverse neuropsychological and motor development in their progeny. One study showed that testing of only high-risk groups would miss one third of pregnant women with overt/subclinical hypothyroidism (4), another study showed that of 61 women with hypothyroidism, 46 (75%) were in the low-risk group, and 9 of 12 women with hyperthyroidism also belonged to the low-risk group (5). In the article by Wang et al., almost 88% of women with hypothyroidism did not have risk factors for thyroid disease. In all of these studies, the risk factors most associated with abnormal thyroid function were family and personal history of thyroid disease, other autoimmune disease, and previous miscarriage. The authors rightly point out that the main argument against universal screening is the lack of a randomized, clinical trial demonstrating a reversal of both obstetric and intellectual abnormalities with maternal thyroxine-replacement therapy.

Among other issues to consider in assessing universal vs. case finding screening, are the need for trimester-specific reference ranges for serum TSH and T_4 assays, including iodine status in a given population; the most appropriate gestational age for screening; which thyroid tests are best suited for disease detection (TSH, T_4 , TPOAb); cost-effectiveness; and the ability to institute both hormonal therapy soon after the diagnosis is confirmed and follow-up monitoring.

The authors concluded that a case-finding strategy for screening thyroid function in the high-risk group would miss about 81.6% of women with elevated serum TSH and 80.4% women with hyperthyroidism.

Proponents of universal screening stressed (3, 6) the almost universal availability to obtain a reliable, rapid turnaround and affordable serum TSH test; a simple and perhaps harmless treatment with levothyroxine; and the difficulty of obtaining proper answers to a specific questionnaire, because of the time it takes to fill it out, language barriers, and lack of understanding of medical terminology. It would be interesting to know whether the responses to the questionnaires given by obstetricians were consistent among the 10 hospitals in the study by Wang et al.

Universal screening could gain further support by the recent publication of Negro et al. (7), which concluded that universal screening, as compared with case finding, for detection and treatment of thyroid hormonal dysfunction during pregnancy did not show a decrease in adverse outcomes in a subgroup of 77 low-risk women diagnosed with subclinical hypothyroidism; 43 of them received levothyroxine treatment and 44 remained untreated. Obstetrical complications were experienced by 43% of the treated group as compared with 91% of the untreated one.

In conclusion, the few studies available confirm that case finding for detection of thyroid dysfunction in pregnancy would miss a significant number of women with thyroid dysfunction, the majority of them with subclinical hypothyroidism or with euthyroid thyroiditis.

In the meantime, health care professionals should decide, based on the evidence available, when and how to assess the need for thyroid testing in women who are planning pregnancy or are newly pregnant.

— Jorge Mestman, MD

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