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Iodine intake in pregnancy—even a little excess is too much

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Abstract

Several studies have linked maternal iodine deficiency during pregnancy with adverse neurodevelopmental outcomes in offspring. A new study warns that excessive iodine exposure might also be detrimental to maternal thyroid health and recommends a lower limit for maternal iodine intake during pregnancy than that currently advised by the WHO.

Iodine is an essential micronutrient for thyroid hormone synthesis. The requirement for iodine increases during early pregnancy, which is due to increased maternal thyroid hormone production, increased renal iodine losses and transfer of iodine to the fetus. Maternal iodine deficiency and subsequent hypothyroidism during pregnancy have adverse effects on the neurodevelopment of offspring, which range from cretinism in cases of severe iodine deficiency to mild defects in cognitive and motor development in cases of mild iodine deficiency.[1]

Shi and colleagues have published the results of the largest cross-sectional study to date in which the associations between urinary iodine concentration (UIC), thyroid gland function and thyroid autoimmunity were examined in pregnant women.[2] The study was carried out in Liaoning Province, which is an iodine-sufficient region in China. UIC and serum markers of thyroid gland function were assessed in 7,190 women at 4–8 weeks gestation. The participants' iodine status was categorized on the basis of UIC (determined by a urine spot assay) as deficient (UIC <100 μg/l), borderline deficient (UIC 100–149 μg/l), sufficient (UIC 150–249 μg/l), more-than-adequate (UIC 250–499 μg/l) or excessive (UI C ≥500 μg/l). A U-shaped relationship between UIC and thyroid gland health was observed, with higher prevalence of hypothyroidism, isolated maternal hypothyroxinaemia and thyroid autoimmunity in participants with UICs at the low and high ends of the spectrum compared with participants in the iodine-sufficient reference group. The lack of iodine substrate for thyroid hormone production probably explains the increased risk of maternal thyroid hypofunction in the iodine-deficient women. In normal individuals, exposure to excess iodine does not lead to iodine-induced hyperthyroidism, as the thyroid gland responds to excess iodine by decreasing thyroid hormone production, a process termed the acute Wolff–Chaikoff effect.[3] When excess iodine exposure persists, an 'escape' from the acute Wolff–Chaikoff effect normally occurs, which is mediated by decreased sodium–iodine symporter

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Competing interests

The authors declare no competing interests.

expression leading to reduced iodine transport into thyroid follicles.[3] The adverse effects of excessive iodine exposure seen in this study might be mediated by a failure of this escape mechanism, which is possibly related to the observed increased prevalence of thyroid autoimmunity.[3] The increased prevalence of thyroid autoimmunity in participants in the groups with high iodine levels was expected; however, the increased prevalence of thyroid autoimmunity in participants in the iodine-deficient groups was surprising.

Among the 6,325 women without detectable anti-thyroglobulin antibodies, circulating thyroglobulin concentrations were higher in iodine-deficient and iodine-excessive groups than in the iodine-sufficient groups. Thyroglobulin has been validated as a biomarker to assess iodine status at a population level in school-aged children,[4] and, as demonstrated by Shi *et al*., is a promising biomarker for use in pregnant women.[2] However, thyroglobulin cannot be reliably measured in women in whom thyroglobulin antibodies have been detected. Moreover, no validated thresholds for thyroglobulin concentrations in pregnancy have been established and the poor reproducibility across different thyroglobulin assays limits the utility of this protein as a surrogate marker of the iodine status of pregnant populations.[4]

Strengths of this study include the enrolment of participants at a very early stage of pregnancy, which is a period in which fetal neurodevelopment might be particularly dependent on adequate maternal thyroid function,[1] and the large sample size. The use of assay-specific and trimester-specific reference ranges to define thyroid dysfunction is an additional strength of the study design. However, one limitation is the use of a spot UIC assay to determine individual iodine status, as this method might have led to some misclassification of participants, owing to substantial day-to-day and diurnal variations in UI Cs, and to the fact that spot UIC is a reflection of recent iodine intake or exposure rather than of chronic individual iodine status.[5]

No information about neonatal thyroid function or subsequent child cognitive development was available from this study. The fetal thyroid gland develops by 10–12 weeks of gestation and is capable of organification of iodine and thyroid hormone production by ~16–20 weeks. When the fetal thyroid gland is functional, it is possible for a fetus to develop hypothyroidism after excess iodine exposure even when the mother remains euthyroid, as the ability of the fetal thyroid to escape from the acute Wolff–Chaikoff effect does not fully develop until ~36 weeks gestation[6]. Adverse effects on cognition in offspring have been associated with mild maternal iodine deficiency,[1] as well as maternal hypothyroidism and hypothyroxinaemia[7]. Traditionally, maternal hypothyroidism has been thought to result from either iodine deficiency or autoimmune thyroiditis[7]. However, the increased risk of maternal subclinical hypothyroidism and maternal hypothyroxinaemia associated with iodine excess that was reported in this study suggests that the risks of even mild iodine excess in pregnancy need to be carefully considered. The lowest prevalences of hypothyroidism, hypothyroxinaemia, and thyroid autoimmunity, as well as the lowest serum thyroglobulin levels observed in the women with UIC of 150–249 μg/l compared with women from the other groups suggest that the current thresholds for iodine sufficiency in pregnant women set by the WHO are appropriate.[8] Current recommended tolerable upper limits (TUL) for iodine intake in pregnancy are quite variable worldwide. The TUL set by

the US Institute of Medicine is 1,100 μg per day,[9] which is higher than the 500 μg per day TUL set by the WHO and the European Food Safety Authority.[8,10] The data from this study suggest that the TUL recommended by the US Institute of Medicine might be too high and should be re-evaluated. The authors suggest that, in iodine-sufficient areas, the TUL should be 250 μg per day for pregnant women. However, this limit would create a very narrow window of optimal iodine intakes. In addition, this proposed limit could be difficult to implement as a public health measure, particularly in regions where food iodine content is not labelled or not actively monitored, and where nutritional iodine intake does not depend on a single source such as iodized salt.

Shi and colleagues have presented one of the first reports from the ongoing Subclinical Hypothyroid during Early Pregnancy (SHEP) study. Additional investigations are needed, in this cohort and in others, to provide increased understanding of the effects of maternal iodine intake on maternal thyroid function in late gestation and on thyroid gland function and neurodevelopment of offspring.

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