

Editorial

# Do Brazilian Pregnant Women Need Iodine Supplementation? A Commentary on the Latest American Thyroid Association Guideline

## *Gestantes brasileiras precisam de suplementação de iodo? Comentário sobre a mais recente diretriz da Associação Americana de Tireoide*

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Iodine is an essential micronutrient required for the production of thyroid hormones, which are critical for homeostasis and neurodevelopment. Because of increased thyroid hormone production, renal iodine excretion and fetal iodine requirements, dietary iodine requirements are higher in pregnancy than they are for nonpregnant adults.<sup>1</sup> Based on this, the World Health Organization (WHO) and the American Thyroid Association (ATA) recommend a daily iodine intake of 250 µg for pregnant and lactating women.<sup>2,3</sup> Iodine deficiency disorder (IDD) in pregnant women could result in harmful effects, including goiter, cretinism, hypothyroidism, growth retardation, pregnancy loss, and infant mortality. Moreover, inadequate iodine intake during pregnancy may lead to neurodevelopmental deficits in offspring, and iodine deficiency is currently considered the leading preventable cause of intellectual impairment worldwide.<sup>4</sup> On the other hand, the excess of iodine may result in fetal goiter and hypothyroidism. Exposures as minor as the vaginal application of povidone-iodine during delivery or local use of disinfectant in newborns can lead to increased serum TSH concentrations<sup>5</sup> and transient neonatal hypothyroidism.<sup>6</sup>

With this information in mind, we read with great interest the 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum.<sup>7</sup> Among other topics, the nutritional aspects related to iodine sufficiency are addressed in section IV, and a supplementation with 150 µg of potassium iodine per day is suggested on Recommendation 6 for women, in most regions of the world, who are planning a pregnancy or currently pregnant. This is optimally

started 3 months in advance of planned pregnancy (strong recommendation, moderate-quality evidence). Could this recommendation improve the quality of the prenatal care of Brazilian pregnant women?

The most efficient method of IDD prevention is salt iodination. Also, ongoing monitoring of population biomarkers, such as urinary iodine concentration, is essential to ensure that population iodine intakes are optimized. In Brazil, the salt iodination is controlled by federal law in partnership with the National Agency for Sanitary Surveillance (Anvisa, in the Portuguese acronym) and the salt productive sector.<sup>8–10</sup> Unfortunately, data on the iodine nutritional status are scarce and contradictory in Brazil. The national project of salt iodination (PNAIsal, in the Portuguese acronym) (which evaluated 477 locations and a total of 18,978 school children) identified Brazil as a country of “more than appropriate” iodine consumption, with a mean urinary iodine excretion (UIE) concentration of 276 µg/L.<sup>11,12</sup> A recent meta-analysis concluded that the majority of the data on this subject are derived from the population in the south/southeast region of Brazil, but the actual overall IDD prevalence is unknown and might still be high in some areas.<sup>13</sup>

Regarding the pregnant population, three studies were published prior to Anvisa's decision to reduce the salt iodine concentration. In the first one, Barca and cols studied 20 pregnant women and showed a median UIE of 167.8 µg/L.<sup>14</sup> The second study evaluated a larger sample (147 women) and observed median UIE of 224 µg/L. The UIE levels ranged from 22 µg/L to 534 µg/L, and 29 women (19.6%) had UIE below 150 µg/L.<sup>15</sup> The third study, published in 2014, evaluated 191 pregnant women aged 18 years and with gestational

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age up to 14 weeks, and it showed a median UIE of 137.7 µg/L. Interestingly, in this study, 19 (9.9%) pregnant women had UIE > 250 µg/L, 63 (33%) had UIE within the normal range (150–250 µg/L), and 109 (57.1%) had UIE < 150 µg/L.<sup>16</sup>

So, there is a part of the pregnant women population that is at risk of IDD and should probably receive supplementation. On the other hand, the majority of the general population and the pregnant women population, specifically, are iodine sufficient, in which case supplementation could induce adverse effects, such as Wolff-Chaikoff effect and neonatal hypothyroidism.<sup>5</sup> Besides that, the same ATA document suggests 500 µg per day as the upper limit of intake of iodine. Considering the Brazilian history of more than appropriate ingestion, supplementation with 150 µg per day may be enough to reach this ceiling, and the pregnant woman and the fetus may be exposed to the effects of excess iodine. Another limiting factor is that UIE, while being an extremely useful tool for assessing the adequacy of iodine in different populations, does not seem to be a good test for evaluating individuals. Variation in UIE concentrations is to be expected, when there is day-to-day and within-day variation in iodine intake, especially in iodine-sufficient areas. Due to diurnal variations, random spot UIE concentration measurement is unlikely to precisely determine the proportion of a population that has a UIE median concentration < 50 µg/L, which indicates iodine deficiency; the data can only be used to describe the central tendency and the dispersion of UIE concentrations for a particular population.<sup>17</sup>

Lastly, virtually all evidence associating mild to moderate iodine deficiency during gestation with subclinical neurological deficiencies in offspring, such as IQ reduction, comes from observational studies.<sup>18</sup> To date, no clinical trial has demonstrated that iodine supplementation during gestation is capable of ameliorating any robust fetal-maternal outcome and only surrogate endpoints (thyroid volume, thyroglobulin levels) were evaluated.<sup>19</sup>

Therefore, we can conclude that the routine supplementation of iodine for every Brazilian pregnant woman is an intervention that needs to be better evaluated. Perhaps, some pregnant women from historically deficient areas of iodine and without access to iodized salt, as well as some other women with restrictive dietary patterns in salt, grains and dairy products, may benefit from iodine supplementation because they present a greater risk of severe deficiency, situation in which there is evidence that supplementation is effective in preventing severe outcomes, such as cretinism.<sup>20</sup> However, efforts are needed to locate this profile of pregnant women within a country with extensive territory and great cultural diversity, such as Brazil, and to provide appropriate supplementation.<sup>21</sup>

#### Conflicts to Interest

Authors declare no conflicts of interest.

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