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Iodine Status in Pregnant Women in Curitiba, Brazil: A Cross-sectional Study of Public Health System Users

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IODINE STATUS IN PREGNANT WOMEN IN CURITIBA, BRAZIL: A CROSS-SECTIONAL STUDY OF PUBLIC HEALTH SYSTEM USERS

Running title: Urinary iodine in pregnant women

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ABSTRACT

Background: Iodine is essential for thyroid hormone synthesis and fetal neurodevelopment. During pregnancy, iodine requirements increase, and deficiency is associated with adverse outcomes. In Brazil, national surveillance does not routinely assess iodine status during pregnancy, despite increased requirements in this period. This study aimed to determine the median urinary iodine concentration (UIC) among pregnant women in the public healthcare system of Curitiba, Southern Brazil.

Methods: A cross-sectional study was conducted (May 2021–August 2023) involving 296 pregnant women across 48 health units from all 10 health districts. Sociodemographic and clinical data were collected, and UIC was classified following WHO criteria. Serum samples from women were assayed for levels of total T4 and thyroid stimulating hormone (TSH). Continuous variables were summarized as medians and interquartile ranges (IQR). Logistic regression explored associations between UIC and clinical variables.

Results: The median (IQR) UIC was 160.4 (IQR: 109,9-248,3) µg/l, indicating overall population adequacy. However, 46% of participants presented individual insufficiency (UIC <150 µg/l). No significant associations were found between UIC and body mass index, TSH, or gestational age ($p > 0.05$). Notably, four health districts had median UICs below 150 µg/l, and women in

medium-vulnerability areas showed higher UICs than those in low or high vulnerability areas.

Conclusion: Although the population median UIC suggests adequacy, the high prevalence of individual insufficiency (46%) is concerning. While universal supplementation is not currently indicated, targeted public health interventions and enhanced monitoring of vulnerable groups are warranted to prevent clinical deficiencies.

Keywords: Iodine, Pregnancy, Micronutrients, Public Health.

INTRODUCTION

Adequate iodine intake is essential for the synthesis of thyroid hormones, which play crucial roles in cellular growth, metabolism, and neurocognitive development (1, 2). Iodine deficiency is associated with several health conditions, including cretinism, stunted growth and development in children and adolescents, and endemic goiter (3).

During pregnancy, the demand for iodine increases due to enhanced renal turnover and excretion, increased maternal thyroid hormone production, and the transfer of iodine and thyroid hormones to the fetus (3-6). For these reasons, the World Health Organization (WHO) recommends a daily iodine intake of 250 μg for pregnant women (7). Severe maternal iodine deficiency has been linked to higher rates of miscarriage, fetal death, and increased perinatal and infant mortality. Additionally, it has adverse effects on the cognitive function of the offspring, representing the leading cause of preventable intellectual

disability worldwide (5, 6). On the other hand, the adverse effects of mild to moderate iodine deficiency during pregnancy remain unclear and require further investigation (3, 8).

In Brazil, public policies on salt iodization for human consumption have successfully reduced the risk of iodine deficiency in the general population. However, pregnant women are not specifically included in the National Survey for the Assessment of the Impact of Salt Iodization, which evaluates the iodine nutritional status of the Brazilian population (9). Concerns about this group intensified in 2013, when the Brazilian regulatory agency mandated a reduction in the iodine content of table salt (10, 11). Furthermore, studies assessing iodine status in pregnant women in Brazil are predominantly regional, show significant variability in their findings, and lack national-level data (12-14).

Given this context, the present study aimed to determine the median urinary iodine concentration among pregnant women attending the public healthcare system in Curitiba, Paraná. These findings could inform local decision-making regarding iodine supplementation for this specific population.

METHODS

Pregnant women aged 18 years or older, who were linked to prenatal care in the public health system between May 2021 and August 2023, were invited to participate in the study at the time of their enrollment in the prenatal care program. The study aimed to recruit mainly first-trimester pregnant women. The number of participants invited was proportional to the number of pregnant women in each of the city's 10 health districts, ensuring representativeness of the city's pregnant population. The

proportional distribution was calculated based on the number of live births recorded in each district. The study was approved by the Ethics Committee of the Pontifical Catholic University of Paraná and subsequently by the Ethics Committee of Curitiba's Municipal Health Department.

Participants who consented to join the study signed an informed consent form. Weight and height measurements were taken, and a structured questionnaire was administered to collect data on the following variables: health district, health unit, age, parity, gestational age (confirmed by ultrasonography), length of residence in Curitiba, profession, household income, current and previous medical history, thyroid diseases, autoimmune conditions, medication use, use of iodine-containing supplements, history of thyroid surgery, use of iodinated contrast agents within the past 8 weeks, family history of thyroid disease, and smoking, alcohol, or drug use.

A midstream urine sample from the first morning void was collected for analysis of urinary iodine concentration (UIC) using the inductively coupled plasma mass spectrometry (ICP-MS) method. Results were expressed in micrograms of iodine per liter of urine (µg/l). Serum samples were assayed for levels of total T4 and thyroid stimulating hormone (TSH) Based on World Health Organization (WHO) guidelines, UIC levels <150 µg/l indicate iodine insufficiency, 150–249 µg/l are considered adequate, 250–499 µg/l are more than adequate, and levels ≥500 µg/l are considered excessive. Although the WHO does not differentiate iodine insufficiency criteria for pregnant women, some authors propose using the criteria for children, with UIC levels <50 µg/l indicating moderate deficiency and <20 µg/l indicating severe deficiency (15, 16).

Statistical analysis

Continuous variables are presented as mean and standard deviation or as median and interquartile range, depending on their distribution. Categorical variables are presented as absolute numbers and percentages. To explore the associations of demographic variables with iodine levels below 150, we used logistic regression. Additionally, scatter plots were created to evaluate the potential association between iodine levels and BMI, as well as TSH levels. All analyses were performed using STATA 18.0 software.

RESULTS

A total of 570 pregnant women agreed to participate in the study. Urinary samples were obtained from 296 patients, who comprised the study´s population. None of these patients were using iodine supplements or had previously undergone iodine therapy or iodinated contrast examinations.

The mean age of the participants was 28.4 ± 5.95 years, ranging from 18 to 44 years, and the mean gestational age was 11.4 ± 7.3 weeks (236 samples were from patients in the first trimester of pregnancy (81,4%), 37 in the second trimester (12,8%) and 17 (5,9%) in the third trimester, with no information on the gestational age for 6 patients). The median urinary iodine concentration (UIC) of the population was 160.4 µg/l. Table 1 shows the general characteristics of the pregnant women included in the study, subdivided into two groups based on UIC: <150 µg/l and ≥150 µg/l. None of the participants reported using iodine-containing medications or iodinated contrast agents in the last 8 weeks.

Table 1: General characteristics of pregnant women included in the study: total, UIC <150 µg/l and UIC ≥150 µg/l. Curitiba, 2023 (n=296)

Characteristic	Overall (n=296)	< 150 (n=137)	≥ 150 (n=159)
UIC - median µg/l (IQR)	160.4 (109.9 – 248.3)	105.5 (62.9 – 126.9)	230.4 (189.9 – 309.6)
Gestational age weeks (mean±SD)	11.4 ± 7.3	12.2 ± 7.9	10.7 ± 6.6
Age - years (mean±SD)	28.5 ± 5.9	28.9 ± 5.9	28.1 ± 6.0
Race (White)	70.8% (n=175)	76.3% (n=87)	66.2 (n=88)
BMI kg/m² (mean±SD)	27.3 ±5.7	27.3 ± 5.9	27.3 ± 5.4
< 18.5	3.2% (n=9)	5.2% (n=7)	1.3% (n=2)
18.5 to 24.9	35.1% (n=100)	34.3% (n=46)	35.8% (n=54)
25 to 29.9	30.2% (n=86)	25.4% (n=34)	34.4% (n=52)
> 30	31.6% (n=90)	35.1% (n=47)	28.5% (n=43)
TSH (µUI/ml – mean ±SD)	2.1±1.6	2.1±1.6	2.2±1.6
TT4 (µg/ml – mean ±SD)	10.5±2.4	10.7±2.4	10.4±2.4
Smoking (yes)	5.7% (n=17)	6.2% (n=10)	5.1% (n=7)
Family history of thyroid disease (yes)	11.1% (n=33)	9.4% (n=15)	13.1% (n=18)

Legend: There were 11 patients with missing data on BMI,67 for TT4 and 64 for TSH; The subgroups based on iodine levels were compared using t-test, Chi-Square, or Mann-Whitney test, depending on the variable. There was no significant difference between groups for any variable. UIC: Urinary Iodine Concentration; IQR: interquartile Range; SD: Standard Deviation; BMI Body Mass Index; TSH: Thyroid Stimulating Hormone; TT4: Total T4.

Figure 1 shows the distribution curve of urinary iodine concentration for the entire study population.

Although the median UIC was above 150 µg/l, suggesting overall iodine sufficiency, a substantial proportion of pregnant women had inadequate levels. Specifically, 137 women (46%) had UIC below 150 µg/l (Figure 2). In contrast, 87 (30%)

had UIC between 150 and 249 µg/l, 66 (22%) between 250 and 499 µg/l, and only 6 (2%) had values above 500 µg/l.

In the subgroup analysis mentioned above, no association was found between UIC and body mass index or gestational age (Figure 3). However, a predictive model based on gestational age revealed a slight, but non-significant, absolute reduction in UIC values as pregnancy progressed (Supplemental Figure S1).

We also explored iodine levels in pregnant women attending 48 Health Units across the 10 health districts of Curitiba. Four of these districts had a median UIC below 150 µg/l: Boa Vista (n = 19, UIC = 137 µg/l), Boqueirão (n = 23, UIC = 138 µg/l), Matriz (n = 24, UIC = 128 µg/l), and Portão (n = 20, UIC = 119 µg/l). Supplemental Table S1 presents the number and percentage of pregnant women from each district, the median UIC for each district, and the proportion of participants enrolled in the municipal prenatal care program.

Finally, we also examined the relationship between iodine levels and social vulnerability. Each Health Unit is classified according to the vulnerability of the population in its geographical area. In the analyzed sample, 77 participants (26.2%) were linked to Health Units in areas of low social vulnerability, 104 (35.4%) in areas of medium vulnerability, and 113 (38.4%) in areas of high vulnerability. The median UIC varied by vulnerability level: 134 µg/l in low-vulnerability areas, 204 µg/l in medium-vulnerability areas, and 148 µg/l in high-vulnerability areas. Figure 4 shows a map of Curitiba illustrating the distribution of social vulnerability and the corresponding median UIC, categorized as ≥150 µg/l or <150 µg/l.

DISCUSSION

Severe maternal iodine deficiency has been associated with higher rates of miscarriage, fetal death, and increased

perinatal and infant mortality. Additionally, it adversely affects the cognitive development of the offspring and is the leading cause of preventable intellectual disability worldwide (5, 6). On the other hand, the adverse effects of mild to moderate iodine deficiency during pregnancy remain unclear and require further investigation (3, 8).

Urinary iodine concentration is considered an indicator of iodine intake, as approximately 90% of iodine is excreted in the urine (17). UIC can be expressed as a concentration (µg/l), relative to creatinine excretion (µg iodine/g creatinine), or as 24-hour excretion (µg/day) (17). For population-level studies, UIC can be assessed using spot urine samples from a representative group, with results expressed as a median in µg/l (17). However, this measure is not suitable for evaluating iodine status in individual cases and should not be used to determine iodine supplementation for a single pregnant woman due to significant daily variability (18).

This study presents important population-based findings from the capital city of a Brazilian state, suggesting that iodine status, as assessed by urinary iodine concentration (UIC), among pregnant women in the city is in accordance with the World Health Organization's recommendation. The WHO recommends that the median UIC for a population of pregnant women should be between 150 and 250 µg/l (7), and the value found in our study was 160.4 µg/l. Local studies on iodine nutritional status in pregnant women in Brazil have revealed conflicting epidemiological findings. A multicenter study in Brazil, covering 11 cities, found an overall median urinary iodine concentration (UIC) of 186.6 µg/l, indicating iodine sufficiency (19). Among these cities, Pinhais-PR, wich is in the metropolitan area of Curitiba, had a median UIC of 198.6 µg/l, and other cities across the Southeast, Northeast, Midwest, North, and South also maintained median values above 150 µg/l (19). Specific studies

in Maranhão (181.3 µg/l) (20), Rio de Janeiro (221 µg/l) (21), Belo Horizonte-MG (216.73 µg/l) (22), and a more recent study in Ribeirão Preto-SP (180 µg/l) (23) confirmed sufficient iodine intake in these locations. However, two cities in the multicenter study, one of them coastal, presented median UIC levels below 150 µg/l (19), as did Diamantina-MG (94.6 µg/l) (24), Ribeirão Preto-SP in an earlier study (137.7 µg/l) (12), and São Paulo (144 µg/l) (13), indicating iodine deficiency.

One factor that may have contributed to this heterogeneity of results is the studied population. Some studies were conducted with populations receiving tertiary care in referral hospitals, while others, like ours, evaluated pregnant women receiving prenatal care in primary health care settings. There are no Brazilian studies comparing populations using the public health system versus the private sector, which could also be an important variable. This significant heterogeneity among different cities in Brazil makes it challenging to establish a generalized approach to iodine supplementation during pregnancy across the country. It is likely that local data will be needed for each state or municipality to determine the iodine status of their specific pregnant population and develop appropriate supplementation recommendations.

Although the median UIC in our population was within the range of 150 to 250 µg/l, we observed that nearly half of our sample (46%) had UIC levels below 150 µg/l. This portion of the pregnant population may be at risk for iodine deficiency, highlighting heterogeneity even within the same population. This proportion also varied widely among Brazilian studies, reaching 40.6% in Maranhão (20), 48.7% in Rio de Janeiro (21), 57% in Ribeirão Preto (earlier study) (12), 38% in Ribeirão Preto (more recent study) (23) and 52% in São Paulo (13). Therefore, even studies with an adequate median UIC often report large portions of the population with low iodine excretion, as observed

in our study. Thus, it is crucial to identify risk factors associated with low iodine excretion.

In our study, we found no association between this finding and body mass index, age, gestational age. These findings differed from the study in Rio de Janeiro, which found that UIC was independently and negatively correlated with age and positively correlated with multiparity and BMI (14). We observed a trend of reduced UIC as pregnancy progressed, as demonstrated by our model. This finding is consistent with other studies, such as Corcino et al. (14), which involved an iodine-sufficient population, and Fischer et al. (25), which studied an iodine-deficient population, highlighting the need for greater attention during the later stages of gestation. Smoking was not associated with iodine deficiency in our study, and the smoking population (n=17) exhibited a higher UIC compared to non-smokers (n=266) (205 µg/l vs. 154 µg/l). Similarly, Johannesen et al. reported in their study that 10% of pregnant smokers had a UIC comparable to that of non-smokers (26).

To understand the differences in UIC across health districts, we analysed the social vulnerability characteristics of the regions. Social vulnerability is a broad concept that encompasses exposure to determinants of the health-disease process, which can be both biological and social (27). In Curitiba, the Vulnerability Index of the Areas Covered by Municipal Health Units (IVAB) was established in 2018 (28), based on the Family Vulnerability Index of Paraná, developed by the Paraná Institute of Economic and Social Development (IPARDES) (29), and population data from the IBGE Census (28). The IVAB is calculated as the average of four dimensions: household adequacy, family profile and composition, access to work and income, and schooling conditions (28).

A systematic review analyzing 18 studies on iodine intake in pregnant women indicated that low income may be associated with inadequate iodine nutritional status. Additionally, lack of access to iodized salt has been linked to lower birth weight (30). Given this, we sought to assess whether urinary iodine concentration (UIC) varied according to social vulnerability in the city. However, we did not find any statistically significant differences between populations at low, medium, and high vulnerability risk (data with p-value to be presented). On the other hand, when analyzing the map of social vulnerability and health districts, using a UIC cutoff of 150, we observed that areas with lower vulnerability tend to have lower UIC values (Figure 4).

Iodine insufficiency, based on UIC WHO criteria, was not identified among populations in more socially vulnerable areas in our study. However, inferring that iodine intake is adequate based on urinary iodine excretion may not be accurate in pregnant women due to iodine transfer to the fetus and potential iodine storage in the placenta (31). For this reason, it would be important to have national or subnational survey data assessing iodine intake through food frequency questionnaires or 24-hour dietary recalls. These surveys should consider iodine-rich foods such as eggs, dairy products, fish, and seafood, as well as iodized salt consumption. Data on iodine intake could help identify specific groups at risk of deficiency among pregnant women, enabling further evaluation of urinary iodine excretion in these groups (31). The Multicenter Study on Iodine Deficiency – EMDI/Brazil is the most extensive study published to date evaluating iodine intake among pregnant women in Brazil (32). It is a cross-sectional study carried out with food consumption data of pregnant women with a 24h dietary recall and calculation of iodine across 11 municipalities with 2247 provided 24-h recalls eligible for this study. The mean usual

iodine intake of pregnant women was 163.1 mcg and “salt” and its respective food group (“spices and condiments”) and food subgroup (“herbs and seasonings”) were the primary contributors to iodine intake of Brazilian pregnant women.

The main strength of our study was providing a comprehensive overview of the UIC among pregnant women in the municipality of Curitiba who use the public healthcare system, including participants from all health districts in the city, with urine samples from 48 Health Units. Additionally, the inclusion of pregnant women linked to primary healthcare eliminates potential biases associated with samples from tertiary institutions. Thus, our results can be applied at the municipal level as a basis for public health policy. A limitation of our study is that we only analyzed UIC, without collecting dietary recall data. This information could have helped in interpreting the significant variability observed in our population, where a high proportion of pregnant women had reduced UIC, despite the median being within the adequate range according to WHO guidelines.

We conclude that the population of pregnant women using the public healthcare system in the city of Curitiba showed a median UIC within the adequate range according to the WHO, reflecting a likely adequate iodine status. Therefore, we cannot recommend universal iodine supplementation for this population. However, the observation that 46% of the studied group had UIC below the adequate threshold suggests the presence of a high-risk group for iodine deficiency. A trend of reduced UIC with the progression of pregnancy indicates that the likelihood of iodine deficiency may increase as pregnancy advances. We did not find other risk factors associated with this finding. Future studies should focus on identifying risk factors linked to low UIC, such as dietary habits, for example.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work the author(s) used Chat GPT in order to improve the readability and language of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

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Data Availability

The data are available from the corresponding author upon reasonable request.

Ethics approval:

Research Ethics Committee, Pontifical Catholic University of Paraná (PUCPR), nº 4.573.801.

Research Ethics Committee of the Municipal Health Department of Curitiba, nº 4.732.618.

Conflict of interest

TPM: Speaker and consultant fees: AstraZeneca, Baxter, Boehringer, Bayer, Lilly, Merck, CSL Vifor, Novo Nordisk, Pfizer and Vantive.

The other authors have no conflicts of interest.

Figure Legends:

Figure 1 – Urinary iodine distribution

Figure 2 - Distribution of categories of urinary iodine concentration in µg/l

Figure 3 - Association between urinary iodine and Body Mass Index (A) and gestational age (B)

Figure 4 – Map of the city of Curitiba illustrating the distribution of the median UIC in different areas, categorized as ≥150 µg/l and <150 µg/l (A) and social vulnerability (risk) (B).

Figure S1 - Predicted urinary iodine by gestational age

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1UrinaryiodineinpregnancyEJCN.docx
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- Table1UrinaryiodineinpregnancyEJCN.docx
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