



## Urinary Iodine Concentration in 24-Hour Urine of Pregnant Women and Its Association with Food and Salt Intake

Mendes AB<sup>1</sup>, Seabra FCA<sup>1</sup>, de Sousa Bechtluft IM<sup>1</sup>, Costa JA<sup>1</sup>, Ajeje LS<sup>1</sup>, Guimarães MM<sup>2,5</sup>, Rodrigues VO<sup>2,5</sup>, de Paiva AR<sup>3</sup>, Silva AC<sup>2,5</sup>, Panconi CR<sup>2,5</sup>, de Souza HD<sup>2,5</sup>, Zimmermann JB<sup>1,2,3,5\*</sup>

<sup>1</sup>Serviço de Ginecologia e Obstetrícia, Faculdade de Medicina de Barbacena (FUNJOB). Barbacena, MG, Brazil

<sup>2</sup>Serviço de Obstetrícia, Faculdade de Medicina de Juiz de Fora (UFJF). Juiz de Fora, MG, Brazil

<sup>3</sup>Clínica de Ginecologia e Obstetrícia Zimmermann LTDA. Juiz de Fora, MG, Brazil

<sup>4</sup>Santa Casa de Misericórdia de Barbacena, Barbacena, MG, Brazil

<sup>5</sup>High Risk Prenatal Care Group, Brazil

Corresponding Author: **Juliana Barroso Zimmermann**

**Address:** Faculdade de Medicina de Barbacena (FUNJOB), Praça Presidente Antônio Carlos, 8, 36202-336, Barbacena, MG, Brazil; E-mail: [julianabz@uol.com.br](mailto:julianabz@uol.com.br)

**Received date:** 16 March 2020; **Accepted date:** 14 April 2020; **Published date:** 18 May 2020

**Citation:** Mendes AB, Seabra FCA, de Sousa Bechtluft IM, Costa JA, Ajeje LS, Guimarães MM, Rodrigues VO, de Paiva AR, Silva AC, Panconi CR, de Souza HD, Zimmermann JB. Urinary Iodine Concentration in 24-Hour Urine of Pregnant Women and Its Association with Food and Salt Intake. *Asp Biomed Clin Case Rep.* 2020 May 18;3(2):119-127.

**Copyright** © 2020 Mendes AB, Seabra FCA, de Sousa Bechtluft IM, Costa JA, Ajeje LS, Guimarães MM, Rodrigues VO, de Paiva AR, Silva AC, Panconi CR, de Souza HD, Zimmermann JB. This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited.

### Abstract

**Introduction:** Iodine is a human body essential element, which exists in various chemical forms, of which iodide, iodine, and elemental iodine are outstanding, existing in constant amounts in saltwater.

**Methods:** It was an observational cross-sectional study, where 37 pregnant women attended under low-risk and high-risk prenatal care were studied from October 2016 to July 2018, attended by the Obstetrics Service of the Barbacena Medicine College and a private clinic in the city of Juiz de Fora. Exclusion criteria were incomplete records and refusal to participate in the study or urine inadequate collection.

**Results:** We studied 37 patients with an average of  $1.5 \pm 0.84$  gestations,  $0.45 \pm 0.62$  births and  $0.15 \pm 0.84$  abortions. The mean age of the patients was  $32.1 \pm 7.2$  years. Due to the consumption of salt, milk, and fish, there was an association between urinary iodine significant ( $p < 0,05$ ).

**Conclusion:** It should be noted that the present study concluded that it is important to take into account the eating habits of these patients.

### Keywords

Urinary Iodine, Thyroid, Iodine, Salt, Nutrition, Pregnant Women

### Introduction

Iodine is a human body essential element, which exists in various chemical forms, of which iodide, iodine, and elemental iodine are outstanding, existing in constant

amounts in saltwater. However, its distribution on land and freshwater is uneven, which shows the importance of food as a source of iodine. Saltwater fish is an excellent source since the ocean is quite rich in

iodine, as well as cheese and milk [1].

This is an important element for the generation of triiodothyronine and thyroxine (T<sub>3</sub> and T<sub>4</sub>) in two thyroid hormones essential for the maintenance of normal metabolism in all cells. These hormones control cell oxidation by interfering in the metabolism of water, proteins, carbohydrates, lipids, and other minerals. Thus, excess thyroid hormone determines hyperthyroidism, and, on the other hand, the hormone deficit determines hypothyroidism [1-3].

To be possible a proper intake, the best strategy is salt iodination. Most of the countries have regulations that establish a content of 20-60µg iodine/g salt, that is, 20-60 mg of iodine per kilogram of salt. In Brazil, the concern with salt iodization began in the early 1950s with Law no. 1944/1983, which made it mandatory to salt iodination to the goiter area [4]. From 2013, a reduction in grams in salt iodination (15 to 45 mg of iodine to each kilogram of the product) was proposed. Although this measure was criticized, it was standardized by ANVISA from 2014 [5,6]. The reasons for this reduction are related to the high salt intake by the Brazilian, the monitoring of the iodine content in the salt, and also by the data of iodine urinary concentration existing. In addition, WHO [2] recommends that for populations where salt intake is around 10 g/day, the salt iodination range should be between 20 and 40 mg/kg.

In Brazil, it is estimated that salt intake is 10 to 12 g/day, which would determine acceptable iodine dosages even for pregnant women [4], reiterating the fact that the Brazilian ingests more salt than recommended and consequently more iodine, which deserves attention. The current WHO recommendation is to consume the equivalent of five grams of salt per day. The Geography and Statistics Brazilian Institute (IBGE) reports that the consumption of salt per capita in Brazil is 10 g/day and the Extractors and Salt Refiners Brazilian Association refers to 14 to 16 g/day [2]. A study carried out at the Espírito Santo Federal University has identified that daily per capita salt consumption in Vitória, capital of the state of Espírito Santo, is in averaged 12.5 grams [6,7].

On the other hand, a deficit of iodine intake has been reported in most European countries. In Portugal, it was found that 83% of pregnant women consume less iodine than it is recommended [1]. The most important pathologies resulting from iodine deficiency are goiter and hypothyroidism. During the fetal period, occurs the neuronal proliferation and migration in the cerebral cortex, hippocampus and ganglionic eminence, axonal growth, and myelination onset, which are maintained after birth, that needs the participation of thyroid hormone (HT) [8]. On the other hand, iodine supplementation in pregnant women improved the children's mental development [9].

Excessive iodine is undesirable, but its consequences are not as serious as its deficit. There is evidence that daily doses of iodine in adults greater than 1,100 µg may become harmful. In pregnant and lactating women, the maximum acceptable amount of iodine intake per day is 600µg [10].

In 2006, the American Thyroid Association (ATA) recommended the supplementation of 150 µg / day of iodine (in polyvitamin or potassium iodide) for all pregnant and nursing women to assure urine iodine levels 150 to 250µg/l [11]. From 2011, this recommendation extended to the preconception period and remained in the consensus of 2017 [11,12]. However, up to the present moment, we cannot extend this recommendation to the Brazilian population, since more information, such as family diet, educational level, nutritional status of the mother and family socioeconomic level can be determinant in the dosage of iodine. In addition, in Brazil, salt iodination is mandatory and regulated by ANVISA, and, therefore, our pregnant women may not present the iodine deficiency identified in other countries [11]. Based on the above, it is proposed to evaluate the urine iodine levels of pregnant women under a prenatal regimen, associating this dosage with diet and socioeconomic level.

## Methodology

### *Methods and Patients:*

The iodine urine dosage is not part of the prenatal routine recommended by FEBRASGO [13]. As the best

exam for the analysis of urinary iodine concentration, the induction coupled mass spectrophotometry has a high cost; it was decided to carry out a pilot study. This is a test study, with a small-scale of the procedures, materials, and methods proposed for particular research. It can be described as a minor version of the complete study, which involves performing all the procedures provided in the methodology so as to enable the adequacy of the instruments in the phase prior to the investigation itself. The importance of conducting a pilot study lies in the possibility of testing, evaluating, revising, and improving research instruments and procedures. To achieve this, the number of participants does not need to exceed 10% of the target sample [14].

Thus, to perform the present study, a sample calculation was made considering the mean urine dosage in Brazilian people. For a 20% beta and 5% alpha error, 158 patients in each group would be necessary, totaling 316 patients. Considering the pilot study, the required sample would be 10% that is 32 patients [15].

It was an observational cross-sectional study, where 37 pregnant women attended under low-risk and high-risk prenatal care were studied from October 2016 to July 2018, attended by the Obstetrics Service of the Barbacena Medicine College and a private clinic in the city of Juiz de Fora. Exclusion criteria were incomplete records and refusal to participate in the study or urine inadequate collection.

All the patients were submitted to anamnesis and physical examination, as well as the usual prenatal propaedeutics, according to the norms of FEBRASGO [13]. From the anamnesis data were collected regarding dietary habits, socioeconomic level, clinical data (age, gestational age, gestation, births, previous abortions, and previous diseases) and physical examination data.

#### *Diet Evaluation:*

Regarding diet, the consumption of milk and dairy products, fish, and salt was evaluated. Fish consumption was evaluated in relation to weekly frequency and quantity. It was considered that the

pregnant woman consumed fish when there was at least one 150g fish fillet at the meal. In relation to frequency, we considered: a) frequent: when the consumption was at least 1x per week; b) rarely: when consumption occurred between eight and thirteen days apart; c) absence of consumption when the patient ingested an amount less than 150g in the meal and/or when consumption occurred at intervals greater than or equal to fourteen days.

The salt consumption was measured from home measurements, according to **Table-1**. The consumption of 5 to 10g of cooking salt was considered normosodic diet. The diet below 5g of cooking salt was considered hyposodic. Values above 10g of cooking salt consumption were considered as increased (hypersodic). The asodic diet was considered when there was a report below 1g per day of salt.

**Table-1: Association between the dosage of Urinary Iodine and thyroid diseases [16]**

Median IU (µg/L)	Intake of Iodine	Nutritional Status
<b>Non Pregnancy</b>		
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Light deficiency of Iodine
100-199	Proper	Great
200-299	More than proper	Risk of induced Hyperthyroidism within 5 to 10 years
>300	Excessive	Risk of induced hyperthyroidism, autoimmune thyroid diseases
<b>Pregnancy</b>		
>150	Proper	Great

The consumption of milk and dairy products was evaluated through home measurements. It was considered that the pregnant woman consumed milk when there were at least two teacups of milk (two servings) or the equivalent in derivatives (yogurt, cheese) per day [16].

In relation to the frequency, it was considered frequent the intake of two portions of milk or shed on three or more days in the week. It was classified as rare, while consumption was identified up to twice weekly.

#### Urinary Iodine:

The concentration of iodine in the urine is the most commonly used biochemical marker for the evaluation of iodine intake and its consequent sufficiency or deficiency. The gold standard for estimating the reliable urinary excretion of iodine is 24-hour urine, stored in a plastic container, and in a refrigerator. The method used for the measurement of iodine in the urine was induction coupled mass spectrometry (ICP-MS), with volume expressed in ml and result in  $\mu\text{g}/24\text{h}$ . Values of urinary iodine were considered as described in **Table-1**, and in gestation,  $150\mu\text{g}/\text{L}$  [16].

#### Statistical Method:

All data was entered and stored in Epi-Info software, version 8.0. The relative risk (RR) values were calculated in  $2 \times 2$  tables. Logistic regression was used to assess the independence of observed effects. For the calculation between means, the Anova or Kruskal Wallis (KW) test was used according to the evaluated variables. The significance level was set at  $p < 0.05$ .

## Results

### Clinical Data of the Patients Studied

We studied 37 patients with an average of  $1.5 \pm 0.84$  gestations,  $0.45 \pm 0.62$  births and  $0.15 \pm 0.84$  abortions. The mean age of the patients was  $32.1 \pm 7.2$  years. In relation to pre-existing diseases, Diabetes Mellitus (DM) was diagnosed in 8.8% of cases, Chronic Hypertension (HAC) in 8.82%, hypothyroidism in 2.0%, and thrombophilia in 6.90 % of cases. When the complications identified during prenatal care were identified, preterm labor was identified in 6.9%, gestational diabetes in 20.7%, preeclampsia in 3.4%, and condyloma in 3.4% of the cases studied.

### Evaluation of Eating Habits:

The use of cooking salt in the diet was investigated. About 55.88% of the patients reported using 5 to 10g of cooking salt per day, considering the usual measurements of the population (1 to 2 teaspoons), and 41.2% of them reported using less salt of cooking (< than a teaspoon). Only one patient reported using an asodic diet (2.9%). In **Table-2**, the consumption of cooking salt was associated with the dosing of iodine in the urine of 24 hours.

Research on milk and dairy products in the diet (yogurt, milk, and cheese) was also evaluated. It was verified that 32 patients (86.5%) reported using milk

**Table-2: Association between milk consumption and derivatives and iodine dosage in 24hrs Urine**

Food Assessment	N	24-hour urine iodine mean	P	F Test
<b>Con. of milk and milk products</b>				
1. Frequently (78.4%)	29	247.6 $\pm$ 89.9	0.00012	11.9
2. Rerely (8.1%)	3	128.6 $\pm$ 1.21		
3. Non (13.5%)	5	67.7 $\pm$ 31.2		
<b>Salt consumption</b>				
1. >5g salt (55.88%)	21	249.2 $\pm$ 101.99	0	11.9
2. 1-5g salt (41.2%)	15	176.1 $\pm$ 85.6		
<b>Fish consumption</b>				
1. Frequently (55.5%)	20	253.7 $\pm$ 108.5	0.02	4.41
2. Rerely (27.8%)	10	168.7 $\pm$ 63.4		
3. Non (16.7%)	6	143.4 $\pm$ 97.4		

and derivatives in their diet, however, 78.4% reported frequent use. The association between milk consumption and milk products was significant ( $p = 0.00012$ ), according to **Table-2**.

Fish consumption was identified, and 20 fish were frequently consumed (55.5%), 10 were rarely consumed (27.8%) and 6 (16.7%) did not consume fish or fish. One patient did not know how to report fish consumption in her daily life. The results are described in **Table-2**.

*The Iodine Dosage and Its Association with the Patient's Origin: Private Clinic or Public Health Service:*

The mean iodine in the urine of 24h was 213.6  $\mu\text{g/l}$  of urine, the minimum dosage being 29 $\mu\text{g/l}$  and the maximum dose was 437 $\mu\text{g/l}$ . A comparison was made between the iodine dosage and the origin of the patients. Although not statistically significant, the iodine dosage in the urine of pregnant women was higher in those from a private clinic when compared to pregnant women in the Barbacena public service

Origin	Public Service	Private Clinic	P	F/X2 Test
24/5000	177.5 $\pm$ 74.3	232.2 $\pm$ 114.6	2.5	0.12
<b>Dosing of Iodine in Urine (Average <math>\mu\text{g/l}</math>)</b>				
<b>Consumption of Milk and Mile Products</b>				
1. No	2	3	1.17	0.4
2. Rarely	0	3		
3. Yes	11	18		
<b>Fish Consumption</b>				
1. No	5	1	0.0001	19.4
2. Rarely	7	3		
3. Yes	1	19		
<b>Salt Consumption</b>				
1. No	8	7	0.04	6.4
2. Yes	4	17		
3. Asodic	1	0		
<b>Diabetes</b>				
	N	N		
1. Gestational diabetes	1	2	0.9	0.2
2. Previous diabetes	1	1		
3. No	11	21		
<b>HAC</b>				
	N	N		
1. No	10	23	1.4	0.2
2. Yes	3	1		
<b>Obstetric History</b>				
	Public Service	Private Clinic	F Test	P
Child-bearing	1.9 + 0.7	1.5 + 0.8	0.18	1.8
Parturition	0.8 $\pm$ 0.7	0.4 $\pm$ 0.5	0.09	2.9
Abortion	0.2 $\pm$ 0.6	0.1 $\pm$ 0.4	0.43	0.61

(Table-3).

### Discussion

The gestational period is critical in metabolic, energetic, and nutritional terms, and the organism must be adequately supplied in its needs, protecting the health of the mother and allowing the adequate development of the fetus. The World Health Organization (WHO) estimates that 13% of the world's population is affected by diseases whose etiology is lack of iodine [14-16].

In this study, the mean of iodine in the 24-hour urine was 213.6µg/L and the minimum dosage was 29µg/l and the maximum was 437µg/l. When the frequency of iodine dosing below the ideal dose (<150µg/L) was evaluated, nine pregnant women (24.3%) were identified, and of these four (10.8%) the urinary dosage was classified as severe to moderate iodine deficiency. These results are compatible with Soares et al (2008), who measured

urinary iodine (single sample) by indirect detection, based on the Sandell-Kolthoff reaction, and showed that 19.7% of the pregnant women presented iodine deficiency [17]. Other studies have shown more important iodine deficiencies in pregnant women [18]. A study conducted by Ferreira et al (2014) found that the median urinary iodine concentration (IUC) was higher than that of the urinary iodine concentration (n = 109) of the pregnant women studied was below the recommended level (median = 137.7µg/l; 95% CI = 132.9 - 155.9), which causes concern, especially considering that these studies were conducted prior to the decrease in iodine concentration in the cooking salt determined by ANVISA [19] (Table-4).

A study conducted at USP's Hospital das Clínicas found that 52% of pregnant women had iodine deficiency, even living in areas considered non-iodine-deprived, with a median of 147µg/l [20]. The IUC dosing method used in this study was the Sandell-Kolthoff reaction in a single sample. Thus, it is important to emphasize that this iodine deficiency in

Table-4: Classification of consumption defined in the study [2]		
Food	Consumption in grams	Consumption in days
<b>Fish</b>		
Yes	Greater than or equal to 150g	a) Frequent: when the consumption was at least 1x per week; b) Rarely: when the consumption occurred between 8 and 13 days apart
No	< 150g	When consumption occurred at intervals greater than or equal to 14 days
<b>Salt</b>		
Normal	5 to 10g	
Hyposodic	< 5g	
Non sodic	< 1g	
Hypersodic	>10g	
<b>Milk and dairy products</b>		
Yes	Intake of at least 2 cups of milk tea (two servings) or equivalent in derivatives (yogurt, cheese) daily	Frequent: When this consumption was identified on 3 or more days in a week. Rarely: It was classified as rare, when this consumption was identified up to twice a week
No	Intake less than 2 cups of milk tea or equivalent in derivatives (yogurt, cheese) daily	When the consumption was identified at intervals greater than or equal to seven days

pregnant women is not an exclusive problem in Brazil. Several countries have been facing such a deficit and measures such as salt iodization have been implemented. In China, Zhejiang universal iodization of salt was carried out as of 2011.

However, even with these measures, urinary iodine was still identified below the ideal in coastal populations (107.54µg/l), through the catalytic spectrophotometry of arsenic- which suggests that measures of iodine supplementation in this population should be evaluated [21]. A study conducted in Europe with 36 pregnant women identified a high frequency of iodine deficiency (83%) even in the 150µg iodine supplementation regimen in the prenatal and postpartum periods [22]. In this study, iodine concentrations were analyzed by inductively coupled plasma mass spectrometry (ICP-MS).

In Ethiopia, the IUC median was 85.7 µg / l, so that 77.6% of the pregnant women (95% CI: 73.0-82.0%) had insufficient iodine intake (UIC <150µg/l). The goiter rate was 20.2% (95% CI: 16.0-24.0%) [23]. Since ICP-MS was also used. Even in Norway, low urinary iodine concentration has been identified in pregnant women with a median of 85µg/l [24]. Thus, our results are compatible with that reported in the literature and although the Brazilian government program avoids the severe iodine deficiency in the great majority of the population, there are still pregnant women exposed to the risk, and support measures should be considered.

When evaluating the association between milk, fish, and salt intake and iodine dosage, it was verified that the higher the intake of these foods, the greater the 24-hour urinary iodine dosage. These data are compatible with those cited in the literature so that the diet is able to modulate iodine dosages in the body. A study conducted in Norway, using the inductively coupled plasma mass spectrometry method, found that women who consumed the highest amount of dairy products (four to nine servings/day) had significantly higher IUC (99µg/l) than women who (57µg/l) or two to three portions/day (83µg/l), however, these values are still far below what is necessary in pregnancy, and therefore, the authors conclude that the diet of

pregnant women is not able to ensure the sufficiency of iodine. Thus, there is an urgent need for public health strategies to ensure adequate iodine nutrition among pregnant women in Norway [24].

Another study in Iceland, also using the ICP-MS method, showed that women who consumed less fish and dairy products had a lower IUC average when compared to those who consumed at least two servings of dairy products per day or consumption of fish twice a week (180µg x 160µg) [25]. In addition, the consumption of iodized salt also allowed an increase of the iodine dosage in our study. These findings are compatible with a study carried out in Catalonia (Spain) where IUC median of 163µg/l was verified, with differences between mountainous and coastal regions (209 versus 142µg/l,  $p = 0.007$ ), so that the regions with higher IUCs were those where people consumed more iodized salt (58% versus 36.4%,  $p < 0.001$ ). This last study made use of the colorimetric technique with a spectrophotometer [26].

Another evaluation was the comparison between the two services in relation to IUC. One of them provides care through the SUS and another a private clinic in the city of Juiz de Fora. When comparing IUC between cities, it was found that pregnant women in the private clinic consume more fish ( $p = 0.001$ ) and salt ( $p = 0.04$ ) when compared to pregnant women in the public service. These data reflect the mean of urinary iodine identified in these two groups. Although not statistically significant, IUC was higher in pregnant women in the private service ( $232.2 \pm 114.6$ ). In Brazil, a possible explanation may be associated with the cost of seafood in our region, since the costs of these foods are higher when compared to the coastal areas. The cost, preparation, and presence of food taboos are examples of limiting factors of fish consumption in Brazil and this is directly related to IUC [27]. However, although salt is a relatively cheap product in our country, higher consumption was also identified in the private clinic population when compared to SUS users. There was no difference between dairy products.

In Brazil, the Ministry of Health still does not recommend the supplementation of iodine in pregnant women routinely. Some authors believe that the

excessive consumption of iodized salt by the Brazilian can overcome iodine deficiencies, even in pregnant women. However, it should be borne in mind that even in areas considered sufficient iodine in Brazil, IUC was below ideal in pregnant women, school children, and the general population [28]. This study, despite being a small sample of the population, was important to identify that even in areas considered sufficient iodine; patients may be exposed to iodine deficiency. In addition, IUC varies with food, especially salt intake, fish, and dairy products. Thus, careful anamnesis is suggested to identify pregnant women at risk. These patients could benefit from prenatal iodine supplementation. It may be suggested that supplementation should be considered in the population exposed to the risk, such as where there is low salt intake or low intake of foods containing iodine.

## References

- [1] Jacob M, Brito N. Iodine supplementation in pregnancy: is it important?. *Revista Portuguesa de Saúde Pública.* 2015 Jun;33(1):107-19.
- [2] Brasil. ANVISA. Resultado do monitoramento do teor de iodo no sal para consumo humano; 2014. Accessed: 2018 Feb 14. Available from: <http://portal.anvisa.gov.br/documents/33916/395584/Relat%C3%B3rio+Pro+Iodo+2014/9fcda63e-a164-41f7-a32b-156399f30f1c>
- [3] Santana-Lopes M, Jacome de Castro J, Marcelino M, Oliveira MJ, Carrilho F, Limbert E, de Estudos da Tiróide E. Iodine and Thyroid: What a Clinic Should Know. *Acta Med Port.* 2012 May;25(3):174-78
- [4] Pontes AA, Rocha AD, Leite DF, Lessa AD, Adan LF. Iodação do sal no Brasil, um assunto controverso. *Arquivos Brasileiros de Endocrinologia & Metabologia.* 2009 Feb;53(1):113-14.
- [5] Brasil. ANVISA. Resultado do Monitoramento do Teor de Iodo no sal; 2013. Accessed: 2018 Feb 14. Available from: <http://portal.anvisa.gov.br/documents/33916/395584/Relat%25C3%25B3rio%2BPro%2BIodo%2B2013.pdf/6fb4fcf1-e33c-4a09-82c9-6d3a90744436>
- [6] Bisi Molina Mdel C, Cunha Rde S, Herkenhoff LF, Mill JG. Hypertension and salt intake in an urban population, Article in Portuguese. *Rev Saude Publica.* 2003 Dec;37(6):743-50. [PMID: 14666304]
- [7] Sarno F, Claro RM, Levy RB, Bandoni DH, Monteiro CA. Estimated sodium intake for the Brazilian population, 2008-2009, Article in Portuguese. *Rev Saude Publica.* 2013 Jun;47(3):571-78. [PMID: 24346570]
- [8] Setian NS. Hypothyroidism in children: diagnosis and treatment. *J Pediatr (Rio J).* 2007 Nov;83(5 Suppl):S209-16. [PMID: 18000629]
- [9] Martins IS. Iodine and mental development of children: a new supplement? *RevPortMed Geral Fam.* 2013;29(5):341-43.
- [10] Public Health Committee of the American Thyroid Association, Becker DV, Braverman LE, Delange F, Dunn JT, Franklyn JA, Hollowell JG, Lamm SH, Mitchell ML, Pearce E, Robbins J, Rovet JF. Iodine supplementation for pregnancy and lactation-United States and Canada: recommendations of the American Thyroid Association. *Thyroid.* 2006 Oct;16(10):949-51. [PMID: 17042677]
- [11] Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, Nixon A, Pearce EN, Soldin OP, Sullivan S, Wiersinga W; American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid.* 2011 Oct;21(10):1081-25. [PMID: 21787128]
- [12] Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, Grobman WA, Laurberg P, Lazarus JH, Mandel SJ, Peeters RP, Sullivan S. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid.* 2017 Mar;27(3):315-89. [PMID: 28056690]
- [13] FEBRASGO. Ficha clínica - Pré Natal. Available from: [www.febrasgo.org.br](http://www.febrasgo.org.br)
- [14] Bailer C, Tomitch LM, D'ely RC. Planning as a dynamic process: the importance of a pilot study for experimental research in applied language. *Revista do Programa de Estudos Pós-Graduados em Linguística Aplicada e Estudos da Linguagem.* 2011;24:129-46.
- [15] Singer J. A simple procedure to compute the sample size needed to compare two independent groups when the population variances are unequal. *Statistics in Medicine.* 2001; 20(7):1089-95.
- [16] Switzerland. World Health Organization and

Food and Agriculture Organization of the United Nations. Vitamin and mineral requirements in human nutrition; 2005. Accessed: 2018 Jul 15. Available from:

<http://apps.who.int/iris/bitstream/handle/10665/42716/9241546123.pdf;jsessionid=7816F2B6E09F050E1A4A130E1A566538?sequence=1>

[17] Soares R, Vanacor R, Manica D, Dorneles LB, Resende VL, Bertoluci MC, Furlanetto TW. Thyroid volume is associated with family history of thyroid disease in pregnant women with adequate iodine intake: a cross-sectional study in southern Brazil. *J Endocrinol Invest.* 2008 Jul;31(7):614-17. [PMID: 18787379]

[18] Erbil Y, Ozluk Y, Giriş M, Salmalıoglu A, Issever H, Barbaros U, Kapran Y, Ozarmağan S, Tezelman S. Effect of lugol solution on thyroid gland blood flow and microvessel density in the patients with Graves' disease. *J Clin Endocrinol Metab.* 2007 Jun;92(6):2182-89. [PMID: 17389702]

[19] Ferreira SM, Navarro AM, Magalhães PK, Maciel LM. Iodine insufficiency in pregnant women from the State of São Paulo. *Arq Bras Endocrinol Metabol.* 2014 Apr;58(3):282-87. [PMID: 24863091]

[20] Mito VCB, Monteiro ACCNG, de Camargo RYA, Borel AR, Catarino RM, Kobayashi S, Chammas MC, Marui S. High prevalence of iodine deficiency in pregnant women living in adequate iodine area. *Endocr Connect.* 2018 May;7(5):762-67. [PMID: 29700098]

[21] Mao G, Zhu W, Mo Z, Wang Y, Wang X, Lou X, Wang Z. Iodine deficiency in pregnant women after the adoption of the new provincial standard for salt iodization in Zhejiang Province, China. *BMC Pregnancy Childbirth.* 2018 Aug 3;18(1):313. [PMID: 30075759]

[22] Stoutjesdijk E, Schaafsma A, Dijck-Brouwer DAJ, Muskiet FAJ. Iodine status during pregnancy and lactation: a pilot study in the Netherlands. *Neth J Med.*

2018 Jul;76(5):210-17. [PMID: 30019676]

[23] Fereja M, Gebremedhin S, Gebreegziabher T, Girma M, Stoecker BJ. Prevalence of iodine deficiency and associated factors among pregnant women in Ada district, Oromia region, Ethiopia: a cross-sectional study. *BMC Pregnancy Childbirth.* 2018 Jun 25;18(1):257. [PMID: 29940879]

[24] Dahl L, Wik Markhus M, Sanchez PVR, Moe V, Smith L, Meltzer HM, Kjellevoid M. Iodine Deficiency in a Study Population of Norwegian Pregnant Women-Results from the Little in Norway Study (LiN). *Nutrients.* 2018 Apr 20;10(4). pii: E513. [PMID: 29677112]

[25] Gunnarsdottir I, Gustavsdottir AG, Steingrimsdottir L, Maage A, Johannesson AJ, Thorsdottir I. Iodine status of pregnant women in a population changing from high to lower fish and milk consumption. *Public Health Nutr.* 2013 Feb;16(2):325-29. [PMID: 22607718]

[26] Vila L, Serra-Prat M, de Castro A, Palomera E, Casamitjana R, Legaz G, Barrionuevo C, Muñoz JA, García AJ, Lal-Trehan S, García A, Durán J, Puig-Domingo M. Iodine nutritional status in pregnant women of two historically different iodine-deficient areas of Catalonia, Spain. *Nutrition.* 2011 Oct;27(10):1029-33. [PMID: 21621389]

[27] Lopes IG, de Oliveira RG, Ramos FM. Perfil do consumo de peixes pela população brasileira. *Biota Amazônia (Biota Amazonie, Biota Amazonia, Amazonian Biota).* 2016 Jun 30;6(2):62-65.

[28] Brasil. Ministério da Saúde: Secretaria de Atenção à Saúde, Departamento de Atenção Básica. Manual Técnico e Operacional do Pró-iodo; 2008. Accessed: 2018 Sept 9. Available from:

[http://bvsms.saude.gov.br/bvs/publicacoes/manual\\_tecnico\\_operacional\\_proiodo.pdf](http://bvsms.saude.gov.br/bvs/publicacoes/manual_tecnico_operacional_proiodo.pdf)