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Iodine Intake Based on a Survey from a Cohort of Women at Their Third Trimester of Pregnancy from the Bosque County Chile

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Abstract

Adequate iodine nutrition is fundamental for all humans and is critical during pregnancy and lactation due to iodine forms part of the structure of thyroid hormones (THs) and it is required for THs function. Iodine is a scarce micronutrient that must be obtained from the diet. Sufficient iodine can be found in the nature from seafood and given it is not frequently consumed by Chileans, public health policies state that table salt in Chile must be iodized. Health plans must be monitored to determine if the intake of iodine is being appropriated and the population has not fallen in deficiency or excess. The aim of this work was to evaluate iodine intake in 26 women at the third trimester of pregnancy.

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Pregnant women are resident from El Bosque a low-income County located in Santiago de Chile. These Chilean pregnant women were recruited by nutritionist at the Centros de Salud familiar (CESFAM). A 24 h dietary recall (24 h-DR) was applied to them to evaluate iodine intake. Samples of urine and blood were taken by health professionals to analyze parameters of thyroid function and to measure urine iodine concentration (UIC). The survey analysis showed that the iodine consumption in these pregnant women derived mainly from salt, bread and milk and not from seafood. The survey analysis indicated that iodine intake was above the requirements for pregnant women. However, the average UIC indicated that iodine intake was adequate, suggesting the need to find a better parameter to determine iodine intake in pregnant women.

Keywords

Iodine · 24-h dietary recall · Pregnancy · Iodine intake

Abbreviations

24-DR	24-Hour dietary recall
BMI	Body mass index
CESFAM	Centros de Salud familiar
cIC	Calculated iodine consumption
Cr	Creatinine
DICTUC	Dirección de Investigaciones Científicas y Tecnológicas de la Pontificia Universidad Católica de Chile
EIC	Estimated iodine consumption
ENS	National Health Survey
fT3	Free T3
fT4	Free T4
hGC	Human chorionic gonadotropin
ICP-MS	Inductively Coupled Plasma Mass Spectroscopy
LOWESS	Locally Weighted Scatterplot Smoothing
NIS	Na^+/I^- symporter
PCA	Principal components analysis
RDA	Recommended dietary allowance
S.E.M	Standard error of the mean
SSMS	Servicio de Salud Metropolitano Sur
tEIC	Theoretical estimated iodine consumption
Tg	Thyroglobulin
TH	Thyroid hormones
TSH	Thyroid stimulating hormone
tT3	Total T3
tT4	Total T4
UIC	Urine iodine concentration
USDA	United States Department of Agriculture
WHO	World Health Organization

8.1 Introduction

Adequate iodine nutrition is fundamental for all humans, and it is critical during pregnancy and lactation. The main biological function of iodine is to be an essential component of the structure of thyroid hormones (HTs) [1]. Iodine is obtained from the diet as iodide, and it is concentrated at the thyroid gland by the Na^+/I^- symporter (NIS) [2]. About the 70–80% of the iodine is concentrated by the thyroid gland. Iodine absorption occurs principally at upper small intestine where all different forms of iodine are reduced to iodide which is transported by NIS action at the apical surface of the enterocyte. NIS expression is regulated mainly by thyroid stimulating hormone (TSH) and iodine itself. TSH stimulates the synthesis of NIS and its targeting to the basolateral plasma membrane of thyrocytes. Meanwhile, acute high levels of iodine in the blood reduces NIS expression by the thyroid gland, this effect is known as the Wollk-Chaikoff effect. After iodide is being released to the circulation, it is taken up by the thyroid gland and kidney depending on physiological needs [3]. During pregnancy there is an increase in the amount of iodine required for the pregnant woman compared to normal adult. This is due to the maternal thyroid gland must synthesize THs for herself and the fetus at least until 20th week of gestation [2]. It has been reported that at the beginning of pregnancy not only TSH stimulates the thyroid gland to transport iodide into the thyroid gland and to increase the THs synthesis, but also the human chorionic gonadotropin hormone (hCG). Thus, the maternal thyroid gland will increase iodide clearance and it will be subjected to a physiological challenge that in many women becomes a physiological stress [2]. In fact, it is highly frequent that at the beginning of pregnancy women developed transient hypothyroxinemia (HTX). It has been reported in humans and in animal models that HTX impairs cognition in the offspring. To overcome iodide deficiency in pregnancy, women are encouraged to increase iodine consumption. Unfortunately, iodine is found in very low concentrations at the soil and in vegetables, fruits, and meat which contributes with the prevalence of iodine deficiency worldwide [4]. To overcome this problem, in Chile, since 1960 public health policies had been developed to ensure that the table salt must be iodized to prevent iodine deficiency [5, 6]. However, the high consumption of salt has caused in Chilean population to be exposed to iodine excess intake and consequently high prevalence of thyroid diseases [7]. In Chile about 24% of the adult population suffers of thyroid diseases [8, 9]. Moreover, it has been reported that iodine deficiency or excess during gestation is responsible for growth retardation, short stature, bone malformations and cognitive impairment in the offspring [10, 11]. For these reasons iodine intake in pregnant women needs to be monitored to prevent the consequences of iodine deficiency or excess in the offspring. Therefore, knowing the status of iodine nutrition and thyroid function in pregnant women will be a value information for the developing of proper health policies. The assessment of iodine status is not an easy task due to all available biomarkers of nutritional iodine status have their limitations. The most frequently biomarker used index is urinary iodine concentration (UIC) [12]. UIC is a sensitive indicator of iodine intake during the days prior to sampling. However, UIC is not indicative of long-term iodine intake and of the iodine nutritional status. UIC can be applied as a population-based indicator of iodine nutritional status [13]. According to the World Health Organization (WHO), a median population of UIC below 100 µg/L for pregnant women is considered indicative of iodine deficiency. While values between 100 and 150 µg/L reflect normal iodine intake and values above 300 µg/L indicate excessive iodine intake [12]. The determination of THs as a biomarker of iodine intake is less sensitive and is only affected when iodine deficiency is severe [13, 14]. TSH can be used as a biomarker for iodine nutritional status mainly when iodine deficiency is also severe [15]. Tg is a thyroid specific protein and precursor of THs. It has been proposed that the levels of Tg in the blood can be used as an iodine status biomarker. This is because exist a positive relationship with thyroid mass increase [16]. During iodine deficiency Tg levels increase in serum. Importantly, to consider is the interference of anti-Tg antibodies in the serum. These antibodies can bind Tg reducing Tg levels and resulting in an inappropriate estimation of iodine status [17]. Moreover, assay reproducibility and standardization is still lacking in Tg available assays [17, 18]. Thyroid physiological alterations related to iodine intake have a U-shaped distribution [19], therefore, public health strategies focused on guaranteeing an adequate intake of iodine in the population should focus on maintaining levels within an optimal range. Scientific evidence has shown that iodine excess can induce physiological changes in susceptible groups, particularly those previously exposed to iodine deficiency, and pregnant or lactating women [20]. Several expert committees have pointed out the need to identify the most important dietary sources of iodine. Thus, this information will contribute to improve the data on the iodine content in foods and beverages [21]. This information will also allow to understand in more detail the population patterns of iodine intake. Therefore, by applying dietary assessment methods to estimate iodine intake, and thus be able to assess iodine status through dietary recommendations [22]. All food intake assessment methods pose several challenges, as many of the instruments used are time consuming for participants and rely on memory, portion estimation, and precise frequency. Additionally, dietary methods must rely on accurate and reliable data about the chemical composition of different macronutrients and micronutrients in foods. Moreover, these methods should include native and traditional foods used from each country and region [23]. Regarding the determination of iodine intake, there are additional limitations, as the iodine content of foods can vary considerably between similar products, for example, as in dairy products or between the same species of seafood [24]. Twenty-four-hour dietary recalls (24 h-DR) are one of the most used dietary methods to qualitatively determine the consumption of one or more foods in nutritional research [23]. 24 h-DR can also be used to assess habitual iodine intake. However, all 24 h-DR developed must be validated for the specific nutrient and population that will be used [25]. On the other hand, the success of these methods relies on the recall and accuracy of whom answer the questions. An advantage of this method is that it is very useful for evaluating foods that contain high levels of a specific nutrient [26]. We think that this method can be applied to determine the intake of iodine in pregnant women population given that iodine must be present in high level in frequent type of food like are salt, bread and milk. Hence, the usefulness of this method will be for evaluating the nutritional contribution of bread and dairy products as a primary source of iodine, given their high and cross-sectional level of consumption in the Chilean population. According to the National Health Survey (ENS), practically the entire population reports consuming bread while 98% report consuming some type of dairy products, which corroborates the massiveness of the foods to be evaluated [27]. Several studies have used this strategy to evaluate iodine consumption and its nutritional sources, particularly in countries where iodine consumption is a constant concern, such as Spain [28], Norway [29, 30], Denmark [31], Poland [32], Australia [33], and England [34, 35]. In Latin America, some studies have been published on the Brazilian population [36]. In Chile there are no studies on the consumption of foods that contribute to iodine nutrition. The aim of this work is to determine the status of iodine nutrition in a cohort of Chilean pregnant women from El Bosque County, a low-income municipality located in Santiago de Chile. For that 24 h-DR was performed and the survey was analyzed by using a Food Processor Software. The iodine content in bread and milk that was used in this study derived from our data. This is the first work that compares iodine intake in Chilean pregnant women based in a 24 h-DR with UIC.

8.2 Methods

Study design and participants: Pregnant women at the third trimester of gestation were recruited at primary health care center from the following Centros de Salud Familiar (CESFAM) of El Bosque County: Carlos Lorca, Cóndores de Chile, Mario Salcedo, Orlando Letelier and Santa Laura from the Servicio de Salud Metropolitano Sur (SSMS). El Bosque is a Municipality located in the southern part of Santiago. According to the 2017 Census, the Municipality is home to 162.505 inhabitants (National Institute of Statistics) [37]. El Bosque has higher rates of poverty than the Metropolitan Region and National averages (14%, 11.1% and 13.7% respectively), as well as higher enrolment in the National Health Fund or public insurance (88.4%, 70% and 76.5%) (Ministry of Social Development) [38]. The inclusion criteria used in this study are shown in Table 8.1. Briefly, adult (> 18 years old) and single pregnancy women were included. Pregnant women that were recruited signed an informed consent and responded a brief health questionnaire to inform about their gestational age, parity, gravidity, weight, height, presence thyroid disease or other disease (chronic or not), daily medication, smoking habit, type, and frequency of intake of multivitamins with or without iodine supplementation. Five mL of blood were taken for measuring thyroid hormones,

Table 8.1 Criteria used for the inclusion of the pregnant women in the study

Inclusion criteria
Healthy women between 18 and 45 years old
Single fetus pregnancy
Non-smokers or smoker
Delivery or cesarean section without use of iodine disinfectants

TSH and thyroglobulin (Tg). Three to five mL of urine sample were taken for iodine and creatinine determination. Both blood and urine were obtained by health professionals that belong to the CESFAMs. Urine and plasma samples were stored at − 20 °C until analyses. This study was approved by the ethical committee of the Servicio de Salud Metropolitano Sur (SSMS) (see ethical approval section).

UIC determination: Urine iodine concentration (UIC) was measured in duplicate at the Laboratorio de Endocrinología e Inmunología from Universidad Andrés Bello by using a modification of the Sandell-Kolthoff reaction with spectrophotometric detection (Epoch, Biotek) and with a method sensitivity of 12 µg /L [39]. Urine samples were frozen and kept at -20 °C until analysis. Briefly, the samples were mineralized by adding ammonium persulfate and homogenized by vortexing at 95°C for 40 min followed by cooling bath at 20–30 min. 50 µL of sample or standard were added to each well of a 96 well plate followed by a solution of arsenic acid and agitated for 1 min. After agitation, a solution of Cerium Ammonium (IV) sulfate was added an incubated for 30 min at room temperature. Then, the absorbance at a 450 nm wavelength was determined using a spectrophotometer. The values were interpolated from a standard curve ranging from 0 to 50 µg/dL of iodine.

Laboratory analyses: Creatinine (Cr) (mg/dL) in urine samples and free T_3 (fT_3) (pg/mL), total T_3 (tT_3) (ng/dL), free T_4 (fT_4) (ng/dL), total T_4 (tT_4) (µg/dL), thyroid stimulating hormone (TSH) (µUI/mL) and thyroglobulin (Tg) (ng/mL) in serum samples were measured in a certified laboratory (IEMA, Providencia, Santiago). Hormones and Tg were measured by chemiluminescence using a Maglumi 2000 and Immulite 2000 equipment respectively. Cr was measured using a BA400 equipment (IEMA, Providencia, Santiago).

24 h dietary recall (24 h-DR): A standard set of questionnaires were designed to collect basic information from participants. This information included health status, dietary information due to allergies, intolerances, food preferences, use of dietary supplements, salt, and condiments consumption. Experienced dieticians performed a 24 h-DR by phone followed by a food portion size estimation. The 24-h diet records included food or drink. Details of the food such as brand, preparation/cooking method, and weight at the time of consumption were registered. To analyze food preparations, the weight of all individual ingredients and the weight of the portion were registered for all the preparation consumed by the patient [40]. Discretionary salt intake, which correspond to salt added during cooking or at the table, was calculated according to standard referent portion sizes as pieces and/or spoons. The amount of iodine in salt was considered as 40 µg/g according to the last modification of the Chilean salt ionization program [5]. The iodine content in milk skim, whole milk, lactose-free milk, powdered milk, and traditional Chilean white bread (marraqueta/hallulla) was determined by Inductively Coupled Plasma Mass Spectroscopy (ICP-MS) (DICTUC). The values obtained by ICP-MS for bread and milk were included in the present study for the calculation of iodine intake. The iodine content values available in the United States Department of Agriculture (USDA) food composition database [41] were used as reference values for the rest of foods. Taking together all this data, the theoretical estimated iodine consumption (tEIC) was computed using the ESHA Food Processor software (version 11.11.32; 2022) by a trained dietician.

Determination of iodine concentration in milk and bread by ICP-MS: Iodine content in whole milk, lactose free whole milk, semi-skimmed liquid milk, liquid skimmed milk, lactose-free liquid skimmed milk, whole milk powder, powdered skim milk from Colún brand and bread white samples (and white traditional Chilean bread named hallula and marraqueta by using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) Briefly, iodine measurement were performed by the Norma ISO 20647:2015. First, a sample of bread or milk is digested in KOH at 105 ± 5 °C during. Then the iodine is stabilized in NH_4OH and $Na_2S_2SO_3$. Then, the samples were reconstituted and filtered. The filtrated sample was analyzed directly at the ICP-MS using praseodymium as internal standard. The quantification was performed through a calibration curve which followed the laboratory requirements: the error for each point was established as < 10% with an r value < 0,998. The set of samples plus blanks, were analyzed by duplicate and the reference material fulfill the acceptance criteria established as: Blank < LD, RSD < 10% with a recuperation of reference material between 90 and 110%. The ICP-MS equipment is located at the Dirección de Investigaciones Científicas y Tecnológicas de la Pontificia Universidad Católica de Chile, (DICTUC) in Santiago, Chile. These experimental values were used to determine the calculated iodine consumption (cIC) for each patient according to the data provided by the patient when interviewed by dietician in the 24 h-RD.

Statistical analysis: Statistical analyses were conducted using the statistical functions in Python SciPy packages (version 1.9.9; available from: https://www.scipy.org/). All plots were drawn using Python Matplotlib package (version 3.6.0; available from: https://matplotlib.org/) and GraphPad Prism 9 (version 9.4.1). Student's T test and Spearman's or Pearson's correlation coefficient (r) was calculated. Correlation will be considered as follows according to r value: 0–0.1 as negligible correlation; 0.10–0.39 as weak correlation; 0.4–0.69 as moderate correlation; 0.7–0.89 a strong correlation and 0.9–1 a very strong correlation according to the criteria proposed by Schober et al., [42]. Standardized values ((Value-Median)/SD) were used to obtain the histogram plots and scatter plots. A Locally Weighted Scatterplot Smoothing (LOWESS) representative curve was added. LOWESS smoothing was applied to show the trends for each variable pair (light red) and each point was colored according to the patient iodine consumption. *P* values were considered statically significant when $*p < 0.05$, $**p < 0.01$ and $***p < 0.001$. Principal components analysis (PCA) was performed using a standardizing method and selecting the principal components by the "Kaiser rule" with eigenvalues > 1. Table S4 shows the PC summary for all PCs generated. PC1 and PC2 account for the 88% of the cumulative variance of the analyzed population.

8.3 Results

8.3.1 Characteristic of Pregnant Women that Participated in the Study

A total number of 72 pregnant women were recruited for this study. From them, only 26 women fulfilled the inclusion criteria. A 88.45% was recruited at CESFAM Carlos Lorca meanwhile a 7.69% and a 3.8% of all the patients were recruited at CESFAM Cóndores de Chile, and CESFAM Mario Salcedo respectively (Table 8.2). The characteristics of the recruited pregnant women are shown at Table 8.3. All patients were residents from El Bosque that have

Table 8.2 Primary health care centers that participate in the study

Primary health service	
CESFAM Carlos Lorca	88.46% (23)
CESFAM Cóndores de Chile	7.69% (2)
CESFAM Mario Salcedo	3.8% (1)

Table 8.3 Characteristics of pregnant women included in the study

Number of total Pregnant women included	26
El Bosque resident patients	100% (26)
Average age (years ± SEM)	30.4 ± 1.1
Average gestational age (weeks ± SEM)	22.8 ± 1.2
Average weight (Kg ± SEM)	76.9 ± 2.9
Average height (cm ± SEM)	159.8 ± 1.2
Average BMI (Kg/m^2 ± SEM)	30.0 ± 1.2
Average gravidity (number ± SEM)	1.9 ± 0.2
Average parity (number ± SEM)	0.8 ± 0.2

an average age of 30.4 years old and average of gestational age of 23 weeks at the time they were recruited for this study. The survey, urine and blood samples were obtained at the third gestation trimester by health professionals. Anthropometrical data showed an average weight of 76.86 Kg and an average height of 159.8 cm. The calculated BMI value for this group of pregnant women was of 30.03. This BMI is considered obese according to WHO guidelines [43]. In fact, a 46% of the participants were considered obese and only a 11% showed a healthy weight. A 92.3% of patients were non-smokers with a very low percentage of chronic diseases as diabetes or hypertension (Table 8.4). Regarding vitamins and supplements consumption the 65.4% of the interviewed women were consuming iron meanwhile the 23.1% were consuming folic acid as prenatal supplements (Table 8.5).

8.3.2 Thyroid Physiological Parameters

To evaluate thyroid function in pregnant women, thyroid physiological parameters were measured. The levels of fT_3, tT_3, tT_4, fT_4, TSH and Tg were determined from blood samples and Cr and UIC were determine in urine samples. The global mean and S.E.M for each parameter can be found at Table 8.6. The mean of all thyroid physiological parameters was observed between the normal ranges for pregnant women [44–47].

Table 8.4 Health status of pregnant women included in the study

Smoking	7.7% (2)
Non-smoking	92.3% (24)
Underweight patients (BMI < 18.5)	3.8% (1)
Healthy weight patients (18.5 < BMI < 24.9)	11.5% (3)
Overweight patients (25 < BMI < 29.9)	30.8% (8)
Obese patients (30 < BMI < 39.9)	46.2% (12)
Extremely Obese (BMI > 40)	3.8% (1)
Insulin resistant	7.7% (2)
Diabetic	7.7% (2)
Hypertensive	3.8% (1)
Hypothyroid	3.8% (1)
Others (Asma. Ulcerative colitis. Hyperemesis. Headache. depression)	7.7% (2)

In parenthesis the number of women with these characteristics is indicated

Table 8.5 Information of supplement and vitamin consumption taken for pregnant women included in this study

Supplements	
Iron	65.4% (17)
Folic acid	23.1% (6)
Calcium	7.7% (2)
Omega 3	3.8% (4)
Vitamins	
Prenatal vitamins	15.4% (8)

In parenthesis the number of women with these characteristics is indicated

Table 8.6 Average for thyroid physiological parameters

Creatinuria (mg/dL ± SEM)	90.03 ± 11.72	(90–300 mg/dL)
Free T_3 (pg/mL ± SEM)	3.188 ± 0.053	(2.5–13 pg/mL)
Total T_3 (ng/dL ± SEM)	170 ± 9.70	(99–257 ng/dL) [40]
Total T_4 (μg/dL ± SEM)	10.98 ± 0.32	(7.3–15.1 μg/dL) [41]
Free T_4 (ng/dL ± SEM)	0.994 ± 0.017	(0.5–4.82 ng/dL) [41]
TSH (μUI/mL ± SEM)	2.025 ± 0.19	(0.3–3.5 μUI/mL) [42]
Thyroglobulin (ng/mL ± SEM)	17.83 ± 4.88	(5.3–25.2 ng/mL) [43]
UIC (μg/L ± SEM)	212.6 ± 19.84	(150–249 μg/L)[a]
I/Cr (μg/g ± SEM)	304.8 ± 34.76	(33–535 μg/g)[b]

[a] National Health Survey (ENS). Chile 2017
[b] Urinary iodine percentile ranges in the United States 2013 (normal ranges)

Individual analysis of thyroid physiological parameters for each patient are shown in Table S1. It was observed values in the normal range for fT_3, fT_4 and Tg. However, one patient had high levels of tT_3, another patient had low levels of tT_3, and one patient had high level of tT_4. Meanwhile, two patients had high levels of TSH and other two patients presented high levels of Tg. Regarding, to the individual values of UIC six patients presented a UIC value over the normal range and three patients had low levels of UIC. The values of UIC were corrected by Cr and the analysis showed that four patients had higher levels of UIC/Cr. Correlation analysis showed the absence of strong associations between thyroid physiological parameters (Fig. 8.2).

8.3.3 Food Iodine Content and Estimated Iodine Consumption

Iodine concentration in food varies greatly between regions because it depends on the soil and high levels of iodine are found in areas that are close to the sea [10, 48, 49]. In Chile the salt is iodized, and it has been shown that the population ingest 10 g of salt daily [50]. Chilean diet has a higher consumption of bread, milk, and salt [50]. Therefore, iodine concentration was measured for two types of highly consumed breads in the Chilean population and different types of milk available in the Chilean market by ICP-MS (see methodology). This methodology presents an increased selectivity and sensitivity for iodine determination [51]. The obtained results are shown in Table 8.7, interestingly we found that semi-skimmed liquid milk (Colún), lactose-free semi-skimmed liquid milk (Colún) and lactose-free skimmed liquid milk (Colún) have high concentrations of iodine 92.40 µg/100 mL, 91.50 µg/100 mL and 87.40 µg/100 mL respectively compared to the other types of milk subtypes (Table 8.7). Moreover, hallulla has the higher iodine concentration compared to marraqueta 22.98 µg/100 g and 8.49 µg/100 g respectively.

8.3.4 Theorical Estimated Iodine Consumption (tEIC) and Calculated Iodine Consumption (cIC)

The theoretical estimated iodine consumption (tEIC) for each pregnant woman of this study was obtained from the analysis of a 24 h-DR by trained nutritionists using the Food processor software. The data from the 24 h-DR was entered into the Food Processor Software to obtain the tEIC. The value of iodine used for bread and milk in the analysis with the Food Processor Software corresponded to the value obtained from the ICP-MS determination (Table 8.7), meanwhile for any other food type the iodine value was the one provided the software manufacturer. The reason for that lies in that bread and milk are frequent consumed by pregnant women and the content of iodine in these types of foods varies greatly in Chile compared to other countries [50] (Table S3). The tEIC for each patient is shown in Table S3. Based on the recommended dietary allowance (RDA) the patient's daily iodine dietary intake was classified as insufficient (<160 µg), adequate (160–220 µg) above the requirements (220 220–299 µg) or excessive (> 300 µg). Interestingly, the distribution of tEIC in this group of patients was 3.84% for those with insufficient iodine intake, 26,9% was under adequate iodine intake, 38.5% was above requirement and 30.8% under excessive iodine intake with a mean of tEIC for this group of pregnant women above requirements. Considering that the population residing at El Bosque County, is considered as a low-income population and that they consume higher amounts of bread, milk and salt, we estimated a calculated iodine consumption (cIC) based on the amounts of these foods consumed by the patiens. The cIC considered the iodide ingested daily only due to bread, milk and salt daily consumed provided by the patient in the 24 h-DR and using the ICP-MS data previously obtained. The individual cIC for each pregnant woman and the mean plus SEM for the study group are shown in Table S2. At the Table 8.8, cIC can be compared to tEIC. The obtained tEIC was of 269.6 ± 16.40 µg/day meanwhile the cIC was of 222.6 ± 16.64 µg/day. Figure 8.1 shows the comparison between tEIC and cIC. The statistical analysis showed that there is not significant difference between tEIC and cIC (Fig. 8.1a)

Table 8.7 Iodine content in Chilean bread (µg/100 mg) and milk (µg/100 mL or µg/100 g) measured by ICP-MS

Whole liquid milk (Colún)	22.60
Lactose free whole liquid milk (Colún)	22.40
Semi-skimmed liquid milk (Colún)	92.40
Lactose-free semi-skimmed liquid milk (Colún)	91.50
Skimmed liquid milk (Colún)	34.80
Lactose-free skimmed liquid milk (Colún)	87.40
Whole powdered milk (Colún)	50.30
Skimmed powdered milk (Colún)	42.40
Marraqueta bread	8.49
Hallulla bread	22.98

Table 8.8 Theoretical estimated iodine consumption (tEIC) and calculated iodine concentration (cIC) for pregnant women analyzed from the 24 h-DR

Patient	tEIC (μg/day)	Classification according reference value[a] (160–220 μg/day[a])	cIC (μg /day)	Classification according reference value[a] (160–220 μg[a])
1	378.71	Excessive	232.17	Above requirements
2	423.01	Excessive	358.76	Excessive
3	167.96	Adequate	100.24	Insufficient
4	270.50	Above requirements	149.33	Insufficient
5	253.57	Above requirements	171.52	Adequate
6	312.15	Excessive	271.79	Above requirements
7	162.63	Adequate	109.20	Insufficient
8	124.84	Insufficient	79.40	Insufficient
9	164.08	Adequate	154.83	Insufficient
10	263.50	Above requirements	225.12	Above requirements
11	249.51	Above requirements	222.15	Above requirements
12	261.95	Above requirements	214.49	Adequate
13	259.81	Above requirements	223.78	Excessive
14	190.39	Adequate	183.68	Adequate
15	295.25	Above requirements	242.87	Above requirements
16	254.83	Above requirements	167.47	Adequate
17	332.42	Excessive	303.97	Excessive
18	265.78	Above requirements	221.22	Adequate
19	384.51	Excessive	362.35	Excessive
20	436.99	Excessive	406.67	Excessive
21	380.34	Excessive	345.28	Excessive
22	190.10	Adequate	129.23	Insufficient
23	310.29	Excessive	285.26	Above requirements
24	241.86	Above requirements	190.49	Adequate
25	207.72	Adequate	172.98	Adequate
26	292.00	Above requirements	264.16	Above requirements
Mean ± SEM	269.6 ± 16.40	Above requirements	222.6 ± 16.64	Above requirements

[a] NIH Recommended Dietary Allowances (RDAs) for Iodine. Insufficient < 160 μg/day; Adequate 160–220 μg/day; Above requirements 220–299 μg/day; Excessive > 300 μg/day

and the correlation analysis showed a strong correlation between both parameters tEIC and cIC (Fig. 8.1b) suggesting that salt, bread, and milk could be the principal types of food contributing with the daily dietary iodide intake of the Chilean pregnant women. A PCA analysis was performed over the variables contributing to tEIC to understand their correlation and contribution to this parameter. Figure 8.1c shows the obtained loading plot. Here we observed the clustering of bread and milk showing a strong correlation between both variables with a moderate correlation with PC1 and PC2. Fish and seafoods presents a moderate correlation with PC1 and week correlation with PC2, on the other hand meat, present negligible correlation with both PC1 and PC2 meanwhile fruits and vegetables present a very strong negative correlation with PC2. Interestingly, there is cluster composed by snacks, rice and noodles and butter/ham/cheese showing

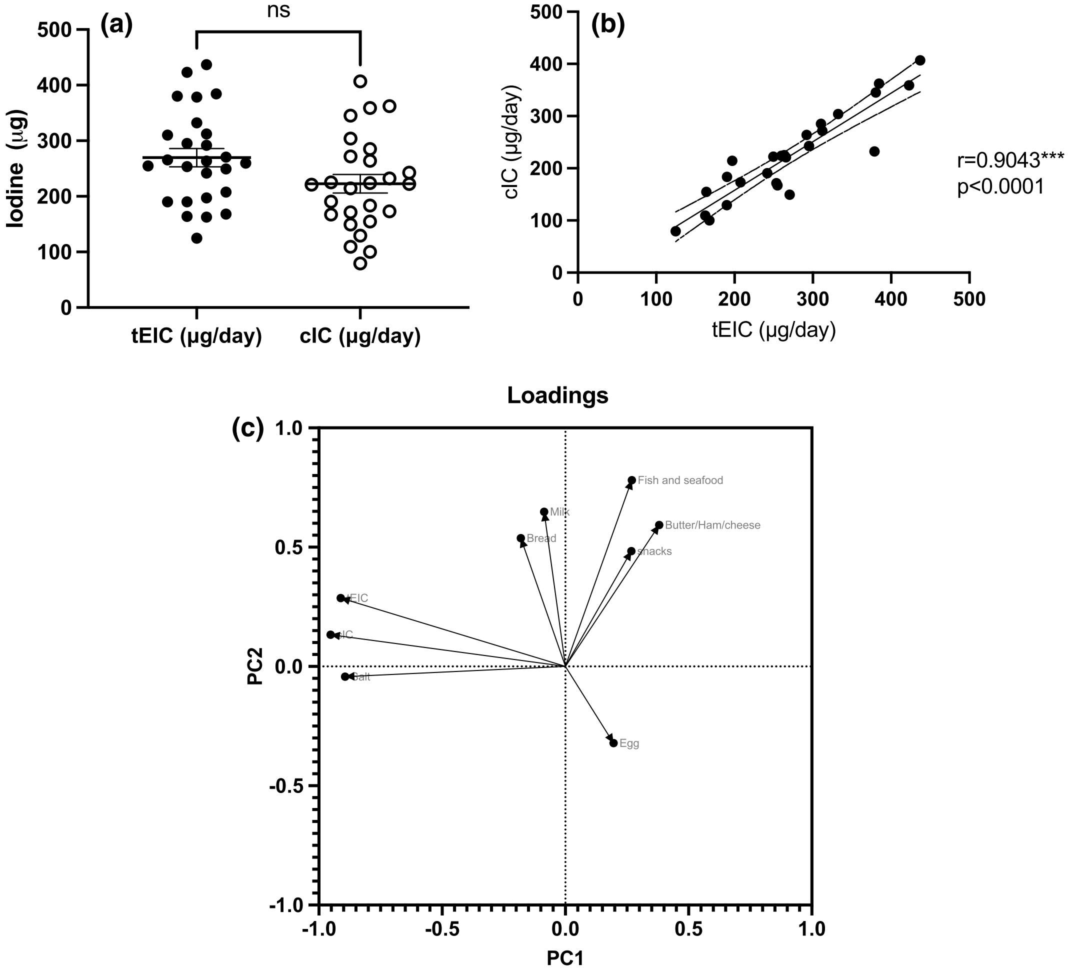

Fig. 8.1 There is a strong correlation between cEIC and cIC. Estimated iodine consumption (EIC) was theoretically calculated from the 24 h-DR using the food processor software (tEIC) and using the bread and milk values determined by ICP-MS (cEIC). **a** Individual values for tEIC and cIC were plotted, statistical analysis indicated that no significant differences are between tEIC and cIC. **b** Correlation plot between tEIC and cIC. a positive correlation value was observed between both parameters. N = 26. Student´s T-test. ns: $p > 0.05$. For B Spearman's correlation analysis r = 0.9043. $p < 0.0001$. **c** PCA analysis. The graph shows the correlation between each variable and the principal components. PC1 and PC2 accounts for 76.8% of the cumulative variance of the population

positive correlation between them and a strong correlation with PC1 but moderate correlation with PC2. Interestingly, salt and eggs does not cluster with any variable presenting opposite directions showing no correlation between them. Nevertheless, salt is clustering with tEIC and cIC which is showing a positive strong correlation between them, with a lesser angle with cIC suggesting a very strong positive correlation between salt and cIC.

8.3.5 Matrix Correlation Analysis

To evaluate the correlation between tEIC, clinical and anthropometric parameters, we perform a correlation analysis matrix. The obtained results are shown in Fig. 8.2. No or weak correlation was observed between tEIC and parameters. A moderate correlation was found between fT_3 and tT_3 and between tT_4 and fT_4. Moreover, a moderate correlation was observed Cr with UIC

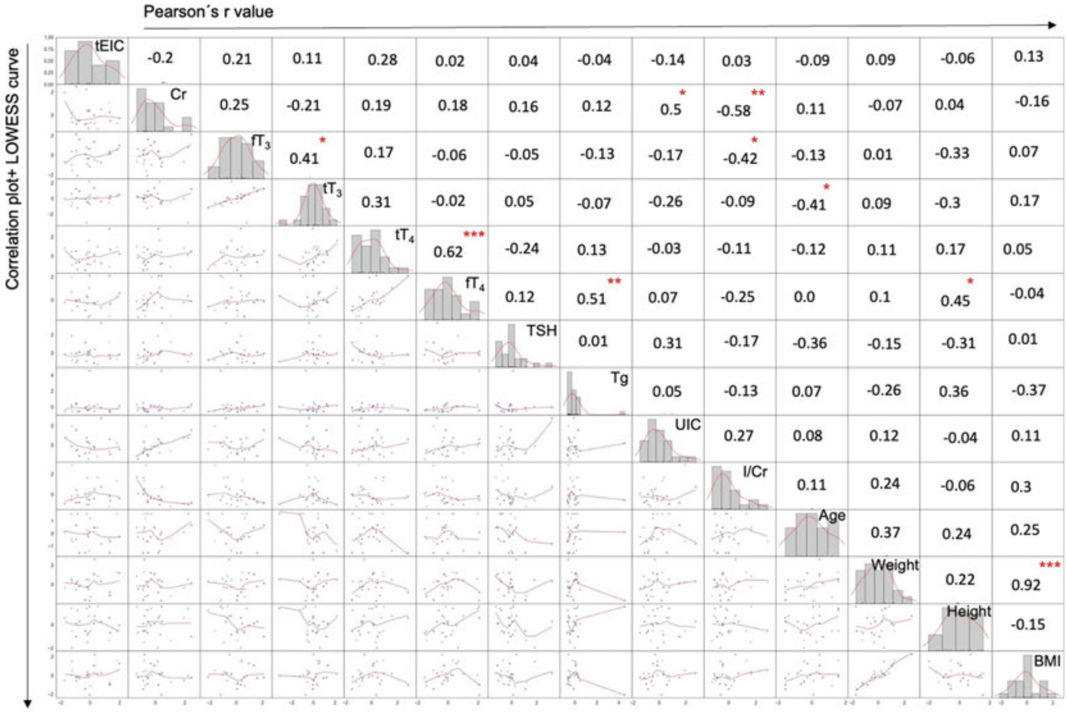

Fig. 8.2 Correlation matrix analysis. The figure shows a correlation analysis between all the clinical parameters including the estimated iodine consumption obtained by the analysis of the 24 h recall 24 h-DR. The squares right next to each histogram plot shows the Pearson's r value for the correlation with the next parameter. The columns below each histogram represent the correlation plot of standardized data and the line represent the LOWESS curve. Pearson´s correlation was considered significant when $*p < 0.05$. $**p < 0.01$ and $***p < 0.001$. EIC: estimated iodine consumption; Cr: Creatinine; fT_3: free T_3; tT_3: total T_3; tT_4. Total T_4; fT_4: free T_4; TSH: Thyroid stimulating hormone; Tg; Thyroglobulin; UIC: Urinary iodine content; I/Cr: Urinary iodine content/Creatinine; BMI: Body Mass Index. N = 26

and I/Cr. Interestingly, a moderate correlation was observed between tT_3 and age, on other hand tT_4 present a moderate correlation with Tg and height. As expected, a strong correlation was observed between weight and BMI. These results are shown in Fig. 8.2.

8.4 Discussion

Proper thyroid function and iodide consumption during pregnancy are essential aspects for fetus development [52]. There is scarce information regarding thyroid function and iodide intake for Chilean pregnant women and this information is necessary to take proper public health decisions. Specially, in Chile where the prevalence of thyroid diseases is ten times higher than most countries. This study contributes with information regarding iodine consumption and the types of foods that contribute to iodine intake in a cohort of pregnant women from Chile. Our data shows that the intake of iodine based on tEIC and cIC is above requirement, and in contrast the UIC and UIC/Cr values fall into adequate. Moreover, this study shows that milk and bread are the type of food besides salt that contributes better to the intake of iodine in the diet of Chilean pregnant women. The iodine concentration in bread and milk determined in this study used ICP-MS, a very sensitive technique [53–55]. The 24 h-DR revealed that bread and milk are the types of food most consume by pregnant women from this study. Therefore these foods were chosen for the analysis. The content of iodine for whole milk was 22,60 µg/100 mL which is similar to the value reported using the same technique by United States (~22,2 µg/100 mL) [55]. Interestingly, the iodine content in semi and skimmed milks was higher than in whole milks (Table 8.7). The highest value was 92,4 µg/100 mL in the semi-skimmed liquid milk and 42,40 µg/100 g for powdered skimmed milk. It has been reported higher values of iodine content by using ICP-MS. Similar to our determination are the case reported from Finland and New Zealand that indicated 540 µg/Kg [48] and 40–150 µg/Kg [49] respectively of iodine content in skimmed milk. *Tinggi* et al., reported 3.48 mg/Kg of iodine in non-fat milk [55] a higher content of iodide that we found. Like *Tinggi* et al., Todorov et al., reported higher values of iodine in non-fat milk (342 µg/100 g) by using ICP-MS. This information is very relevant for chilean public health medicine to aware that pregnant women consuming skim milk should reduce the salt intake to avoid high iodine ingestion [53, 56]. *Dahl* et al., reported 23, 2 µg/100 mL of iodine content in non-fat milk using ICP-MS [57]. The reason for these variations on iodide concentration in milk between different countries and between whole and skimmed milk are unknown. Factors like the region, manufacture procedures and period of the year could be interesting possibilities to analyze for the variations on iodine content in milk. We found that the content of iodine in Chilean bread (marraqueta) was 8,49 µg/100 g this value indicated that the amount of iodine in Chilean bread was lower than the reported for *Leiva* et al., in 2002. In fact, they reported 760 µg/g for hallulla and 830 µg/g for marraqueta [6]. The reduction of iodine content in bread can be due to the modification of the iodization health plan in Chile aimed to reduce the intake of iodine [5]. In fact, the iodine content in 8.49 µg/100 g for marraqueta and 22.98 µg/100 g for hallulla were similar to 5.6 µg/100 g reported by Chilean Iodine Educational Bureau in 1952, before the startup of iodization health plan in Chile [58]. In this work, based on the analysis of the 24 h-DR the tEIC applied to pregnant women we found that this population has an iodine intake above the recommended dietary based on the range given by NIH Recommended Dietary Allowances (RDAs) for iodine [59]. The same conclusion was obtained if we only considered the iodine intake due to the consumption of bread, milk, and salt (cIC, Table S2). Both tEIC and cIC values fall above the requirements stablished for proper iodine intake during pregnancy (Table 8.8 and Fig. 8.1). In fact, no significant differences were observed between tEIC and cIC (Fig. 8.1a). Moreover, a strong correlation was found among these values (Fig. 8.1b), suggesting cIC can be used as a fairly approximation to determine the daily intake of iodine in pregnant women population. Interestingly, iodine content from bread, milk, and salt (cIC) accounted for the ~ 80% of tEIC, indicating that these foods are the main contributors to the daily iodine intake in our group of pregnant women. Based on Fig. 8.1c we would like to emphasize that the values of iodine in both tEIC and cIC correlated better with iodine in salt, milk, and bread than with the value of iodine in seafood. This observation is very relevant because seafood has high iodine content, suggesting that this group has low consumption of seafood. UIC and UIC/Cr were evaluated in the same group of pregnant women that the survey was applied (Table 8.6). The average values obtained for UIC and UIC/Cr indicated that this group of pregnant women had an adequate of iodine intake (Table 8.6). However, we did not find correlation between tEIC or cIC and UIC or UIC/Cr (Fig. 8.2). Mainly, all pregnant women studied in this work showed normal levels of thyroid hormones, TSH and Tg and one or two cases showed values over or lower the normal range (Table S1) [44–46]. Based on Fig. 8.2 UIC or UIC/Cr did not correlate with thyroid hormones or TSH suggesting that THs and TSH does not reflex or correlate with UIC or UIC/Cr. Therefore, we emphasize the necessity to search for better parameters to follow thyroid function and iodine intake individually in pregnant women. This study recruited a small cohort of pregnant women that have in common that they are resident of the same Chilean County, and they were at the same gestational age when the survey and biological samples were taken. Therefore, our conclusions can only be interpreted for this group and cannot be extrapolated to other Chilean pregnant groups. However, our study indicate that it is necessary to analyze the iodine content in the food and to measure thyroid parameters like thyroid hormones, TSH, Tg, UIC and UIC/Cr to obtain more representative date for Chilean pregnant women. Specially, all these information is important because in Chile the prevalence of thyroid disease is around 24% [5, 27].

8.5 Conclusion

In this work we reported the iodine intake obtained from a 24 h-DR survey in a small cohort of pregnant women was above requirements. These women are from the same Chilean county and were at the same gestational age. The average of cEIC fall above requirements based on the range of proper iodine intake given by RDA. Our data support that the iodine consumption in these pregnant women derived mainly from salt, bread, and milk and not from seafood or other types of food analyzed in the 24-h-DR. This is the first study that incorporates the content of iodine for Chilean bread and milk determined using the ICP-MS, a very sensitive technique for iodine determination. This determination showed that the intake of iodine is above requirements in a low-income population. Even though, cIC did not correlate with the UIC of these pregnant women and the UIC falls in adequate iodine consumption, the above presented results emphasize the need to find a better parameter and to combine different methodologies to assess iodine intake in pregnant women.

Statements and Declarations

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Disclosure of Interests All authors declare they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval was granted by the Ethical Committee at the Servicio Metropolitano de Salud Sur (SSMS) MEMORANDUM No: 070/2020.

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