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Nutrition

Excess iodinuria in infants and its relation to the iodine in maternal milk

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ABSTRACT

Objective: Iodine is an essential micro nutrient, and a deficiency or excessive intake of this mineral is related to changes in thyroid function. In Brazil, both deficiency and excessive intake of iodine are common; however, excessive intakes have recently been observed. Thus, the objective of the present study was to assess the iodine concentration in maternal milk, taking into account the salt iodine concentration of the participating households and in the infants' urine.
Method: Urine samples from 33 infants (less than 6 months of age), maternal milk samples and samples of the kitchen salt used by the mothers were collected. The iodine levels in the urine and maternal milk were assessed by ICP-MS; the iodine levels in the salt were assessed by titration.
Result: The median iodinuria value in the infants was 293 μg/L; the mean iodine concentration was 206 μg/L in the maternal milk and 39.9 mg I/kg in the salt. There was a positive correlation between the iodine concentration in the maternal milk and the infant iodinuria value.
Conclusion: The median infant iodinuria was elevated due to the high iodine concentration present in the maternal milk. High iodine values were caused by high salt iodine levels, which should be reduced.

Introduction

Iodine is a major component for the formation of thyroid gland hormones [1] which are directly related to the growth and development of human beings. Much attention has been devoted to the effects of iodine deficiency on the cerebral development of fetuses and infants because iodine deficiency is considered to be the most common cause of predictable mental defects [2].

The use of iodinated salt, first used in Switzerland in 1920 [1,2], has prevented iodine deficiency in Brazil and in most countries of the world. However, it has been shown that excessive iodine intake might be associated with clinical disorders such as Hashimoto thyroiditis and hyperthyroidism in many countries, including Brazil [3].

Urinary iodine excretion is correlated with the iodine intake of a population. The urinary iodine is the main biochemical marker used to assess the nutritional status of iodine; the urinary iodine levels are correlated with the severity of disorders attributed to deficient or excessive iodine intakes [2]. According to the World Health Organization, an iodinuria value below 100 μg/L is an indicator of iodine deficiency; values above 200 μg/L are considered to be more than adequate and values above 300 μg/L indicate toxicity in children older than six years [4,5]. However, in infants, the iodine intake is considered to be adequate when the urinary iodine concentration is higher than 100 μg/L; however no upper limit of urinary iodine has been established to diagnose iodine excess.

Maternal milk is a major and essential source of iodine for breastfed infants; its composition is directly related to the maternal diet [6]. An excessive iodine intake may lead to changes in the nutritional iodine status of breastfed infants.

The objective of the present study was to determine the iodine concentration in maternal milk, while taking into account the iodine concentration in the salt present in the participating households and the urinary iodine levels in the infants.

Materials and methods

The study was conducted with 33 infants (0–6 months of age) and their mothers. All infants were breastfed but not all of them on an exclusive basis. A questionnaire was provided to the mothers to assess the general characteristics of the group. The study was approved by the Research Ethics Committee (protocol HCRP no. 3643/2009, Universidade de São Paulo, Ribeirão Preto); only the infants whose mothers provided written informed consent were included in the study.

Urine samples were collected at the Health Care Center of the city of Guariba. These samples were obtained using an infant urine

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Table 1
General characteristics of infants (0–6 months of age) at birth and on the day of the study.[a]

Variable	Mean	Standard deviation	Minimum	1st quartile	Median	3rd quartile	Maximum
Birth length (cm)	47	2.5	43	46	47	48	53
Birth weight (kg)	3.05	0.51	1.75	2.76	3.1	3.41	3.94
Gestational age	38.05	1.4	32	38	38	39	39
Infant's age on the day of collection (days)	78	44.5	7	45	90	120	150

[a] Collection of samples of infant's urine, maternal milk and mother's kitchen salt.

Table 2
Iodine concentrations in the infant's urine, maternal milk and salt.

Iodine concentration	Mean	Standard deviation	Minimum	1st quartile	Median	3rd quartile	Maximum
Urine (μg/L)	470	432	40	211	293	544	1760
Maternal milk (μg/L)	206	112	51	113	206	257	560
Salt (mg iodine/kg salt)	39.9	11.3	13.1	31.7	42.1	46.7	63.5

collector and stored in an appropriate flask for later analysis; a small amount of the kitchen salt used in the mother's residence was provided in a flask.

A mass spectrometry with an inductively coupled plasma source (ICP-MS) [7] was used to determine the iodine concentration in maternal milk and in the infant's urine. The spectrometer used was an ICP-MS ELAN 6100 Sciex® (PerkinElmer Instruments, Ribeirão Preto, SP, Brazil). All the materials used, including the volumetric flasks, beakers, tips and tubes, were decontaminated by immersion in a 10% (v/v) HNO_3 solution for 24 h and then rinsed 3–5 times in Milli-Q water and dried under a laminar flow hood before use.

Before analysis, we calibrated the prepared samples and the iodine solutions by diluting (1:49, 50 μg/L sample or calibrator with 2450 μg/L diluent) with an aqueous solution of tetramethylammonium hydroxide containing 10 μg/L tellurium as the internal standard. The I^+ ions were measured at 127 m/z. Sodium sulfite (Na_2SO_3), which was used as a reducing agent to stabilize the iodide in the calibration solutions, had an intermediate calibration action. The diluent, which consisted of Na_2SO_3 (20 mg/L) and 18 ΩM cm ultrapure water, was added to the controls, blanks and samples. This was added to a Ryton pulverization chamber that utilizes a GemTip cross-flow II Ryton nebulizer for the sample introduction. A 200 ms permanence time was used for the I^+ ions. The readings, which were repeated three times, consisted of one reading per repetition and 25 scans per reading. The RF power used was 1.2 kW, and the flow of the nebulizer argon gas was 1.01 L/min. The detection limit was determined as 3 SD of the concentration measured in 20 base samples.

The iodine content in the salt used for human consumption was measured according to the technique reported by the Health Ministry, 1966 [8]. Ten grams of the salt and 200 mL of distilled water were transferred to a 500 mL Erlenmeyer flask. The solution was mixed until all the crystals were dissolved, and 5 mL of 1 N sulfuric acid was added. Then, 1 mL of a 10% potassium iodide solution (brown-yellowish color) was added, followed by the addition of 2 mL of a 1% starch solution containing potassium dichromate as an indicator (blue color). The released iodine was then titrated by the dropwise addition of a 0.005 N sodium thiosulfate solution using a 10 mL buret until a green metallic clear color appeared. The sodium thiosulfate volume used was read from the buret, and the iodine content was calculated with the following equation.

$$\text{mg iodine/kg salt} = V \cdot f \cdot 126.9/p$$

V, volume of the sodium thiosulfate solution used in titration.
f, solution factor of 0.005 N sodium thiosulfate obtained from the volume of the standard solution (potassium dichromate) divided by volume of the sodium thiosulfate solution used in the preparation of 0.1 N sodium thiosulfate.
p, amount of the salt sample in grams.

The iodine concentrations measured in the infants' urine samples were compared to the reference values reported by the World Health Organization [4] to determine either iodine deficiency or adequacy in the study population. The data obtained from the kitchen salt were compared to the reference values reported by the National Agency of Sanitary Vigilance (ANVISA, 2003) by means of the RDC resolution no. 32 of February 25, 2003 [9].

An exploratory data analysis was first carried out. The Spearman correlation coefficient (r) was used to determine the correlation between the variables of interest (iodinuria values and the iodine concentration in the maternal milk and kitchen salt). The 95% confidence intervals (CI) for the coefficients were also calculated. All analyses were carried out using the SAS 9.2 software.

Results

Table 1 shows the general characteristics of the infants. The mean infant age was two and a half months; most infants were born at term with a mean birth length of 47 cm and a mean birth weight of 3.05 kg, i.e., above the 2.50 kg minimum.

The frequency distribution of the 33 infants in terms of gender, gestation period, type of delivery and feeding method revealed that 67% were boys, 85% were born at term, 64% were born by cesarean section and 79% were exclusively breastfed.

Table 2 shows that the median urinary iodine excretion in 0–6 months old infants was 293 μg/L; three infants had iodinuria values that were below 100 μg/L. The mean iodine concentration in the maternal milk and in the kitchen salt was 206 ng/mL and 39.9 mg I/kg salt, respectively. The concentration of iodine in urine, maternal milk and salt had a high variance. Table 3 shows the distribution of the urinary iodine concentration depending on the salt iodine:

Table 3
Number of samples based on the iodine concentrations present in the salt and the urine.

Values	μg iodine/L urine				
mg iodine/kg salt	<100	100–200	200–300	>300	Total
	n	n	n	n	n
<20	0	0	1	0	1
20–60	2	4	9	16	31
>60	1	0	0	0	1
Total	3	4	10	16	33

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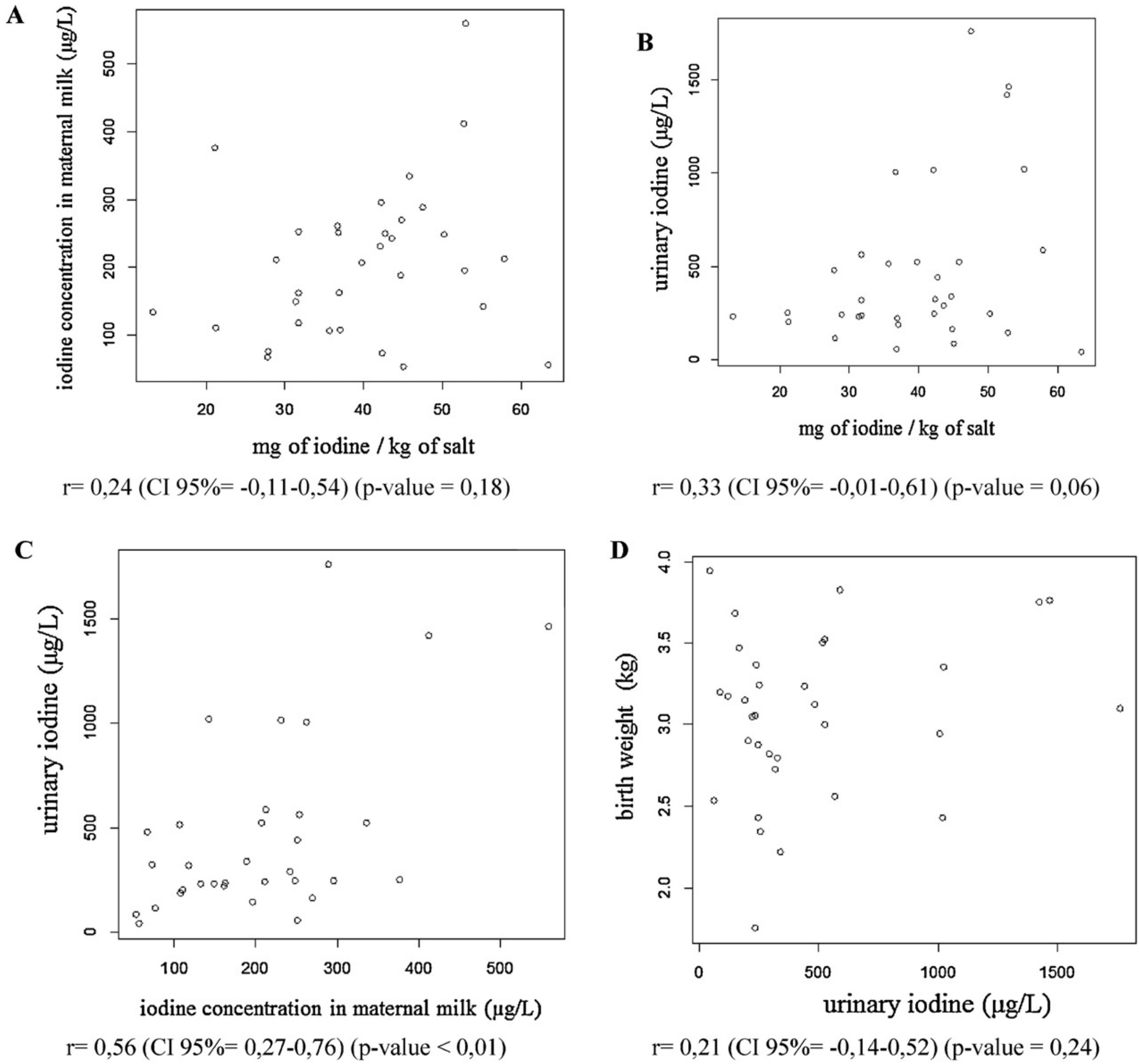

Fig. 1. Dispersal graphs, Spearman correlation coefficients (*r*) and confidence interval of *r* (CI). (A) Correlation between the iodine concentration in salt (mg of iodine/kg of salt) and the iodine concentration in maternal milk (µg/L); (B) correlation between the iodine concentration in salt (mg of iodine/kg of salt) and the iodine concentration in infant urine (µg iodine/L); (C) correlation between the iodine concentration in maternal milk (µg/L) and the iodine concentration in infant urine (µg iodine/L); (D) correlation between the urinary iodine concentration (µg/L) and the infant birth weight (kg).

49% of the participants had iodinuria values higher than 300 µg/L, and the iodine concentration in the salt ranged between 20 and 60 mg iodine/kg salt.

There was a significant correlation between the iodine concentration in the maternal milk and the infants' iodinuria values ($p < 0.01$), i.e., the higher the iodine concentration in the maternal milk, the higher the infant's iodinuria was. There were no significances for the other graphs presented in Fig. 1.

Discussion

Iodine intake regulates the urinary iodine excretion; an excess of iodine is directly excreted into the urine [10]. Breastfed infants, between the ages of 0 and 6 months, acquire iodine mainly through the maternal milk, which has iodine concentrations ranging from 5.4 to 2140 µg/L (median: 62 µg/L), as reported in the literature [11].

The iodine present in maternal milk is derived from the mother's diet. The most important sources of iodine in the maternal diet vary depending on the variations in diet worldwide but include seafood, iodinated salt and, in some regions, dairy foods. In Switzerland, it has been observed that breastfed infants have lower iodinuria values than non-breastfed infants [12], which might indicate an iodine deficiency in the maternal milk. According to Mulrine et al. [13], the iodine concentration in maternal milk during the first six months postpartum is reduced in women who already have iodine deficiency; this is reflected in the infant's iodinuria values.

According to Fomon [14], the iodine concentration in maternal milk is usually much higher than the maternal serum levels of iodine and is proportional to intake. In addition, the iodine levels in maternal milk are highly variable in different world populations and may also vary during the day and from one day to another [15]. In this study, the mean iodine concentration in the maternal milk was 206 µg/L, with a range of 51–560 µg/L.

Because milk is a main and essential source of iodine for breastfed infants and its composition is related to the mother's diet [6], the

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mother's iodine intake may lead to changes in the iodine nutritional status of this population group [11].

The World Health Organization [4] recommends the fortification of salt with iodine at a level of 20–40 mg iodine/kg salt. According to ANVISA [9], in Brazil this recommendation is 20–60 mg iodine/kg salt. The present study showed an adequate iodine concentration in the kitchen salt consumed by the mothers because the mean value detected was 40 mg iodine/kg salt. Although this mean concentration is adequate, the intake of this nutrient by the mother may be excessive; there were salt samples with very high iodine content and other iodine sources may have been consumed including sea fish. This was evident by the high iodine concentration present in the maternal milk.

An excessive daily iodine intake was observed in a school population in the State of São Paulo and may contribute to higher risks of thyroid function disorders such as subclinical hyperthyroidism (in the elderly) and chronic autoimmune thyroiditis (in the adult population) [16]. For this reason, in Brazil, the concentration of iodine in salt should be between 15 mg/kg and 47 mg/kg to be considered acceptable [3].

However, there is no legislation about the iodine concentration in infant formulas, which may influence the nutritional status of infants. Although the present study did not show a significant difference between the exclusively breastfed infants and the infants receiving complementary foods, another study showed that infants who did not receive infant formula had lower iodinuria values than bottle-fed babies [12]. This may have been due to the fact that the cited study was conducted in Switzerland, where nursing women have a mild iodine deficiency. In contrast, in Brazil, there is an excessive iodine intake.

As stated previously, the urinary iodine excretion can reveal an iodine deficiency or excess in the infant's diet, and the data on this biochemical marker may define the urgency for correcting the iodine intake of infants and their mothers [17].

In this study, the iodinuria levels were found to be very high in infants, with a median of 292 μg iodine/L urine and a maximum value of 1760 μg iodine/L urine. Similarly, a study involving 145 children from two schools, one in the rural area and the other in the urban area, showed that 62% of the rural children and 91% of the urban children had iodinuria values higher than 300 μg/L [18]. Another study conducted in six different Brazilian states, showed that the median iodinuria concentration in children was 360 μg/L [19].

Regarding the reduced child growth and neurodevelopment and the increased infant mortality due to iodine deficiency [20,21] there is a need for more iodine per body weight (kg) during infancy when there is an increased utilization of the thyroid hormones [22]. This study showed that almost one tenth of the breastfed infants had urinary iodine concentrations below 100 μg/L; however, the overall population was not iodine deficient. It was not possible to determine whether this population has an excessive intake of this mineral or not due to lacking reference levels for upper urinary iodine in infancy as mentioned in the introduction.

The urinary iodine level in infants was significantly correlated with the maternal milk iodine concentration, i.e., the higher the iodine concentration was in the maternal milk, the higher the infant's iodinuria value. Similarly, a study conducted in Denmark showed that the infants of mothers with low iodine concentrations in their breast milk had low urinary iodine concentrations [23].

Conclusion

This study showed a high iodine concentration in maternal milk and a high iodinuria value in breastfed infants in a Brazilian population, indicating an excessive consumption of this micro nutrient. Most of the kitchen salt samples analyzed had 20–40 mg iodine/kg salt, in agreement with Brazilian recommendations; however, they were in the upper concentration range according to other countries' recommendations. A positive correlation was found between the iodine concentration in the maternal milk and the infant iodinuria value.

Therefore, the high iodine values in infants' urine and in the maternal milk warrant a possible reduction in the iodine levels in salt currently recommended in Brazil.

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