



Original article

Nutritional status of iodine in children: When appropriateness relies on milk consumption and not adequate coverage of iodized salt in households



Marta Taida García Ascaso^{a,*,1}, Purificación Ros Pérez^a, Esmeralda Colino Alcol^a, Agustín López López^a, Carmen de Lucas Collantes^a, Isabel Millán Santos^b, Elise Tessier^c, Susana Ares Segura^d

^a Servicio de Pediatría, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain

^b Servicio de Estadística, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain

^c London School of Hygiene and Tropical Medicine, London, UK

^d Servicio de Neonatología, Hospital Universitario La Paz, Madrid, Spain

ARTICLE INFO

Article history:

Received 7 April 2018

Accepted 13 February 2019

Keywords:

Urine iodine
Iodized salt
Childhood
Adolescence
Iodine-rich foods

SUMMARY

Background & aims: Iodine deficiency inhibits the normal development of human beings and is the leading cause of preventable mental retardation. Our study aims to update the urinary iodine concentrations and the intake of iodized salt in children in Madrid (Spain).

Methods: A cross-sectional study was designed where 217 children aged 3–14 years old were studied. A nutritional survey including the intake of iodized salt and other iodine-rich foods was performed. In addition, the urinary concentration of iodine was determined in each patient.

Results: Near 60% of the surveyed households routinely used iodized salt. Significant differences in age, sex, country of birth, or country of birth and parents educational levels and iodized salt consumption were not found. The median of the urinary iodine level (120 µg/L; interquartile range 80–184) was significantly higher in boys than girls and more elevated in younger children. Iodized salt and milk consumption significantly increased the concentration of urinary iodine. Children who drank less than two glasses of milk per day and did not consume iodized salt have four times the risk of iodine deficiency compared to children who daily drank at least two glasses of milk and consumed iodized salt ($P < 0.001$).

Conclusions: The nutritional level of iodine in the children studied is appropriate despite the low consumption of iodized salt. This is due to the consumption of dairy products and milk. The younger the child, the better his/her iodine nutritional level. Teenagers studied are at higher risk of iodine deficiency.

© 2019 European Society for Clinical Nutrition and Metabolism. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Iodine is an essential trace element for the formation of thyroid hormones, which are crucial for somatic and cognitive development of individuals. The recommended iodine intake is 90 µg/day (birth to 8 years), 120 µg/day (children 9–13 years), 150 µg/day (adolescents and adults), and 250–300 µg/day during the pregnancy and lactation periods [1]. According to the World Health Organization (WHO), iodine deficiency remains the leading preventable nutritional cause of mental retardation, affecting more than 1 billion people worldwide, most of them children and newborns [2]. Although iodine deficiency is prevalent in developing countries, mild or moderate iodine deficiency is not uncommon in

Abbreviations: ANOVA, Analysis of variance; IGN, Iodine Global Network; IQR, Interquartile range; IS, Iodized salt; NIS, Noniodized salt; OR, Odds Ratio; SD, Standard deviation; UIC, Urinary iodine concentration; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

* Corresponding author. Servicio de Pediatría, Hospital Universitario La Moraleja, Madrid, Spain.

E-mail address: martagarciaascaso@gmail.com (M.T. García Ascaso).

¹ Present address: Servicio de Pediatría, Hospital Universitario La Moraleja, Av. de Francisco Pi y Margall, 81, 28050 Madrid, Spain.

<https://doi.org/10.1016/j.clnesp.2019.02.007>

2405-4577/© 2019 European Society for Clinical Nutrition and Metabolism. Published by Elsevier Ltd. All rights reserved.

industrialized countries; it has been shown that about 20% of the world's population is at risk [3]. To determine the nutritional status of iodine in a population, WHO and the Iodine Global Network (IGN) recommend using urinary iodine concentration (UIC) (in $\mu\text{g}/\text{L}$) as the most practical biochemical estimate of recent iodine intake. The median UIC is used to express the global nutritional level of iodine in a population, although this median does not take into consideration the intra-individual variation [4,5]. According to international rules, the normal values of median UIC are between 100 and 199 $\mu\text{g}/\text{L}$ corresponding to a daily oral iodine intake of 150–299 μg (Table S1) [5,6]. UIC in school-age children is considered the best indicator of iodine status in the general population, although there are recent concerns on whether this can be applicable to other population groups such as pregnant women.

According to the WHO, the most common way of knowing the nutritional status of iodine in a region is to obtain data on the domestic use of iodized salt (IS), as this is the main vehicle of iodine consumption [7,8]. WHO recommended using IS in $\geq 90\%$ of all households to guarantee an adequate iodine nutritional status [9]. However, the United Nations Children's Fund (UNICEF) reported only 37 countries reaching a 90% of IS household consumption in 2012 [10]. Overall, according to recent studies, the iodine status has improved during the last decades in many countries including Spain [11–14]. Nevertheless, children, pregnant women and vegan/vegetarian people are still at risk of suffering iodine deficiency [15–17].

Iodine deficiency in Spain has been known since 1899, and published work in 1993 showed mild iodine deficiency [18,19]. Recent regional and multicenter studies in school children have shown some improvement in UIC since the nineties of the past century; however IS consumption is still below that recommended [20]. There are also other foods with high iodine content, some of them with a natural origin as fish and seafood. Dairy products (especially cow's milk) may also contain high levels of iodine related with agriculture and cattle industry methods; unfortunately, these policies are not completely regulated yet.

The present study aimed to assess the UIC in relation with IS and other iodine-rich food intake in children from Madrid and to know the related individual and familiar features as well as the dietary habits.

2. Methods

2.1. Participants and study design

An observational, cross-sectional study was conducted at the Pediatric Department at the Puerta de Hierro-Majadahonda Hospital to assess iodine status, and IS and other foods intake of children aged 3–14 years. The study was conducted from April 2011 to October 2012. The region sampled has middle to high socioeconomic status and a population under 18 years of 90,000. A total of 217 children were recruited. Exclusion criteria were children with known thyroid disorder or those that have received iodine contrast in a radiological investigation.

2.2. Variables assessed

UIC for each child was measured by taking a 10 ml fasting sample of urine. Each sample was frozen within the first 6 h at $-80\text{ }^{\circ}\text{C}$ in the Pharmacy Laboratory of the Hospital Puerta de Hierro (Majadahonda, Madrid, Spain). Later on, samples were transported in a portable refrigerator to the Laboratory of Biochemistry at Hospital La Paz (Madrid, Spain) for analysis. UIC was determined using the modified Benotti-Benotti method [21,22]. This is a colorimetric method based on the role of iodine as

a catalyst in the reduction of yellow tetra-ammonium cerium (IV) sulfate to the colorless cerous form by arsenite (Sandell-Kolthoff reaction). To eliminate interfering substances, a previous digestion step using ammonium persulfate ($100\text{ }^{\circ}\text{C}$, 60 min) was performed [23]. The results were read spectrometrically on microtiter plates as previously described [24]. Analyses were performed at La Paz University Hospital Foundation for Biomedical Research in Madrid, Spain. Neither Multistix[®] nor Combur Test D[®] test strips were used for urine sampling and/or manipulation because they contain iodine [25].

Each child was given a questionnaire, which included questions about place of birth, time since arrival to Spain (if not born here), congenital hypothyroidism screening result at birth, parents' birthplace and education, family history of thyroid diseases, and consumption of IS and other iodine-rich foods. Dietary survey included the frequency of consumption: milk (number of glasses per day), dairy products (number of cups of yogurt, custard, and/or cream caramel per day), eggs, fish, seafood, cheese (times per week) and IS (used for cooking: yes/no). Weight and height were registered. Data were normalized for sex and age and expressed in standard deviations (SD) according to standardized published tables [26,27].

2.3. Statistical analyses

The sample size required for this study was calculated by accepting an alpha risk of 0.05 for an accuracy of $\pm 6.5\%$ in a bilateral contrast for an estimated proportion of 65% of pathological UIC (normal interval 100–199 $\mu\text{g}/\text{L}$), 5% replenishment rate. Data were presented using statistics of central tendency and dispersion: mean and SD or median and interquartile range (IQR) or extreme values. The data corresponding to qualitative variables were expressed as absolute value of percentages. The Kolmogorov-Smirnov test was used to assess whether the variables followed a normal distribution. The comparison between the continuous variables between two groups was made using the Student's *t*-test for independent data. The non-parametric Mann-Whitney test was used when the normality hypothesis was rejected in the comparison of 2 samples and the Kruskal-Wallis test in the comparison of 3 or more samples. Analysis of variance (ANOVA) followed by the Bonferroni multiple comparison test was used to compare 3 or more means. The relationship between continuous (ordinal) variables was established using the Pearson correlation quotient and Spearman's non-parametric correlation.

The contrast between the categorical variables was performed using the normal χ^2 or χ^2 test corrected by Yates in the case of expected frequencies < 5 and the linear trend test χ^2 for 2×2 tables. A logistic regression model was conducted which included the statistically significant independent variables from the univariate analysis showing a significant association with iodine deficiency. The results were expressed as Odds Ratio (OR) and the 95% confidence interval (95% CI). The SPSS software (version 14) was used for data analysis. The statistical significance level was set at 5%.

2.4. Ethics

This study was approved by the Ethics Research Committee of Hospital Puerta de Hierro-Majadahonda (Madrid, Spain) in March 2011. The parents signed an informed consent before enrolling the child after full explanation of the purpose and nature of all procedures. If the child was over 11 years old, he/she signed the informed consent as well. The procedures followed were in accordance with the Helsinki Declaration of 1975, revised in 2008.

3. Results

3.1. Description of the population

A total of 217 children were studied (107 girls and 110 boys), making three different age groups: a) preschoolers (3–6 years); 38.7% of the total sample; b) school age children (7–10 years); 33.6%; and c) adolescents (11–14 years); 27.6%. Ninety one percent of the children were born in Spain, 4.2% in Latin America and the remaining (4.6%) in other European countries, Asia, or North Africa. Children born in Spain had normal values in metabolic screening tests. The majority of parents were born in Spain (79% fathers and 66% mothers). Regarding the level of parental studies, the question was asked whether primary, secondary (Bachelor and/or Vocational Training), or university studies. Mothers' academic levels (primary, secondary or vocational training and university) were 12.7%, 38.0% and 49.3%, respectively whereas fathers' academic levels were 17.1%, 40.2% and 42.7%, respectively. According to the interview, 53.1% of the patients' families had at least one first or second degree member with some type of thyroid pathology. In the whole sample, the mean SD values for weight, height, and body mass index were: 0.285 ± 1.319 , -0.078 ± 1.079 , and -0.047 ± 1.301 respectively; whereby the population was considered to be representative of the child population according to published values.

3.2. Dietary habits

Twelve families were unaware of the type of salt they used. Of those who knew the type of salt consumed at home, 59.5% used IS. Table 1 displays the consumption of IS compared to that of non-iodized salt (NIS) according to the different variables for which each child was questioned. The mean consumption of IS was similar in

Table 1
Intake of iodized (IS) y noniodized salt (NIS) in relation with individual and familiar variables.^a

Variable	Intake		P
	IS (%)	NIS (%)	
Age group (years)			
3–6	46 (57.5)	34 (42.5)	0.589
7–10	40 (59.7)	27 (40.3)	
11–14	36 (62.1)	22 (37.9)	
Sex			
Female	62 (62.0)	38 (38.0)	0.479
Male	60 (57.1)	45 (42.9)	
Ethnicity			
Child			
Native	113 (60.4)	74 (39.6)	0.389
Immigrant	9 (50)	9 (50)	
Mother			
Native	92 (59.7)	62 (40.3)	0.908
Immigrant	39 (58.8)	20 (41.2)	
Father			
Native	99 (61.1)	63 (38.9)	0.305
Immigrant	22 (52.4)	20 (47.6)	
Academic education			
Mother			
Primary	15 (55.6)	12 (44.4)	0.762
Secondary/VT	50 (65.8)	26 (34.2)	
University	57 (57.6)	42 (42.4)	
Father			
Primary	22 (62.9)	13 (37.1)	0.326
Secondary/VT	51 (63.8)	29 (36.3)	
University	47 (55.3)	38 (44.7)	
FTD			
No	51 (56.0)	40 (44.4)	0.274
Yes	70 (63.6)	40 (36.4)	

^a FTD: familial thyroid disorder; VT, vocational training.

all age groups and in both genders. Likewise, the child's or parents' place of birth or academic levels, as well as family thyroid pathology did not show significant differences in IS consumption in children.

The results obtained on the routine consumption of iodine-rich food are shown in Table 2. Consumption of these foods was high, especially fish (42% children consumed at least 3 times/week), cheese (53% ate at least 3 times/week) and milk (52% consumed at least 2 glasses of milk per day).

3.3. Relationship between IUC and personal/familiar features and dietary habits

The median UIC was 120.00 (IQR 80–184) $\mu\text{g/L}$ with a significant difference between children who consumed IS (median 136.50; IQR 94–209 $\mu\text{g/L}$) and those who did not (median 110.50; IQR, 64–162 $\mu\text{g/L}$); $P = 0.006$. Table 3 shows the overall results of the UIC according to the ranges established by the WHO. There were 7 children with values higher than 500 $\mu\text{g/L}$, considered as probable iodine poisoning, and 37.8% of the total had <100 $\mu\text{g/L}$ (iodine deficiency) whereas 12% had <50 $\mu\text{g/L}$. Table 4 shows UIC adjusted by socio-demographic characteristics of the population. UIC was higher in boys and in the youngest group. The median UIC in the adolescents group (11–14 years) was at the limit of iodine deficiency. There were no differences in UIC among children or parents born in or out of Spain. In addition, UIC was influenced neither by parents' studies nor by any familial thyroid pathology.

The UIC medians were compared according to the different food consumption and are shown in Table 5; only consumption of milk <2 glasses/day (UIC 102.00 $\mu\text{g/L}$; IQR 60–147) vs. ≥ 2 glasses/day (UIC 132.00 $\mu\text{g/L}$; IQR 96–235) was statistically significant.

A logistic regression was conducted with the variables that had been associated with iodine deficiency in the invariant analysis: age, gender, consumption of IS and number of milk glasses per day (Table 6). The oldest group, children who did not consume IS regularly or those who took less than 2 glasses of milk per day, had more than 2-fold increased risk of iodine deficiency.

Further comparative studies were carried out according to the consumption of IS associated to milk consumption, the following results were obtained: children who did not take IS and took less than 2 glasses/day (UIC median 90.00 $\mu\text{g/L}$; IQR 48.00–141), children who took IS but drank less than 2 glasses of milk per day (UIC median 118.00 $\mu\text{g/L}$; IQR 70.50–170.50), children who did not take IS but drank at least 2 glasses of milk/day (UIC median 124.00 $\mu\text{g/L}$; IQR 85.00–231.00), and children who took IS and at least 2 milk glasses daily (UIC median 143.50 $\mu\text{g/L}$; IQR 105.25–236.75). A logistic regression to assess the effect of independent variables on achieving UIC >100 $\mu\text{g/L}$ was performed. Odds Ratio expressed the risk of having an UIC <100 $\mu\text{g/L}$. Table 7 shows that the non-consumption of IS or taking less than 2 glasses of milk per day increased the risk of iodine deficiency by 2-fold. If both factors overlap, the risk exceeded 4-fold.

4. Discussion

Our results reveal that the iodine nutritional level in children of the Community of Madrid is overall within the range of normality, although a considerable percentage (37.9%) has UIC in the mild to moderate range of deficiency. Only 59% of the families surveyed routinely used IS at their home, which is well below the 90% recommended by the WHO. Our results are consistent with a study published in 2006 in this region, which revealed that 65.5% of the population aged 10–19 years consumed IS and also with the national study Tirokid (population 6–7 years old) that reflected a consumption of IS of 69.8% [20,28]. More recent studies carried out

Table 2
Frequency of consumption of iodine-rich foods.

Frequency of consumption (%)	Fish	Seafood	Cheese	Eggs	Algae	Milk	Dairy
Never	2.3	64.7	21.2	1.6	98.1		
<1/week	5.2	19.1	2.6	3.6	1.4		
1–2/week	49.7	16.3	22.8	76.6	0.5		
≥3/week	42.8	0	53.4	18.2			
Never						5.5	4.6
<1/day						3.7	12.9
1/day						38.2	50.7
2/day						26.7	18.0
>2/day						25.8	13.8

Table 3
IUC values of the population studied.

IUC (µg/L)	No. of children (%)
<20	1 (0.5)
20–49	24 (11.5)
50–99	56 (25.9)
100–199	87 (40.3)
200–299	35 (16.2)
>299	13 (6.0)

in South Spain (2015) showed a 30.9% use of IS, which is even smaller and extremely concerning [29]. During the nutritional survey, parents recalled the salt brands they were using at home and whether the container specified the word “iodized” or not. There were a total of 17 different brands but their iodine content was not determined since its actual concentration in the salt may be lower than the described on the package due to different factors such as local conditions of production, packaging, and/or storage [30–32].

Table 4
IUC (µg/L) vs. individual and familial variables.^a

Variable	Median (P25–P75)	P
Age group (years)		
3–6	148.50 (95–231)	0.001
7–10	119.00 (85–159)	
11–14	100.00 (58–145)	
Sex		
Female	116.00 (64–168)	0.028
Male	126.00 (90–213)	
Ethnicity		
Child		0.15
Native	121.00 (83–187)	
Immigrant	88.00 (48–174)	
Father		0.59
Native	137.00 (63–195)	
Immigrant	117.50 (79–178)	
Mother		0.37
Native	134.50 (74–198)	
Immigrant	117.50 (80–179)	
Academic education		
Father		0.590
Primary	138.00 (89–179)	
Secondary/VT	122.00 (83–187)	
University	177.00 (82–208)	
Mother		0.961
Primary	112.00 (88–182)	
Secondary/VT	119.00 (76–201)	
University	124.50 (84–117)	
FTD		
No	120.00 (77–185)	0.66
Yes	121.00 (84–193)	

^a FTD: familial thyroid disorder; VT, vocational training.**Table 5**
Relationships between medians of IUC (µg/mL) and consumption of iodine-rich foods.

Food	N	Frequency of consumption ^a	IUC ^b (IQR)	P
Fish	142	<3	118.00 (89.75–186.50)	0.315
	74	≥3	129.50 (89.75–178.75)	
Seafood	139	<1	116.00 (70.00–179.00)	0.075
	76	≥1	136.50 (95.00–206.25)	
Cheese	114	<3	118.50 (72.25–181.25)	0.405
	103	≥3	125.00 (82.25–192.50)	
Eggs	132	<1	93.00 (57.00–137.00)	0.188
	84	≥1	124.00 (182.00–192.00)	
Algae	211	Never	120.00 (81.00–189.00)	0.543
	4	≥1	120.00 (41.00–154.75)	
Milk	103	<2	102.00 (60.00–147.00)	<0.001
	114	≥2	132.00 (95.50–234.50)	
Dairy ^b	148	<2	117.50 (72.25–187.74)	0.504
	69	≥2	130.50 (88.25–178.00)	

^a Expressed in times per week, except in the case of milk (glasses per day) and dairy products (number of dairy products per week).^b Not including cheese.**Table 6**
Multivariate study of the relationships between IUC and the associated variables.^a

Variable	OR	Confidence interval (p)
Age groups (years)		
7–10 vs. 3–6	1.4	0.7–3.1 (0.338)
11–14 vs. 3–6	2.6	1.2–5.6 (0.012)
Sex		
Female vs. male	1.7	0.9–3.1 (0.087)
Salt consumption		
NIS vs. IS	2.1	1.1–3.9 (0.018)
Milk intake (glasses/day)		
<2 vs. ≥2 glasses	2.2	1.1–3.9 (0.018)

^a IS, iodized salt; NIS, noniodized salt; OR, Odds ratio.

The percentage of IS consumption was not influenced by any of the individual or family variables. This contrasts with previous results suggesting that the country of origin and the level of parental studies do affect IS consumption, although this trend has not been detected in all studies [33–35]. These differences may be explained by the type of immigration in Madrid, with a predominance of parents from Latin America, generally with a knowledge about the

Table 7
Iodine deficiency risk related to iodized salt and milk consumption.^a

Variable	OR	Confidence interval (p)
Group 3 vs. group 4	2.46	1.03–5.87 (0.04)
Group 2 vs. group 4	2.79	1.25–6.22 (0.01)
Group 1 vs. group 4	4.16	1.78–9.51 (<0.001)

^a Group 1: no IS and drink less than 2 milk glasses/day. Group 2: take IS but drink less than 2 milk glasses/day. Group 3: no IS but drink ≥2 milk glasses/day. Group 4: take IS and drink ≥2 milk glasses/day. OR, Odds Ratio.

importance of IS consumption greater than other studies that analyzed populations of Maghreb origin. The proportion of children born out of Spain was less than 10%, so the differences between Spanish and non-Spanish children may be more difficult to establish [36]. The type of salt used in the school canteen (those children who ate at school), and the iodine content of processed foods were not known.

The median UIC value (120 µg/L) was similar to values previously reported in other Spanish provinces [20,29,35,37,38]. The data of the Tirokid study were somewhat higher than ours, probably because the mean age of the children examined (6–7 years old) was different to that of our study where almost one third of the children were >11 years, when UIC was significantly lower [20]. An study performed in the Basque Country showed that children in the age range of 6–26 months had adequate UIC levels (median, 127 µg/L), regardless of the low IS consumption and in probable relation to high consumption of milk, which would also coincide with our results in children 3–6 years old [39]. It is disturbing to realize that in the adolescent population (11–14 years) the median UIC was 100 µg/L, this is, at the limit of deficiency. There may be a potential in women of childbearing age with the subsequent risk of fetal harm [40,41]. From our results, it should be noted that using UIC in school-age children as a single reference for the general population may not be accurate, missing vulnerable groups such as pregnant women where iodine deficiency is most harmful. Comparative studies in Thailand and China showed that, when studying a group of schoolchildren and their pregnant mothers, the children group presented an optimal level of iodine while their mothers were mostly iodine deficient [42,43].

The low IS consumption rate (59%) contradicts with the UIC median within normal limits, especially in younger children. UIC was correlated with IS consumption, which remains the ideal vehicle to guarantee adequate universal iodine coverage, but the percentage consumption in Madrid is low. However, as demonstrated by this study, higher UIC is also associated with increased consumption of dairy products, with a clear positive correlation with the number of milk cups consumed daily. Other studies have also previously noted that milk and its derivatives are the true “responsible” for improvement in the nutritional iodine level of many populations and countries [34,44,45]. However, this “silent prophylaxis” is not regulated and has unequal levels of iodine content in different brands of milk both in Spain and the United States [44,45]. Since the iodine content is not indicated in the labeling of these milk containers, consumption is arbitrary. Changes in the regulation of hygienic measures and feeding of cattle patterns could cause a decrease in the amount of iodine contained in the milk, prompting to iodine deficiency as is already happening in other countries [46,47]. In the present study, the amount of iodine in the milk used in the children’s households was not determined. Commonly, milk brands do not report their iodine content that may depend on many factors, such as iodine content and level of iodine supplementation of feed, farm management or teat dipping with iodine-containing substances [45,48,49].

Our estimation of iodine deficiency risks according to four different diet-related groups agrees with national results published in the Tirokid study, but in our population it is even more worrisome, since the median UIC in children who neither consume IS nor drink at least 2 glasses of milk per day were already at iodine deficiency level (90 µg/L), whereas in the national study the reported value was 146 µg/L [20]. As pointed out above this difference may be attributable to the age differences of the children examined. Like in other studies, gender also influenced UIC, being higher in boys [20]. Although some studies have also shown an influence of fish or egg intake on UIC [50], neither impact in our study nor in a previous one [20] was noted.

Based on the above comments, the nutritional level of iodine in children in Madrid is within the normal range. Although the levels of iodine in children is related to IS consumption, other factors must be considered, especially the consumption of milk, and certain iodine-rich medicines or the systematic use of povidone iodine solution [51–53].

Despite UIC in our population is in optimal range, there are still some challenges to overcome. First, it is important to improve the families’ knowledge about the IS, since many parents stayed in the interviews that IS and sea salt were the same while others believed that iodine could be harmful to the thyroid gland [2]. Secondly, if families start using salt for cooking, it should be emphasized that the salt should always be iodized and that they should frequently consume marine foods rich in iodine [3]. The consumption of milk in our population is high — as in other Spanish regions— and this product exerts a real prophylaxis for iodine deficiency. However, companies should be requested to be transparent about their livestock policies and to report, on each labeling, the amount of iodine in the milk product [7]. School canteens should be compelled to use only IS [8]. It is important to monitor what medications, including topical ones, children use. Very high amounts of iodine, sometimes in the toxic range, can be harmful, especially in young children. Additionally, it would be also necessary to force companies to sell natural or homeopathic products with controlled amount of iodine levels.

One limitation of our study is that it was performed in a single center. Our population comes from an area with a medium-high socioeconomic level (49% of mothers and 42% of parents had university education) that may influence dietary habits *i.e.*, lower consumption of iodine at a lower socioeconomic level [54]. However, our results are superimposable with the national study [20]. The strength of the present study was that the performance of UIC and the dietary survey were performed at the same time and no patient rejected the study, thus reducing the possibility of selection bias.

It is important to continue raising awareness of the importance of IS in Spain, as the reality is far from optimal; in this way, it is necessary to implement adequate policies from the Government and to reach an adequate citizens and health workers education.

Statement of authorship

All authors contributed to the study design, recruited the subjects, and discussed the results. M.G.A., S.A.S. and P.R.P. were who conceived the study initially. M.G.A. and I.M.S. analyzed the results. E.T. was involved in the original design of the study. M.G.A. wrote the first draft of the manuscript and all authors revised and approved the final version.

Conflict of interest statement

We declare that we have no conflict of interest.

Funding sources

There is no funding source.

Acknowledgements

We are grateful to all the children and families who participated in this study. We thank Dr. Soledad Santacruz, Dep. of Bioquímica, Hospital Universitario La Paz Madrid, for laboratory analysis of the urine samples.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnesp.2019.02.007>.

References

- [1] World Health Organization. United Nations Children's Fund and Council for Control of Iodine Deficiency Disorders. In: Assessment of iodine deficiency disorders and monitoring their elimination. A guide for programme managers. 3rd ed. Geneva: WHO Press; 2007 Accessed March 13, 2018 at http://apps.who.int/iris/bitstream/10665/43781/1/9789241595827_eng.pdf.
- [2] Delange F. Iodine deficiency as a cause of brain damage. *Postgrad Med J* 2001;77:217–20. <https://doi.org/10.1136/pmj.77.906.217>.
- [3] World Health Organization and United Nations Children's Fund. Iodine deficiency in Europe: a continuing public health problem. Geneva: WHO Press; 2007. Accessed March 18, 2018 at, http://apps.who.int/iris/bitstream/10665/43398/1/9789241593960_eng.pdf.
- [4] Ristic-Medic D, Piskackova Z, Hooper L, Ruprich J, Casgrain A, Ashton K, et al. Methods of assessment of iodine status in humans: a systematic review. *Am J Clin Nutr* 2009;89:2052S–69S. <https://doi.org/10.3945/ajcn.2009.27230H>.
- [5] König F, Andersson M, Hotz K, Aeberli I, Zimmermann MB. Ten repeat collections for urinary iodine from spot samples or 24-hour samples are needed to reliably estimate individual iodine status in women. *J Nutr* 2011;141:2049–54. <https://doi.org/10.3945/jn.111.144071>.
- [6] World Health Organization. Urinary iodine concentrations for determining iodine status in populations. Geneva: WHO Press; 2013. Accessed March 18, 2018 at, http://apps.who.int/iris/bitstream/10665/85972/1/WHO_NMH_NHD_EPG_13.1_eng.pdf.
- [7] Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. *Lancet* 1983;322:1126–9. [https://doi.org/10.1016/S0140-6736\(83\)90636-0](https://doi.org/10.1016/S0140-6736(83)90636-0).
- [8] Zimmermann MB, Andersson M. Update on iodine status worldwide. *Curr Opin Endocrinol Diabetes Obes* 2012;19:382–7. <https://doi.org/10.1097/MED.0b013e328357271a>.
- [9] World Health Organization Secretariat, Andersson M, de Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. *Publ Health Nutr* 2007;10:1606–11. <https://doi.org/10.1017/s1368890007361004>.
- [10] United Nations Children's Fund. The state of the world's children 2012: children in an urban world. Utica NY: Brodock Press, Inc.; 2012. Accessed March 18, 2018, at, https://www.unicef.org/sowc/files/SOWC_2012-Main_Report_EN_21Dec2011.pdf.
- [11] Mohammadi M, Azizi F, Hedayati M. Iodine deficiency status in the WHO Eastern Mediterranean Region: a systematic review. *Environ Geochem Health* 2018;40:87–97. <https://doi.org/10.1007/s10653-017-9911-z>.
- [12] Sun D, Codling K, Chang S, Zhang S, Shen H, Su X, et al. Eliminating iodine deficiency in China: achievements, challenges and global implications. *Nutrients* 2017;9:361. <https://doi.org/10.3390/nu9040361>.
- [13] Nerhus I, Odland M, Kjellevoid M, Midtbø LK, Markhus MW, Graff IE, et al. Iodine status in Norwegian preschool children and associations with dietary iodine sources: the FINNS-KIDS study. *Eur J Nutr* 2018. <https://doi.org/10.1007/s00394-018-1768-0>.
- [14] García-Ascaso MT, Ares-Segura S, Ros-Pérez P. Is iodine nutrition in the Spanish pediatric population adequate? Historical review and current situation. *Endocrinol Diabetes Nutr* 2018;65:458–67. <https://doi.org/10.1016/j.endinu.2018.05.011>.
- [15] Brantsæter AL, Knutsen HK, Johansen NC, Nyheim KA, Erlund I, Meltzer HM, et al. Inadequate iodine intake in population groups defined by age, life stage and vegetarian dietary practice in a Norwegian convenience sample. *Nutrients* 2018;10:230. <https://doi.org/10.3390/nu10020230>.
- [16] Pearce EN. Iodine nutrition: recent research and unanswered questions. *Eur J Clin Nutr* 2018;72:1226–8. <https://doi.org/10.1038/s41430-018-0226-7>.
- [17] Sobiecki JG, Appleby PN, Bradbury KE, Key TJ. High compliance with dietary recommendations in a cohort of meat eaters, fish eaters, vegetarians, and vegans: results from the European Prospective Investigation into Cancer and Nutrition—Oxford study. *Nutr Res* 2016;36:464–77. <https://doi.org/10.1016/j.nutres.2015.12.016>.
- [18] Rubio y Galí F. *Clinica social. Rev Ibero-amer Ciencias Méd* 1899;2:50–78.
- [19] Escobar del Rey F. Nuevos estudios sobre deficiencia de yodo en España. *Endocrinología* 1993;40:205–10.
- [20] Vila L, Donnay S, Arena J, Arrizabalaga JJ, Pineda J, García-Fuentes E, et al. Iodine status and thyroid function among Spanish schoolchildren aged 6–7 years: the Tirokid study. *Br J Nutr* 2016;115:1623–31. <https://doi.org/10.1017/s0007114516000660>.
- [21] Benotti J, Benotti N. Protein-bound iodine, total iodine, and butanol-extractable iodine by partial automation. *Clin Chem* 1963;12:408–16.
- [22] Benotti J, Benotti N, Pino S, Gardyna H. Determination of total iodine in urine, stool, diets, and tissue. *Clin Chem* 1965;11:932–6.
- [23] Shelor CP, Dasgupta PK. Review of analytical methods for the quantification of iodine in complex matrices. *Anal Chim Acta* 2011;702:16–36. <https://doi.org/10.1016/j.aca.2011.05.039>.
- [24] Aakre I, Strand TA, Bjørø T, Norheim I, Barikmo I, Ares S, et al. Thyroid function among breastfed children with chronically excessive iodine intakes. *Nutrients* 2016;8:398. <https://doi.org/10.3390/nu8070398>.
- [25] Pearce EN, Lazarus JH, Smyth PP, He X, Smith DF, Pino S, et al. Urine tests strips as a source of iodine contamination. *Thyroid* 2009;19:919. <https://doi.org/10.1089/thy.2009.0120>.
- [26] Hernández M, Castellet J, Narvaiza JL, Rincón JM, Ruios I, Sánchez E, et al. *Curvas y tablas de crecimiento*. Madrid: Garsi; 1988.
- [27] Carrascosa Lezcano A, Fernández García JM, Fernández Ramos C, Ferrández Longás A, López-Siguero JP, Sánchez González E, et al. Estudio transversal español de crecimiento 2008. Parte II: valores de talla, peso e índice de masa corporal desde el nacimiento a la talla adulta. *An Pediatr (Barc)* 2008;68:552–69. <https://doi.org/10.1157/13123287>.
- [28] Donnay Candil S, Saavedra Blanco MA, Gorgojo Martínez JJ, Brito Sanfiel M, Fernández Moreno A, del Cañizo Gómez FJ. Consumo de sal yodada en pacientes de consultas de endocrinología de tres áreas sanitarias de la Comunidad de Madrid. *Endocrinol Nutr* 2006;53:536–42. [https://doi.org/10.1016/S1575-0922\(06\)71145-7](https://doi.org/10.1016/S1575-0922(06)71145-7).
- [29] Olmedo Carrillo P, García Fuentes E, Gutiérrez Alcántara C, Serrano Quero M, Moreno Martínez M, Fernández T Ureña, et al. Evaluación del estado de nutrición yódica en población general en la provincia de Jaén. *Endocrinol Nutr* 2015;62:373–9. <https://doi.org/10.1016/j.endonu.2015.06.006>.
- [30] Diosady LL, Alberti JO, Mannar MG, Stone TG. Stability of iodine in iodized salt used for correction of iodine-deficiency disorders. *Food Nutr Bull* 1997;18:1–9. <https://doi.org/10.1177/156482659701800409>.
- [31] Donnay Candil S, Abel Pareja M, Escobar Del Rey F. Disponibilidad de sal yodada y su contenido real de yodo. *Endocrinol Nutr* 1999;46:224–7.
- [32] Dasgupta PK, Liu Y, Dyke JV. Iodine nutrition: iodine content of iodized salt in the United States. *Environ Sci Technol* 2008;42:1315–23. <https://doi.org/10.1021/es0719071>.
- [33] Peris Roig B, Atienzar Herráez N, Merchante Alfaro AA, Calvo Rigual F, Tenías Burillo JM, Selfa Moreno S, et al. Bocio endémico y déficit de yodo: ¿sigue siendo una realidad en España? *An Pediatr (Barc)* 2006;65:234–40. <https://doi.org/10.1157/13092160>.
- [34] Arrizabalaga JJ, Larrañaga N, Espada M, Amiano P, Bidaurrezaga J, Latorre K, et al. Evolución del estado de nutrición de yodo en los escolares de la Comunidad Autónoma del País Vasco. *Endocrinol Nutr* 2012;59:474–84. <https://doi.org/10.1016/j.endonu.2012.03.012>.
- [35] Serra-Prat M, Díaz E, Verde Y, Gost J, Serra E, Puig Domingo M. Prevalencia del déficit de yodo y factores asociados en escolares de 4 años. *Med Clin (Barc)* 2003;120:246–9. [https://doi.org/10.1016/S0025-7753\(03\)73667-7](https://doi.org/10.1016/S0025-7753(03)73667-7).
- [36] Morreale de Escobar G, Escobar del Rey F. Consequences of iodine deficiency for brain development. In: de Vijlder J, Morreale de Escobar G, editors. *The thyroid and the brain*. Stuttgart: Schattauer Verlag; 2003. p. 33–56.
- [37] Delgado E, Díaz-Cadorniga FJ, Tartón T, Bobis ML, Valdés MM, Méndez A. Erradicación de los trastornos por deficiencia de yodo en Asturias (España): 18 años de yodoprofilaxis con sal. *Endocrinol Nutr* 2004;51:492–6. [https://doi.org/10.1016/S1575-0922\(04\)74655-0](https://doi.org/10.1016/S1575-0922(04)74655-0).
- [38] Zubiaur Cantalapiedra A, Zapico Álvarez-Cascos MD, Ruiz Pérez L, Sanguino López L, Sánchez Serrano FJ, Alfayate Guerra R, et al. Situación nutricional de yodo en la población escolar de Alicante. *An Pediatr (Barc)* 2007;66:260–6. <https://doi.org/10.1157/13099688>.
- [39] Arena Ansótegui J, Empananza Knörr JI. Estudio de la ingesta de yodo en los niños de 6 meses a 3 años de edad de Guipúzcoa. *An Pediatr (Barc)* 2012;76:65–8. <https://doi.org/10.1016/j.anpedi.2011.07.007>.
- [40] Morreale de Escobar G, Escobar del Rey F. El yodo durante la gestación, lactancia y primera infancia. Cantidades mínimas y máximas: de microgramos a gramos. *An Esp Pediatr* 2000;53:1–15. [https://doi.org/10.1016/S1695-4033\(00\)77404-2](https://doi.org/10.1016/S1695-4033(00)77404-2).
- [41] Morreale de Escobar G, Escobar del Rey F. Metabolismo de las hormonas tiroideas y el yodo en el embarazo. Razones experimentales para mantener una ingesta de yodo adecuada en la gestación. *Endocrinol Nutr* 2008;55:7–17. [https://doi.org/10.1016/S1575-0922\(08\)76239-9](https://doi.org/10.1016/S1575-0922(08)76239-9).
- [42] Gowachirapant S, Winichagoon P, Wyss L, Tong B, Baumgartner J, Melse-Boonstra A, et al. Urinary iodine concentrations indicate iodine deficiency in pregnant Thai women but iodine sufficiency in their school-aged children. *J Nutr* 2009;139:1169–72. <https://doi.org/10.3945/jn.108.100438>.
- [43] Wong EM, Sullivan KM, Perrine CG, Rogers LM, Peña-Rosas JP. Comparison of median urinary iodine concentration as an indicator of iodine status among pregnant women, school-age children, and nonpregnant women. *Food Nutr Bull* 2011;32:206–12. <https://doi.org/10.1177/156482651103200304>.
- [44] Pearce EN, Pino S, He X, Bazrafshan HR, Lee SL, Braverman LE. Sources of dietary iodine: bread, cows' milk, and infant formula in the Boston area. *J Clin Endocrinol Metab* 2004;89:3421–4. <https://doi.org/10.1210/jc.2003-032002>.
- [45] Soriguier F, Gutierrez-Repiso C, Gonzalez-Romero S, Oliveira G, Garriga MJ, Velasco I, et al. Iodine concentration in cow's milk and its relation with urinary iodine concentrations in the population. *Clin Nutr* 2011;30:44–8. <https://doi.org/10.1016/j.clnu.2010.07.001>.
- [46] Li M, Waite KV, Ma G, Eastman CJ. Declining iodine content of milk and re-emergence of iodine deficiency in Australia. *Med J Aust* 2006;184:307.
- [47] Donnay S, Vila L. Erradicación de la deficiencia de yodo en España. Cerca, pero no en la meta. *Endocrinol Nutr* 2012;59:471–3. <https://doi.org/10.1016/j.endonu.2012.05.011>.

- [48] Flachowsky G, Franke K, Meyer U, Leiterer M, Schöne F. Influencing factors on iodine content of cow milk. *Eur J Nutr* 2014;53:351–65. <https://doi.org/10.1007/s00394-013-0597-4>.
- [49] van der Reijden OL, Zimmermann MB, Galetti V. Iodine in dairy milk: sources, concentrations and importance to human health. *Best Pract Res Clin Endocrinol Metab* 2017;31:385–95. <https://doi.org/10.1016/j.beem.2017.10.004>.
- [50] Capdevila Bert R, Marsal Mora JR, Pujol Salud J, Anguera Farran R. Estudio de prevalencia de la deficiencia de yodo en una población escolarizada de 6 años. *An Pediatr (Barc)* 2010;72:331–8. <https://doi.org/10.1016/j.anpedi.2009.12.023>.
- [51] Pyati SP, Ramamurthy RS, Krauss MT, Pildes RS. Absorption of iodine in the neonate following topical use of povidone iodine. *J Pediatr* 1977;91:825–8.
- [52] Silva JE. Effects of iodine and iodine-containing compounds on thyroid function. *Med Clin North Am* 1985;69:881–98. [https://doi.org/10.1016/S0025-7125\(16\)30995-6](https://doi.org/10.1016/S0025-7125(16)30995-6).
- [53] Arena Ansotegui J, Emparanza Knörr JI. Los antisépticos yodados no son inocuos. *An Pediatr (Barc)* 2000;53:25–9. [https://doi.org/10.1016/s1695-4033\(00\)77409-1](https://doi.org/10.1016/s1695-4033(00)77409-1).
- [54] Novaković R, Cavelaars A, Geelen A, Nikolić M, Iglesia Altaba I, Roman Viñas B, et al. Socio-economic determinants of micronutrient intake and status in Europe: a systematic review. *Publ Health Nutr* 2014;17:1031–45. <https://doi.org/10.1017/s1368980013001341>.