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Iodine status and thyroid function among Spanish schoolchildren aged 6–7 years: the Tirokid study

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Abstract

I deficiency is still a worldwide public health problem, with children being especially vulnerable. No nationwide study had been conducted to assess the I status of Spanish children, and thus an observational, multicentre and cross-sectional study was conducted in Spain to assess the I status and thyroid function in schoolchildren aged 6–7 years. The median urinary I (UI) and thyroid-stimulating hormone (TSH) levels in whole blood were used to assess the I status and thyroid function, respectively. A FFQ was used to determine the consumption of I-rich foods.

Abbreviations: AC, autonomous communities; ID, iodine deficiency; IS, iodised salt; P25 and P75, 25th and 75th percentiles; RV, reference values; TSH, thyroid-stimulating hormone; UI, urinary iodine; UIC, urinary iodine concentration.

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A total of 1981 schoolchildren (52 % male) were included. The median UI was 173 μg/l, and 17·9 % of children showed UI < 100 μg/l. The median UI was higher in males (180·8 v. 153·6 μg/l; P < 0·001). Iodised salt (IS) intake at home was 69·8 %. IS consumption and intakes of ≥2 glasses of milk or 1 cup of yogurt/d were associated with significantly higher median UI. Median TSH was 0·90 mU/l and was higher in females (0·98 v. 0·83; P < 0·001). In total, 0·5 % of children had known hypothyroidism (derived from the questionnaire) and 7·6 % had TSH levels above reference values. Median TSH was higher in schoolchildren with family history of hypothyroidism. I intake was adequate in Spanish schoolchildren. However, no correlation was found between TSH and median UI in any geographical area. The prevalence of TSH above reference values was high and its association with thyroid autoimmunity should be determined. Further assessment of thyroid autoimmunity in Spanish schoolchildren is desirable.

Key words: Iodine status: Iodine deficiency: Thyroid function: Urinary iodine

I deficiency (ID) is still a worldwide public health problem[1]. A wide variety of disorders results from ID, ranging from goitre and psychomotor development retardation up to cretinism in more severe cases. ID is considered the most common cause of preventable mental impairment worldwide[2]. Thyroid hormones produced by the mother have a key role in brain development and maturation of the fetus[3]; thus, a low concentration of maternal thyroid hormones negatively impacts the health of the fetus. ID could be involved in this situation, and thus it could be prevented by adequate I intake to meet the increased I needs during pregnancy. It has been reported that mild or moderate ID during pregnancy is associated with low intelligence quotient (IQ)[4]. Likewise, higher prevalence of goitre, lower IQ and increased auditory threshold have been detected among children with insufficient I intake[4,5].

Use of iodised salt (IS) is one of the best methods to adequately fulfil I requirements[2], and has been accessible to the Spanish population, with an I content of 60 mg/kg, since 1983. IS consumption has always been voluntary and, except for some regions, no comprehensive public health programme has been implemented to promote it[6]. The WHO considers Spain as a zone with an adequate I intake[7], based on local/regional studies conducted in the late 1990s, early 2000s and later[6,8]. However, until now, no national study has been conducted in Spanish schoolchildren. The aforementioned regional studies coincided with a remarkable increase in the consumption of IS and other sources of I, such as dairy products, and described median urinary I (UI) within the World Health Organization[2] range corresponding to an adequate I intake in school-age children (100–199 μg/l). There is no information concerning the I content in food products, with the exception of milk[9] despite the use of flour supplemented with IS by some bakeries.

The assessment of ID disorders is the first step towards achieving the goal of their sustainable elimination. Children are a sensitive population to ID; in fact, data from two independent surveys of micronutrient consumption among European children have shown that maximum and minimum average I intakes were below the reference standard for both sexes in the east and west[10]. It was necessary to assess the current I status of the Spanish children population, along with its geographical distribution. This would in turn facilitate the implementation of targeted public health campaigns.

Thyroid hormones are involved in somatic growth, neurodevelopment and metabolic pathways, which are essential during childhood[11]. In the last few years, thyroid function has been studied in paediatric groups for its relationship with obesity[12] or diabetes type 1[13], but nationwide studies in paediatric populations are not common[14]. In spite of the fact that neonatal hypothyroidism screening is universal in Spain, little information is available on the prevalence of thyroid dysfunction among healthy Spanish schoolchildren. The present study also aimed to generate normative data for thyroid function in school-age children in our country.

Methods

Participants and study design

An observational, multicentre and cross-sectional study was conducted in the seventeen regions, autonomous communities (AC), compiling Spain, to assess the I status of children (primary objective), prevalence of UI < 100 μg/l and thyroid disorders in schoolchildren aged 6–7 years. Each Spanish AC is divided into one or more provinces. In AC with one single province, the one was selected for the study. In AC with two to four provinces, two provinces were randomly selected, and in AC with more than four provinces three were randomly selected for the study. The capital of each province was selected by default for sampling. In addition, one of the province towns having 2000–20 000 inhabitants was randomly selected. One school in the capital and one in the chosen town were randomly selected, and all schoolchildren of the first grade of primary school, which corresponds to 6–7-year-old children, were recruited (each school had one or two first-grade classes with twenty-five students each). Children from the capital represented the urban population, whereas those from the smaller town represented the rural population. The recruitment was conducted over 2 years (2010 and 2011) during the school year period (October to December and January to June).

Variables assessed

The main objective of the present study was to establish the I status of children by assessing the median UI concentration (UIC) of the population. In addition, parents or legal guardians answered a questionnaire, and blood thyroid-stimulating hormone (TSH) levels of the children were also measured. The parents filled in a questionnaire, which included questions about parents' birthplace and education, family or child history of goitre or thyroid dysfunction, medical treatments used, I use for wound disinfection in the last month, surgery in the last 6 months and consumption of IS and other I-rich foods. Foods with known high I content were chosen, especially dairy products[9] and sea fish. Some studies have shown that I supplements for egg-laying chickens increase the I content in eggs, which might contribute to increased I intake in the population[15]. The FFQ was designed to assess the frequency of consumption and portion size of I-rich foods: milk (number of glasses per d) and yogurt (number of cups of yogurt per d); eggs (number per week); fish and cheese (times per week of consumption); and IS (used for cooking: yes/no). Parents were requested in the questionnaire to look at the salt package label to check whether it was iodised or not. The consistency of responses over time, of the six questions of our simplified FFQ, was analysed by a test–re-test, which was conducted in forty-one parents of children aged 6–7 years. Concordance rates varied between 0·71 and 0·95. The results were also expressed in 'dairy servings'. A single serving was considered as one glass of milk (200–250 ml) or two yogurt cups (250 ml total). In Spain, the yogurt cups consumed by children have a volume of 125 ml each. In the 'Results' section, the frequency of consumption of foods has been categorised according to the recommendations of the Spanish Society of Community Nutrition[16]: fish consumption, ≥3 times/week; egg consumption, 3 units/week; and dairy consumption, ≥2 servings/d.

The primary variable was the median UI of the population. The World Health Organization[2] considers a median value of UI between 100 and 199 μg/l as an adequate I status in schoolchildren, a value <100 μg/l as insufficient (50–99 μg/l, mild ID; 20–49 μg/l, moderate ID; <20 μg/l, severe ID) and values ≥200 μg/l as above requirements (≥300 μg/l, excessive). A 20-ml non-fasting sample of urine was obtained from each participant for UI assessment. Each sample was stored in a portable refrigerator and was subsequently frozen at −20°C. Samples were transported to the Malaga Biomedical Research Institute (Hospital Regional Universitario Carlos Haya, Malaga, Spain) for analysis in a container with dry ice to ensure that they stayed frozen and were stored again at −20°C until processing. The laboratory used the modified Benotti and Benotti method for UI determination. A previous digestion of the urine sample was made with chloric acid, followed by the Sandell–Kolthoff reaction, in which I acts as a catalyst for the reduction of Ce (IV) to Ce (III) by As (III). The intra- and inter-assay CV were 2·01 and 4·53 %, respectively. The UI assay is subjected, three times a year, to a programme of external quality assessment for the determination of I in urine by the Spanish Association of Neonatal Screening. We performed the quality control in triplicate and the reference material was Seronorm™ Trace Elements Urine (SERO AS), with a mean z score of 0·3.

TSH was assessed in whole blood dried on Whatman 903 filter paper (Whatman Neonatal Screening cards are manufactured and quality released in compliance with the FDA Quality System Regulation) and submitted to a fluoroimmunometric assay (AutoDELFIA™ Neonatal hTSH test kit; PerkinElmer Inc.) at the Newborn Screening Laboratory, Hospital Clínic. The normal range for TSH was 0·07–1·82 mU/l, with intra- and inter-assay CV of 1·82 and 3·67 %, respectively. A drop of blood was collected from the child, with consent from the child and his or her parents, by a finger stick applied directly onto the filter paper. The drop was allowed to dry at room temperature and the filter paper was stored in an envelope at 4°C until it was processed in the laboratory. This sample was obtained at the same time as the urine sample.

Statistical analyses

According to previous studies conducted in local areas of Spain, the prevalence of ID (UI <100 μg/l) was estimated as 20 %. The sample size needed, assuming an ID prevalence of 20 % and an accuracy of ±1·5 %, was 2370 individuals. As it was estimated that 10 % of values would be lost for analysis, the sample size required was 3100 individuals.

Categorical variables were described by absolute and relative frequencies, whereas quantitative variables were described by mean values, medians, standard deviations, percentiles 25 (P25) and 75 (P75) and number of valid cases. The Kolmogorov–Smirnov test was used to assess whether the variables followed a normal distribution. Missing data were not included in the analyses and were considered as lost.

The UIC was assessed as a continuous variable in the overall population as well as when assessed as a function of another variable (sex, consumption of I-rich foods, geographical area or parents' educational level). The comparison of UI among the groups was performed by the median test. All results obtained by the median test were confirmed by Mann–Whitney or Kruskal–Wallis tests, according to the number of groups (two or more). The association between UI, TSH and consumption of I-rich food units was assessed by Spearman's correlation coefficient.

A binary logistic regression analysis was performed to assess the possible effect of the demographic characteristics and consumption of I-rich foods on UI ≥100 μg/l. The χ^2 test (or exact Fisher's test, when necessary) was used for the exploratory analysis of the possible risk factors in the case of categorical variables, and the median test was used in the case of quantitative variables. Those variables with a P value above 0·20 in the corresponding bivariate analyses were pre-selected. In order to select the definitive model, different methods of variable selection, automatic as well as manual, were tried.

In order to calculate the TSH reference values (RV) of our population, only children without known thyroid disease and a UI between 100 and 200 μg/l were considered. Extreme cases and outliers were excluded following the method of Tukey. The remaining sample showed normal distribution of TSH for the calculation of RV. Thus, the RV were obtained according to the recommendations of the International Federation of Clinical Chemistry[17], by calculating the 95 % CI for the mean of TSH and standard deviations. The prevalence of thyroid dysfunction was operationally defined as the percentages with 95 % CI of children with TSH values above (defined as hypothyroidism) or below (defined as hyperthyroidism) RV. Median TSH has been used for descriptions and comparisons among groups.

The software SPSS version 17 was used for data analyses. The statistical significance level was set at 5 %.

Ethical statement

The present study was approved by the Ethics Research Committee of Hospital de Mataró (Barcelona, Spain) functioning according to the 3rd edition of the *Guidelines on the Practice of Ethical Committees in Medical Research* issued by the Royal College of Physicians of London. The parents or legal guardians of the children signed an informed consent after full explanation of the purpose and nature of all procedures and before enrolling the child for the study. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2008.

Results

Description of the population

A total of 1981 schoolchildren were assessed in eleven AC (Table 1; Fig. 1), covering 74·7 % of the entire Spanish population. The study could not be conducted in the other six AC (Canary Islands, Cantabria, Galicia, La Rioja, Murcia and Valencia) because of administrative constraints.

Table 1 shows the socio-demographic characteristics of the children, along with their geographical distribution. In all, 52 % were male and over half lived in rural areas. In total, 85 % or more of both parents were from Spain and 2 % were uneducated.

Urine and whole blood samples were obtained from 1750 and 1729 children, respectively.

Iodine status

The median UI was 173 (P25–P75 117·5–237·2) μg/l. The percentage of children with UIC within the adequate range (100–199 μg/l) was 44·1 % (95 % CI 41·7, 46·4); UI below 100 μg/l was detected in 17·9 % (95 % CI 16·1, 19·7) (Fig. 2). UI below 100 μg/l and below 50 μg/l were more frequently observed in girls (61·1 and 57·5 %, respectively), in children whose parents had less than high school-level education (21·6 and 30·6 %, respectively) and in those children who did not consume IS (37 and 45·7 %, respectively). Median UI was significantly higher in males than in females (181 v. 154 μg/l; $P<0·001$) and differed significantly between regions, although none showed median values lower than 100 μg/l (Table 2). UI was not influenced by living area (rural or urban), by parents' birthplace, I use for wound disinfection in the last month or surgery in the last 6 months (data not shown). Nevertheless, median UI from samples collected in spring (178 (interquartile range (IQR) 134–240) μg/l) was significantly higher ($P<0·001$) than UI from samples collected in winter and autumn (150 (IQR 99–226) μg/l and 153 (IQR 105–219) μg/l, respectively). No samples were collected in summer.

Table 1. Socio-demographic characteristics of the population (*n* 1981 children)
(Numbers and percentages)

	n	%
Sex*		
Male	816	52·4
Female	741	47·6
Area type		
Rural	1046	52·8
Urban	935	47·2
Regions		
Andalusia	48	2·4
Aragon	193	9·7
Asturias	89	4·5
Balearic Islands	93	4·7
Castile-La Mancha	212	10·7
Castile-Leon	328	16·6
Catalonia	177	8·9
Madrid	119	6
Navarra	159	8·0
Basque Country	363	18·3
Extremadura	200	10·1
Father's ethnicity		
Native	1689	86·8
Immigrant	257	13·2
Father's education		
Uneducated	43	2·2
Primary education	607	31·3
Secondary education	770	39·7
Higher education	521	26·8
Mother's ethnicity		
Native	1684	85·5
Immigrant	286	14·5
Mother's education		
Uneducated	33	1·7
Primary education	462	23·5
Secondary education	755	38·4
Higher education	715	36·4
Thyroid disorder		
In the child	15	0·8
Familial	652	33·5
I disinfection (last month)	289	14·7
Surgery in the last 6 months	36	1·8

* The sex was not specified in 424 (21·4 %) patients.

Urinary iodine concentration according to dietary habits

The prevalence of IS consumption was 69·8 % (95 % CI 68, 72) (Table 2). IS consumption only refers to IS intake at home and not IS that is consumed through processed foods. The median consumption of glasses of milk and yogurt cups per d was 2 (P25–P75 1–2) for each of the two food products. The median consumption of dairy servings was 2·5 (P25–P75 2–3). In all, 64·8 % of children consumed ≥2 glasses of milk/d. In total, 81 % of children consumed ≥2 dairy servings/d. The median consumption of cheese and saltwater fish was 2 (P25–P75 2–4) and 2 (P25–P75 2–3) times/week, respectively. The median of consumption of egg units per week was 2 (P25–P75 2–3). In all, 41 % of children consumed saltwater fish ≥3 times/week, 45·5 % consumed ≥3 eggs/week, and 80 % consumed cheese at least once a week.

Consumption of I-rich foods differed neither between sexes nor between the 231 children who did not provide a urine sample and those who did. There was no association between consumption of saltwater fish, eggs or cheese and higher UI (Table 3).

The group of children who consumed IS showed a significantly higher median UI ($P<0·001$) and a lower percentage of children with UI <100 μg/l ($P=0·003$) compared with the group that did not consume IS (Table 3). Intakes of 1 yogurt cup or ≥2 glasses of milk/d were also associated with statistically significant higher median UI and lower prevalence of children with UI <100 μg/l, as compared with no yogurt intake or <2 glasses of milk/d (Table 3). Among children who did not consume IS, a significant but weak correlation between the number of glasses of milk and UI was observed ($r_S=0·122$; $P=0·005$) (Fig. 3).

A logistic regression to assess the effect of independent variables on achieving UI >100 μg/l was performed: consumption of ≥2 dairy servings/d (OR 1·8; 95 % CI 1·02, 3·34; $P=0·043$), IS consumption (OR 1·4; 95 % CI 1·11, 1·90; $P=0·007$) and male sex (OR 1·9; 95 % CI 1·46, 2·47; $P<0·001$) showed a significant independent effect.

The combined effect of IS and high milk consumption (≥2 glasses/d) resulted in a significantly ($P<0·001$) higher

Fig. 1. Map of Spain with regions of study. ▩, Study completed; ▢, partial study; □, region not studied.

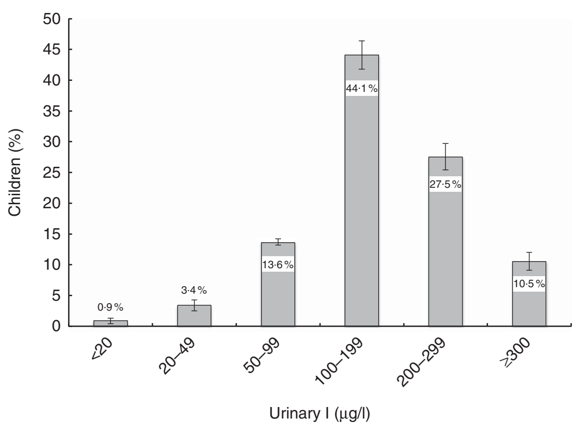

Fig. 2. Urinary iodine (µg/l) distribution among Spanish schoolchildren. Values are percentages, with 95 % CI represented by vertical bars.

median UI (189 (P25–P75 128–254) µg/l) than IS or milk consumption alone (165 (P25–P75 116–227) and 167 (P25–P75 113–225) µg/l, respectively). In cases with no IS consumption and low milk consumption (<2 glasses/d), the median UI was significantly lower than in cases with IS consumption alone (146 (P25–P75 97–204) *v.* 165 (P25–P75 116–227) µg/l; $P = 0.046$). Higher parental education was associated with higher median UI ($P < 0.001$) and implicated higher intakes of IS and milk ($P \leq 0.0001$ and $P = 0.001$, respectively) (data not shown).

Thyroid function

Only fourteen children presented with or had a history of thyroid disorder: ten had known hypothyroidism (0·5 %; 95 % CI 0·23, 0·92) (three were treated with levothyroxine and the other seven showed slightly elevated TSH concentrations), one hyperthyroidism, one known increase in antithyroglobulin antibodies, one non-specified thyroid gland disorder and one surgery for thyroglossal duct cyst.

The TSH RV in whole blood were 0·07–1·75 mU/l for males, 0·14–1·82 mU/l for females and 0·10–1·78 mU/l for the overall population. Median TSH was 0·90 (P25–P75 0·62–1·28) mU/l and was higher in females than in males (0·98 *v.* 0·83 mU/l; $P < 0.001$) (data not shown). No correlation was observed between UI and TSH concentrations. The prevalence of thyroid dysfunction is shown in Table 4.

Family history of hypothyroidism (first-, second- or third-degree relatives) was present in 9·3 % of children (161/1729). In these cases, the median TSH (0·99 *v.* 0·89 mU/l; $P = 0.036$) and the prevalence of hypothyroidism (14·9 *v.* 6·8 %; $P = 0.001$) were significantly higher than in those children with no family history. No correlation was found between prevalence of elevated TSH and median UI in any geographical area. TSH > 3·56 mU/l, twice the upper limit of the reference value (ULRV), was detected in nine cases (0·52 %; 95 % CI 0·23, 0·98).

Discussion

This is the first population-based study conducted to assess the UI in schoolchildren of Spain as a whole. The median UI observed (173 µg/l) indicates an adequate I-related nutrition in schoolchildren, according to World Health Organization[2] criteria. This fact reflects the substantial change in I intake experienced by the Spanish population since the introduction of IS in 1983, evolving from being an ID endemic region[18] to a population with adequate median UI in the late 1990s[6].

This median UI is higher than that of the Spanish adult population (117·2 µg/l)[19], as it has been described in other

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Table 2. Regional distribution of median urinary I (UI) levels, proportion of children with UI <100 µg/l and proportion of children consuming iodised salt*
(Medians and 25th–75th percentiles (P25–P75))

			UI (µg/l)				
Autonomous communities	nmd	*n*	Median	P25–P75	UI <100 µg/l (%)	UI <50 µg/l (%)	Iodised salt consumption (%)
Asturias	6	83	205	146–284	12·0	0·0	77·3
Basque Country	67	296	187	127·4–251	15·9	4·1	71·4
Navarra	16	143	184	135–232	11·9	2·1	60·8
Castile-La Mancha	13	199	175	118–241	17·6	4·5	77·8
Extremadura	21	179	172	122–249	13·4	3·4	67·7
Aragon	14	179	168	112–223	20·7	3·4	80·4
Andalusia	11	37	165	103–241	21·6	13·5	75·0
Madrid	14	105	165	105–235	21·0	5·7	59·6
Catalonia	21	156	163	118–218	13·5	1·9	76·0
Castile-Leon	43	285	156	96–221	26·0	6·7	61·1
Balearic Islands	5	88	149	106–232	20·5	6·8	65·5
Total	231	1750	173	118–237	17·9	4·3	69·8

nmd, Number of subjects with missing data.
* The *P* values for the differences among regions in median UI, population percentage with UI <100 and 50 µg/l and iodised salt consumption were $P=0{\cdot}011$ (median test), $P=0{\cdot}004$ (χ^2 test), $P=0{\cdot}016$ (χ^2 test) and $P<0{\cdot}001$ (χ^2 test), respectively. The difference is not significant if Andalusia is excluded in case of UI <50 µg/l.

studies[20], which might be explained by a higher consumption of milk and dairy products among children as compared with adults, as it was observed in the Spanish enKid study (>500 g/d in the 2–5-year-old group *v.* 350 g/d in the 18–24-year-old group)[21].

The current adequate concentration of UI in Spanish schoolchildren has been achieved by the consumption of IS and also of milk and dairy products, which are known to be important factors influencing UI levels in Spanish children[15,22]. Likewise, in a study conducted in Northeast Italy, an adequate I status was achieved only when IS was combined with daily milk intake[23], in agreement with our data showing the higher impact of the combination of daily milk and IS intake on UI than either one alone. Recently, low milk intake has been associated with ID in UK adolescents[24]. Although some studies have also shown an influence of fish or egg intakes on UI[22], their impact in our study was null.

To guarantee an adequate I concentration, the World Health Organization[2] aimed for >90 % of families to consume IS. A preliminary study[25] has analysed the I content of different IS brands available in the Spanish food market. The mean and median I contents of IS samples were 63·5 (SD 23·0) and 60 (P25–P75 51–70) µg of I/g of salt, respectively. The study showed a wide range of variation in I concentrations among different IS brands but did not find significant differences among regions. In Spain, only 70 % of families consume IS and yet the I concentration was adequate; thus, milk, which in Spain has an average I concentration of 259 (SD 58) µg/l[9], and dairy products seem to have supplied the rest of I. Children with IS consumption and intake <2 glasses of milk/d showed similar median UI compared with those who consumed ≥2 glasses of milk/d but did not consume IS. Furthermore, children with low milk (<2 glasses) and no IS consumption also showed an adequate median UI, which probably indicates the existence of other I sources. Excessive I concentrations have been associated with increased thyroid volume in response to thyroid dysfunction[26]. Our results showed that 10 % of children had UI >300 µg/l (Fig. 2). Although these data do not necessarily identify a population with I excess, they prompt for close monitoring of the iodisation of salt and of other putative food products. UI also showed seasonal variations from spring (higher UIC) to winter (lower UIC), as previously observed in other studies[27], which might be explained by the variability of I content in milk throughout the year[9].

Boys showed significantly higher median UI than girls, which could be justified by the higher energy and I intake in boys[21]; however, the results from the FFQ of boys and girls did not differ significantly.

Nevertheless, a very recent study[28] has warned about how hydration status can interfere with UIC values even in large surveys. This factor must be considered as well as urine volume or body surface area when we consider differences between children and adults, boys and girls or seasonal variations.

This is the first time that TSH RV were assessed in Spanish schoolchildren. Our survey detected high prevalence of elevated TSH (7·6 % overall). Previous studies conducted in two Spanish provinces showed similar data[29,30], which could be explained by the use of adult TSH RV, with a lower upper limit than those of the children[31]. However, in our study, we used RV calculated in the study's population itself. The study by Lazar *et al.*[32], conducted in 121 000 children aged 6 months to 16 years, showed lower prevalence of elevated TSH (3·3 %) than our study, although similar prevalence of cases with TSH concentrations compatible with clinical hypothyroidism. The recent study by Johner *et al.*[33] has shown an association between higher I intakes and a shift in TSH towards higher levels in children. According to those authors, the high prevalence of elevated TSH observed in our population should not be considered as a higher risk for (subclinical) hypothyroidism. Furthermore, the improved I status in children can be a plausible explanation for a physiological variant, corresponding to an euthyroid situation, with slightly elevated TSH[33]. Only cases with initial highly elevated TSH levels show greater risk of evolving to clinical hypothyroidism[32]. In our population, 0·52 % of the children had TSH levels twice the ULRV, and thus were at risk for developing clinical hypothyroidism. Our study

Table 3. Effects of different variables on ioduria
(Numbers and percentages)

Variables	Children		Median UI (µg/l)	P†	UI <100 µg/l		P‡	Correlation: food consumption/UI	
	n	%			n	%		r	P
Sex									
Male	816		181	<0·001*	119	14·6	<0·001*	–	
Female	741		154		181	24·4			
I disinfection									
None	1477	85·2	174	0·743	270	18·3	0·240	–	
Yes	256	14·8	172		39	15·2			
Iodised salt									
None	521	30·2	158	<0·001*	114	21·9	0·003*	–	
Yes	1197	69·8	180		191	16			
Fish consumption								– 0·016	0·498
<3 times /week	1018	59	174	0·405	173	17	0·257		
≥3 times/week	706	41	171		135	19·1			
Glasses of milk								0·117	<0·0001*
<2 glasses/d	611	35·2	160	<0·001*	124	20·3	0·047*		
≥2 glasses/d	1123	64·8	182		185	16·5			
Yogurt consumption								0·037	0·125
None	76	4·5	152	0·001*	20	26·3	0·046*		
≥1 cup/d	1621	95·5	185		270	16·7			
Dairy servings§									
<2 servings/d	324	18·8	148	<0·001*	72	22·2	0·022*	–	
≥2 servings/d	1416	81·3	188		238	16·8			
Cheese consumption								– 0·038	0·118
None	282	16·7	178	0·45	48	17·1	0·92		
≥1/week	1405	83·3	172		245	17·5			
Eggs consumption								0·023	0·332
<3/week	967	55·5	170	0·23	166	17·3	0·77		
≥3/week	775	45·5	178		139	18			
Area type									
Rural	937	53·5	168	0·180	171	18·2	0·670	–	
Urban	813	46·5	177		142	17·5			
Parents education									
Uneducated	23	1·2	114	<0·001*	35 %		0·004*	–	
Primary education	348	17·6	163		19·1 %				
Secondary education	752	38·1	168		20 %				
Higher education	850	42·9	181		14 %				

UI, urinary I.
* Significant P values.
† Median test.
‡ χ^2 Test.
§ Dairy serving (one): one glass of milk (200–250 ml) or two yogurt cups (250 ml total).

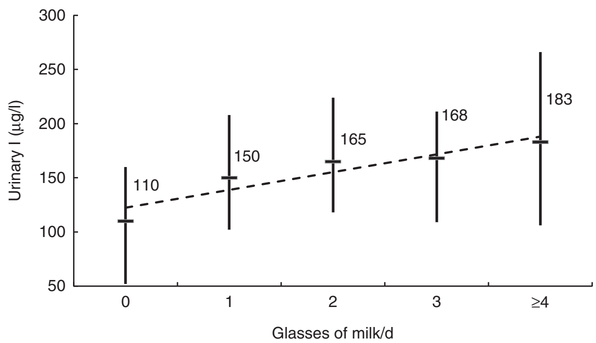

Fig. 3. Correlation between urinary iodine and milk consumption among children who did not consume iodised salt. P, percentiles; ⊥, median of urinary iodine (P25, P75).

Table 4. Prevalence of thyroid dysfunction

	TSH RV (mU/l)	TSH levels below or above TSH RV (*n* (%))	95 % CI (%)
Male	0·07–1·75	Below: 0 (0·0)	–
		Above: 64 (8·1)	6·1, 10·1
Female	0·14–1·82	Below: 4 (0·5)	0·1, 1·4
		Above: 54 (7·3)	5·4, 9·3
Overall	0·10–1·78	Below: 2 (0·1)	0·01, 0·4
		Above: 131 (7·6)	6·3, 8·9

TSH RV, TSH reference values in whole blood; TSH, thyroid-stimulating hormone.

design did not include a follow-up period, which would have allowed us to study the evolution of these cases. The prevalence of low TSH (0·1 %) was similar to that observed in Galicia (0·1 %) and lower than that detected in Almeria (0·6 %)[29,30].

The median TSH concentration, as well as the prevalence of elevated TSH, was significantly higher in children with a family history of hypothyroidism, in agreement with a recent study showing increased TSH concentrations in the adolescent offspring of women who had had hypothyroidism or antithyroid peroxidase (TPO) antibodies during pregnancy, as compared with those of euthyroid mothers or mothers negative for anti-TPO antibodies[34]. The prevalence of a positive family history of thyroid diseases in children with subclinical hypothyroidism and carrying non-synonymous mutations in the TSH receptor gene is twice that of patients with no mutation[35]. Thus, our cases with family history of hypothyroidism could probably have a genetic predisposition to develop further thyroid pathology. García-García *et al.*[30] observed a prevalence of thyroid autoimmunity (TA) (between 2·4 and 5 %) directly related to I intake among children aged 1–16 years with adequate I intake. The association between I prophylaxis and induction of autoimmunity, and thus hypothyroidism, could not be confirmed in our study, as anti-TPO antibodies were not assessed.

Although six AC did not participate in the study, three (Valencia, Andalusia and Galicia) had recent available data regarding I nutrition in schoolchildren[18,30,36], which were comparable with the present data. Thus, the lack of these data will, most likely, not cause a great deviation in our results. One other limitation of the present study is that the labelling of IS was not checked by the investigators, although parents were requested to do so. Some other limitations are the lack of anthropometric and anti-TPO antibodies data, variables that might have had some influence on TSH results, and of thyroxine, which would have helped to better assess thyroid dysfunction. Likewise, the analysis of creatinine in urine could have reduced the variability involved in casual urine sampling. Despite these limitations, the present study is the first one conducted on the I status of a representative sample of schoolchildren in Spain. I-rich foods are the most important determinants of UIC. The enKid study conducted in 3534 individuals (2–24 years old) representative of the Spanish population showed that the intake pattern along the school years (2–5 and 6–9 years) regarding dairy products and fish was very homogeneous[21]. Thus, the UI data of our 6–7-year-old children are probably similar to that of the extended group aged 2–9 years.

In conclusion, 30 years after the initiation of voluntary consumption of IS, I intake is adequate, but IS intake at home is not the only I source in recent years. Although the potential contribution of processed foods to the I status in Spanish schoolchildren might be currently lower than that in other European countries[37,38], it is necessary to monitor and control the iodisation of foods, as a putative risk of I deficit or excess in the future might exist, while it is necessary to promote the consumption of IS to achieve the WHO target of 90 % of household consumption. Prevalence of TSH above RV is high, and although in most cases it will most likely spontaneously normalise, more studies are needed to determine whether these elevated TSH concentrations are associated with an increase in TA.

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L. V. and M. S.-P. designed the research; L. V. analysed the data and had primary responsibility for the final content; S. D., J. J. A., J. Arena, J. P., E. G.-F., J. L. M., A. L.-G., L. M. L., A. V., Z. M., O. B., E. G., J. A. M., G. M., F. V., E. M., M. R., Y. T., P. B.-V., M. A., P. S., J. Aranda and C. G.-R. conducted the research; L. V., S. D., J. J. A., E. G.-F., C. García-Rey and I. V. wrote the

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