CLINICAL STUDY

Iodine intake and prevalence of thyroid autoimmunity and autoimmune thyroiditis in children and adolescents aged between 1 and 16 years

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Abstract

Objectives: To determine the status of iodine nutrition in children and adolescents in Almería, Spain. To calculate prevalence of thyroid autoimmunity (TA) and autoimmune thyroiditis (AT) in pediatric ages and to research into associated factors.

Methods: Cross-sectional epidemiological study. By a multistage probability sampling 1387 children and adolescents aged between 1 and 16 were selected. Physical examination was carried out including neck palpation. Parents were asked about eating habits as well as about social and demographic aspects. Urinary iodine, free thyroxine, TSH, antiperoxidase and antithyroglobulin antibodies were measured. TA was diagnosed when any antibody was positive and AT when autoimmunity was associated with impaired thyroid function or goitre. Results are shown using percentages (and its 95% confidence interval). To study associated factors we used multiple logistic regression, quantifying the relation with odds ratio (OR), and multiple lineal regression.

Results: Median urinary iodine concentration was 199.5 µg/l. The prevalences of TA and AT were 3.7% (2.4–5.0) and 1.4% (0.4–2.4). TA is associated with female sex (OR 2.78; $P < 0.001$) and age (OR 1.30; $P < 0.001$). Iodine status is associated with the intake of milk and dairy product ($P < 0.001$) and vegetable ($P = 0.021$) but not with use of iodized salt at home ($P = 0.1$).

Conclusions: The iodine supply in children and adolescents in our city is optimal. Milk and dairy products are the most important iodine sources. TA and AT are prevalent in pediatric ages in our city mainly in females and older subjects.

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Introduction

Iodine deficit causes high morbidity in pediatric ages producing psychomotor and growth retardation, goitre and hypothyroidism. To optimize this trace element remains a medical challenge (1). Iodine sufficiency in turn increases the possibilities of suffering from an autoimmune thyroid disease (2, 3, 4).

Autoimmune thyroiditis (AT) is a destruction of the thyroid gland mediated by lymphocytes and cytokines. Its aetiology shows the importance of predisposing genetic factors as proved by the fact that a third of cases had a family history of autoimmune thyroid diseases and also by the finding of genes that predispose the subjects to them (5, 6). However, the onset of the disease must be triggered by environmental factors, especially iodine supply (2, 3, 4). The iodination of thyroglobulin (TG) stimulates the production of antibodies and the proliferation of lymphocytes, which are its pathogenic bases (7). We know that the prevalence of AT increases

exponentially decades after supplying iodine in previously deficient areas (8, 9) and also that areas with good iodine supply present prevalences between three and five times higher than those found in deficient areas of the same region (10, 11).

No study has estimated the prevalence of autoimmune thyroid disorders in children and adolescents living in Spain. Our study aims to describe iodine intake among children and adolescents in our city, to calculate the prevalence of thyroid autoimmunity (TA) and AT in pediatric ages and to analyze the variables associated with iodine status and with the presence of autoimmune thyroid disease.

Materials and methods

We conducted an observational cross-sectional epidemiological study on a population sample. The study was focused on the city of Almería and the subjects were

residents aged between 1 and 16. Almería is a city on the Spanish south coast comprising ~180 000 inhabitants.

Accessible population was obtained from two sources: the Medical District and the Education Office. Data from children aged from 1 to 4 were obtained from the list given by the Medical District of Almería in which all children living in the city are registered for screening for hypothyroidism and phenylketonuria. It virtually coincides with the target population. The district has nine community health centres; 5453 children constitute the cohort of children born between January 2003 and December 2004. Subjects older than 4 correspond to the total number of students registered in November 2004 in the 44 state schools, 26 state-subsidised and private schools of Nursery (4–5 years old) and Primary (6–12 years old) education as well as in the 18 state schools and ten state-subsidised and private schools of Secondary education (12–16 years old) in our city. A total of 17 934 children between 4 and 12 years of age and 9823 aged between 12 and 16 were eligible.

A multistage probabilistic sampling was carried out. The primary units were the community health centres of the Medical District and the schools of Nursery, Primary and Secondary education. We randomly selected four community health centres, six schools of Nursery and Primary education (four state and two private) and six schools of Secondary education (four state and two private). Afterwards, three groups of every academic level were selected and all the students in the above-mentioned groups were asked to take part in the study.

Assuming a TA prevalence of 10%, a 95% confidence interval and a precision of 3%, the minimum sampling size needed was 359 individuals aged between 1 and 6, 376 between 6 and 12, and 370 between 12 and 16. We selected 550 individuals in each age group in case any of them refused to take part in the study.

Inclusion criteria were that the participants were residents of Almería and aged between 1 and 16 years. Anybody suffering from any endocrine or systemic disease was excluded.

Anthropometric and physical examination data were obtained for each individual. We looked for signs of pubertal development (testicular volume of at least 4 ml in males and breast development in females) and presence of goitre according to the international criteria (12).

Parents were questioned about the following socio-demographic variables: origin (Spanish or immigrant and if so of what origin); socio-economic and cultural: employment situation (employed, unemployed, retired/disabled, housewife or student); education level (no education, primary or vocational, secondary or university); eating habits: frequency of fruit, vegetables, milk and dairy products, meat, fish, eggs and legumes intake, and how often they eat unnecessary foods, such as baked goods, sweets and snacks; type of salt (iodated or not) and type of oil consumed at home.

Samples of total blood and a urine specimen were collected. Serum free thyroxine (normal range 0.9–1.7 ng/dl), serum TSH (normal range 0.2–4.2 mU/l), antiperoxidase antibodies (TPO ab) (normal value <34 U/ml) and anti-TG antibodies (TG ab; normal value <115 U/ml) were assayed by electrochemiluminescence immunoanalysis (Roche Diagnostics).

Urinary excretion of iodine was assayed by Benotti method (13) in a sample of urine and expressed as micrograms of iodine per litre of urine. Epidemiologic criteria for assessing iodine nutrition based on median urinary iodine concentrations of school-age children and adults are: iodine deficiency, <100 µg/l; adequate iodine nutrition, 100–199 µg/l; above requirements, 200–299 µg/l; and excessive, >300 µg/l (12).

Table 1 Characteristics of study participants.

Variable	Percentage (95% CI)	Mean (95% CI)	s.d.
Sex			
Females	48.8 (46.2–51.4)		
Males	51.2 (48.6–53.8)		
Age (years)		8.37 (8.13–8.61)	4.5
Pubertal status			
Prepubertal	63.6 (62.4–64.8)		
Pubertal	36.4 (35.4–37.4)		
BMI (kg/m ²)		18.7 (18.5–18.9)	3.9
Ethnicity			
Spanish	89.7 (88.1–91.3)		
Maghribian	4.4 (3.4–5.4)		
Latin American	4.4 (3.4–5.4)		
Other	1.5 (0.9–2.1)		
Father's employment situation			
Employed	87.7 (86.0–89.3)		
Unemployed/retired	12.3 (10.6–14.0)		
Mother's employment situation			
Employed	65.8 (63.3–68.3)		
Unemployed/housewife	34.2 (31.7–36.7)		
Father's education level			
No education	4.2 (3.1–5.3)		
Primary	43.0 (40.4–45.6)		
Higher	52.8 (50.2–55.4)		
Mother's education level			
No education	3.1 (2.2–4.0)		
Primary	40.0 (37.4–42.6)		
Higher	56.9 (54.3–59.5)		
How often they consume			
Fruit (per day)		0.82 (0.78–0.85)	0.58
Vegetables (per day)		0.73 (0.70–0.76)	0.44
Milk and dairy products (l/day)		0.67 (0.65–0.69)	0.25
Meat (per week)		4.07 (3.95–4.20)	1.88
Fish (per week)		2.86 (2.76–2.95)	1.38
Eggs (per week)		2.36 (2.28–2.45)	1.28
Pulses (per week)		2.89 (2.79–3.00)	1.53
Baked goods (per week)		2.19 (2.00–2.38)	2.80
Sweets (per week)		2.19 (1.93–2.44)	3.74
Snacks (per week)		1.71 (1.52–1.89)	2.51
Type of oil consumed:	89.2 (87.6–90.8)		
olive			
Type of salt consumed:	47.3 (46.4–48.2)		
iodized			

95% CI, 95% confidence interval.

Concentrations above 500 µg/l were regarded as contamination.

TA was diagnosed when any thyroid antibody was positive and AT when TA were associated with impaired thyroid function (TSH values above 4.2 mU/l or below 0.2 mU/l) or goitre.

Fieldwork was carried out from September 2007 to June 2010. Those in charge of questioning and examining individuals were physicians who followed a programme of training and criteria standardization. Consistency among criteria was assessed by obtaining a consistency coefficient of 0.90.

Software Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 17.0 for Windows was used to conduct the statistical analysis and Epidat 3.0 was used for the sample size calculation. In descriptive statistics qualitative variable results are expressed in percentages and 95% confidence intervals (95% CIs) and quantitative variables are expressed in mean (95% CI) $\pm$ s.d. To study the relation between TA (dichotomous dependent variable) and independent variables, we used binary and multiple logistic regressions quantifying the relation with odds ratio (OR (95% CI)). To study the relation between urinary excretion of iodine (continuous dependent variable) and independent variables, we used binary and multiple lineal regressions. $P < 0.05$ was considered to have statistical significance.

The study was approved by the Research and Ethical Committees of Torrecárdenas Hospital.

Written informed consent from the parents or tutors and the individuals themselves (if they were older than 12) was obtained after full explanation of the purpose and nature of all procedures used.

Results

A total of 1387 children and adolescents enrolled in the study (478 aged between 1 and 6, 505 between 6 and 12, and 404 between 12 and 16).

A description of the samples is given in Table 1. Our city has received a high number of immigrants in recent years (10.3% of children have a foreign origin, mainly Maghribian and Latin American). The rate of unemployment is high (only 87.7% of fathers and 65.8% of mothers state that they are employed), and the rate of parents with no education is 4.2% of fathers and 3.1% of mothers. Regarding eating habits, fruit, vegetables, fish, eggs and pulses intake is not sufficient but our children and adolescents eat enough dairy products and too much unnecessary food (baked goods, sweets and snacks). In 47.3% of families iodized salt was used.

The urinary iodine concentration was 209.1 (± 101.4) µg/l (median 199.5 µg/l). Of the probands, 15.2% had a concentration below 100 µg/l indicating iodine deficiency and 19.9% were above 300 µg/l indicating excess (Table 2). Iodine status is associated

Table 2 Clinical and laboratory findings of study participants.

Variable	Percentage (95% CI)	Mean (95% CI)	s.d.
Goitre	4.8 (3.4–6.2)		
Ia	3.4 (2.4–4.4)		
Ib	1.1 (0.6–1.6)		
II	0.3 (0.0–1.2)		
TSH (mU/l)		2.79 (2.71–2.87)	1.48
Free thyroxine (ng/dl)		1.32 (1.30–1.33)	0.22
Hyperthyroidism	0.6 (0.0–1.8)		
Hypothyroidism	0.2 (0.0–0.8)		
Antiperoxidase antibodies (U/ml)		10.31 (8.62–12.00)	32.1
Antiperoxidase antibodies +	2.1 (1.6–2.6)		
Antithyroglobulin antibodies (U/ml)		31.94 (23.09–40.78)	167.9
Antithyroglobulin antibodies +	3.0 (2.1–3.9)		
Thyroid autoimmunity	3.7 (2.4–5.0)		
Isolated thyroid antibodies	2.3 (1.4–3.2)		
Autoimmune thyroiditis	1.4 (0.4–2.4)		
Simple goitre (without ab)	3.7 (2.4–5.0)		
Urinary iodine excretion (µg/l)		209.1 (203.0–215.3)	101.4
<100	15.2 (14.5–15.9)		
50–100	12.1 (11.6–12.6)		
20–50	2.4 (1.4–3.4)		
<20	0.7 (0.0–2.0)		
100–200	35.1 (34.6–35.6)		
200–300	29.8 (28.4–31.2)		
>300	19.9 (18.4–21.4)		

95% CI, 95% confidence interval.

with the intake of milk and dairy products (ml/day; adjusted β 0.06; $P < 0.001$) and vegetables (times a day; adjusted β 20.7; $P = 0.021$), but not with use of iodized salt at home (adjusted β 13.6; $P = 0.10$). Urinary iodine was as good in those who do not use iodized salt (208.8 ± 101.3 µg/l) as in those who use it (222.4 ± 101.4 µg/l).

The serum concentrations of thyroid hormones are shown in Table 2. In 5.0% of the probands the TSH concentration was > 4.2 mU/l. A clear indication for hypothyroidism with a concentration > 10 mU/l was found in only 0.2% and for hyperthyroidism with a concentration < 0.2 mU/l in 0.6%. Goitre was diagnosed in 4.8%.

The prevalence of TA and AT is shown in Table 2. TA was found in 3.7% of children and adolescents: TPO ab was found in 2.3% and TG ab in 3.0%. Thus, the frequency of AT in the study population defined by positive antibodies combined with goitre or abnormal TSH concentration was 1.4% and isolated TA was 2.3%. Prevalence of goitre and abnormal thyroid function is higher in subjects with TA (Table 3).

Table 4 shows TA and AT prevalence and its 95% CI for each age, sex, pubertal status and iodine intake groups. In females the prevalence was higher than in males ($P < 0.001$). Female preponderance was also found in prepubertal children ($P = 0.03$). There were

Table 3 Prevalence of goitre and abnormal thyroid function in subjects with and without thyroid autoimmunity and in different iodine intake groups.

	Goitre	TSH <0.2 µU/ml	TSH >4.2 µU/ml	TSH >10 µU/ml
Thyroid autoimmunity				
Positive (%)	25.5	5.9	3.9	5.9
Negative (%)	4.0	0.4	4.8	0.0
P value	<0.001	<0.001	0.70	<0.001
Iodine intake				
Deficient	6.2	0.0	2.5	0.0
Adequate	3.9	1.3	4.3	0.0
Above requirements	3.3	0.6	6.4	0.6
Excessive	3.8	0.0	6.2	0.5
P value	0.26	0.36	0.36	0.36

differences among age groups as well. The highest prevalence is found in the group of individuals aged between 12 and 16 and the lowest in the group aged between 1 and 6 ($P < 0.001$), and between pubertal vs prepubertal subjects ($P < 0.001$). Differences in TA and AT prevalence between iodine intake groups did not reach statistical significance.

Variables related to TA were female sex (OR 2.78 (1.89–5.28); $P < 0.001$) and age (OR 1.30 (1.15–1.46); $P < 0.001$).

Discussion

Children and adolescents of Almería have a sufficient intake of iodine as shown by the median urinary iodine excretion (UIE) and goitre prevalence. The studies on children and adolescents in Andalusia, our region, published up to now have shown high goitre prevalence (between 19 and 37%), which is associated with an insufficient intake of this trace element, whereas median UIE were low within acceptable levels, between 109 and 130 µg/l (14, 15, 16). However, recent papers studying other Spanish regions showed an optimal iodine intake with median UIE between 150 and 200 µg/l in children older than 6 (17, 18), as well as in children younger than 6 and infants (19, 20), although iodized salt had not become widespread in any of the regions.

In many areas, the intake of dairy products was proved to be strongly associated with iodine supply (21, 22, 23, 24) and this has been the case in our region (15, 16) too. Milk and dairy products are an important source of iodine; in fact, they now have a higher amount of iodine (25, 26). An analysis of 45 brands of milk in Spain showed that the concentration of this trace element has doubled now (259 µg/l on average) compared with 20 years ago. As a result, if children take the recommended half a litre of dairy products a day, they will have a sufficient iodine supply (26).

With regard to the frequency of autoimmune thyroid disorders, as it is directly proportional to age and iodine intake of the population, very different data can be

found in published papers. The prevalence of TA in adults is around 10–13% and that of AT is 3–5% (in the elderly it goes up to 9.5%) (2, 3, 4). The only data from Spain available show a prevalence of TG ab of 9.7% and TPO ab of 3.4% (27) in a sample of 400 individuals including adults and children older than 6 with a median UIE of 120 µg/l.

Despite the few data on prevalence in paediatric ages, we know that it is higher among adolescents although this pathology can appear even in children younger than 2 (2, 3, 4). In regions with an optimal iodine supply, prevalence of AT ranges between 2.5% and 3.6% in Greece (28), 2.6% in India (29), 2.9% in Sardinia (30), 3.0% in Berlin (31) and 3.6% in Turkey (32). These results are similar to ours as they include only children older than 6. In regions where the median UIE reaches 200 µg/l, prevalences are very high, for example, 5.1% in Sweden (33) and 9.6% in the north west of Greece (9); even in these two studies all children were older than 12.

The consequences that an excess of iodine may entail for our health are less well known than those produced by a deficit. A recent study in China associated excess of iodine with intellectual deficit as it showed that students with a median UIE of 228 µg/l due to the consumption of water with a high concentration of iodine have an intellectual quotient nine points lower than average. However, authors do not know whether this fact is mediated by the induction of autoimmune thyroid disease (34).

Children and adolescents of Almería have an optimal iodine supply. The main source of this trace element in their diet is not salt but dairy products. Among children and adolescents, autoimmune thyroid disease is very prevalent, especially after the onset of puberty. Our study shows limitations in its design that prevent us from comparing different socioeconomic strata or ethnic

Table 4 Prevalence (% and 95% CI) of thyroid autoimmunity, and autoimmune thyroiditis in individuals aged 1–16, in each group of age, sex, pubertal status and iodine intake.

	Thyroid autoimmunity	Autoimmune thyroiditis
Total group	3.7 (2.4–5.0)	1.4 (0.4–2.4)
Males	2.3 (1.1–3.5)	0.8 (0.0–2.8)
Females	5.0 (3.4–6.6)	1.9 (0.9–2.9)
Prepubertal	2.4 (1.2–3.6)	0.5 (0.0–1.8)
Males	1.5 (0.2–2.8)	0.0 (0.0–0.6)
Females	3.3 (2.3–4.3)	0.9 (0.3–1.5)
Pubertal	6.8 (4.2–9.4)	3.0 (1.4–4.6)
Males	3.9 (1.4–6.3)	2.4 (1.1–3.7)
Females	8.1 (5.8–10.4)	3.6 (1.6–5.6)
12–16 years old	6.2 (4.9–7.5)	3.2 (0.0–6.5)
6–12 years old	4.6 (2.6–6.6)	1.2 (0.0–2.4)
1–6 years old	0.6 (0.0–2.6)	0.0 (0.0–0.9)
Iodine intake		
Deficient	2.6 (1.3–5.1)	1.3 (0.0–4.5)
Adequate	2.9 (1.3–6.3)	1.3 (0.1–3.1)
Above requirements	4.6 (2.9–7.8)	1.6 (0.1–3.7)
Excessive	5.0 (2.6–9.6)	1.4 (0.0–4.1)

minorities. It would be interesting to design these studies to identify subpopulations with a deficiency and those with an excessive supply and to create different action plans for each of them.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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