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ORIGINAL ARTICLE

Iodine sources and iodine levels in pregnant women from an area without known iodine deficiency

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Summary

Objective An adequate iodine intake during pregnancy is essential for normal development of the foetus. The World Health Organization (WHO) recommends that the median urinary iodine concentration (UIC) in a population of pregnant women should range between 150 and 249 μg/l. The aim of this study was to evaluate iodine status and to examine the main sources of iodine in pregnant women from an apparently iodine-sufficient area.

Methods Six hundred pregnant women in the third trimester completed a food frequency questionnaire, and iodine was measured in urine samples. Urinary iodine concentrations were described in the whole population and in subgroups according to their frequency of intake of milk, fish, eggs, bread and iodized salt, as iodine supplements.

Results The median UIC was 104 μg/l (n = 600), however, the median was higher among women who had a high milk intake (117 μg/l), used iodized salt (117 μg/l) or who were supplemented with iodine (141 μg/l). Women receiving iodine supplementation who also consumed more than one cup of milk per day had median UIC higher than 150 μg/l. In multivariate models, women with moderate and high milk intake had lower risk of having UIC below 150 μg/l [OR (95% CI): 0·42 (0·22–0·82) and 0·29 (0·15–0·55) respectively], after adjustment for potential confounders.

Conclusions On the basis of WHO criteria, the iodine status of pregnant women was inadequate in this area. Milk was the most important dietary source of iodine, and iodine supplementation was also an important source of iodine, although not enough to reach the current recommendations.

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Introduction

Iodine is an essential micronutrient required for normal activity of the thyroid hormones, which are necessary for normal growth and neurodevelopment of the foetus during pregnancy.[1] Iodine deficiency during this critical period could result in brain damage to the foetus.[1–3] Thus, it is important for pregnant women to consume foods rich in iodine. Milk and fish are known to contain relatively high amounts of iodine[4,5], as does iodized salt, an important dietary source of iodine provided in most populations as an intervention strategy for iodine deficiency control and prevention.[6]

Urinary iodine concentration is currently the most practical biomarker for assessing the iodine nutrition in a population, although not in individuals.[6–8] The World Health Organization (WHO) recommends a median urinary iodine concentration (UIC) of at least 100 μg/l, not more than 20% of values below 50 μg/l, and a use of adequately iodized salt in at least 90% of households to prevent iodine deficiency disorders in the general population.[6] In pregnant women, iodine requirements are thought to be higher as there is an increment in thyroid hormone synthesis to provide for the needs of the foetus, and there is an increased loss of iodine in the urine resulting from an increased renal clearance of iodine during pregnancy.[1,8,9] The WHO recently increased their recommended iodine intake during pregnancy and suggested that a median UIC concentration should range between 150 and 249 μg/l.[7] Most pregnant women in areas of marginal or low iodine intakes require either supplementation with iodine or a high intake of foods rich in iodine to reach this levels.[10]

Some parts of Spain have had historical problems of endemic goitre described during the 1970s and 1980s; however, the situation improved after information campaigns for eradicating iodine deficiency.[11] Recent studies in some areas very close to Sabadell showed iodine sufficiency in the general population.[12] Nevertheless, some recent studies in Spain suggest that pregnant women may still be at risk of iodine deficiency.[12–14]

The objectives of this study were to evaluate the current status of iodine nutrition based on WHO criteria and to assess the main sources of iodine in a population of pregnant women from an apparently iodine-sufficient area.

Methods

Study population

A population-based birth cohort was established in the city of Sabadell (Catalonia, Spain). Six hundred and fifty-seven pregnant women who visited the public health centre of Sabadell for an ultrasound in the first trimester between July 2004 and July 2006 were recruited. Food intakes during the previous month was assessed by a food frequency questionnaire (FFQ) administered by two trained nurses, during the third trimester of pregnancy. The frequency of food intake was reported per day, week or month, and portions were reported based on standard referent portion sizes, as pieces, glasses, cups, spoons, centilitres or grams. The questionnaire is an adapted version of the FFQ developed by Willett,[15] and it has been already used and validated in the general population in Valencia (Spain).[16] Information on education, social class (using the CIUO-88 code), demographic factors, marital status, maternal disease and obstetric history, multivitamin supplement use, parity, alcohol consumption and smoking habits during pregnancy was obtained by questionnaire. Gestational age and anthropometric measures were collected from clinical records. Informed consent was signed and the study was approved by the ethics committee of the Institut Municipal d'Investigació Mèdica, Barcelona.

Urinary iodine analysis

Urine iodine concentration in a spot urine sample was measured in a total of 600 women in the third trimester of pregnancy, using paired-ion reversed phase high performance liquid chromatography with electrochemical detection and a silver working electrode.[17] Urine samples were stored at −20 °C until they were delivered to the reference laboratory (Normative Public Health Laboratory of Bilbao, Basque Country).

Statistical analysis

Urinary iodine concentrations were estimated in groups of women classified according to their use of iodine supplementation during pregnancy (either as specific potassium iodide supplements or multivitamin tablets containing between 100 μg and 200 μg of iodine each) or their intakes of several foods know to be rich in iodine: iodized salt, milk, fish (total fish, and the subgroups of lean and fatty fish, shellfish and molluscs), eggs and bread. Results were given as medians, geometrical mean values, percentiles (PC) 25 and 75, as well as the percentage of women with UIC below 50 μg/l and 150 μg/l. The Kruskal–Wallis test was used to compare UICs between groups. Additionally, logistic regression models were used to assess the relation between dietary iodine sources and UIC after adjustment for potential confounders (gestational age, mother's weight and age, season and time of sample collection, mother's diagnosis with thyroid alterations and mother's smoking habits). All statistical analyses were conducted with the STATA 8.2 (Stata Corp LP, College Station, TX, USA) statistical software package. The level of statistical significance was set at 0·05.

Results

Table 1 shows the characteristics of the study population according to UIC level. There were no statistically significant differences between the groups with higher and lower UICs.

The UIC in the whole population and in the different groups of pregnant women according to their reported food intakes is shown in Table 2. The median UIC overall was 104 μg/l and 72% of the women who had concentrations below 150 μg/l. Iodine supplementation and milk intake were positively related with UIC (*P*-values: 0·002 and 0·000 respectively). When total dairy products intake (milk, cheese and other dairy products) was studied, the results were very similar to milk intake alone (data not shown). The use of iodized salt and high intake of shellfish, molluscs and eggs seemed to be slightly related with higher UIC, although differences were not statistically significant.

When iodine supplement users were excluded, iodine concentrations were lower (the median was 101 μg/l), however milk intake was still positively related with UICs (Table 3).

Table 4 shows UIC in iodine supplemented women according to their consumption of milk, eggs and use of iodized salt. These iodine supplemented women with moderate or high milk intake had a median UIC above 150 μg/l. Iodine supplemented women who had also been using iodized salt during the last month had a median UIC of 141 μg/l.

Table 1. Characteristics of the study population according to the urinary iodine concentration (UIC)

	UIC <150 μg/l (*n* = 429)	UIC >150 μg/l (*n* = 171)
Gestational age at examination (weeks)*	34 (28–40)	34 (30–39)
Mother's weight before pregnancy (kg)*	62 (43–143)	63 (39–134)
Mother's age (years)*	31 (18–43)	32 (18–42)
Season at urine extraction (%)		
Winter	24	31
Spring	28	22
Summer	26	21
Autumn	22	26
Time at urine extraction (%)		
Before 10 am	42	34
10 pm–12 am	45	48
After 12 am	13	18
Mother's thyroid alterations diagnosed (%)		
No	92	95
Yes	8	5
Mother's smoking during pregnancy (%)	17	16
Maternal education (%)		
High school	30	27
Secondary school	43	40
Primary school or less than primary school	27	33

*mean (range).

Table 2. Urine Iodine concentration (μg/l) in pregnant women at the third trimester of pregnancy according to food intake patterns

	n	Median (μg/l)	Geometric mean (μg/l)	PC 25 (μg/l)	PC 75 (μg/l)	% UIC <50 μg/l	% UIC <150 μg/l	Kruskal–Wallis
All women	600	104	103	65	164	13	72	
Iodine supplementation								
No	547	101	100	64	159	14	73	0·002
Yes	53	141	141	71	259	4	57	
Iodized salt								
No	531	104	102	65	161	14	73	0·453
Yes	69	117	110	66	188	10	62	
Milk (full-fat, low fat and skimmed)								
<once/day	96	78	80	55	115	20	85	0·000
1–2 times/day	234	100	100	68	155	14	73	
>2 times/day	266	117	115	74	187	11	65	
Fish (includes all kinds of fish)								
<4 times/week	164	94	100	62	172	16	73	0·478
4–7 times/week	240	107	107	69	175	12	69	
>7 times/week	192	108	100	64	151	13	74	
Lean fish								
<once/day	111	94	99	62	147	14	76	0·282
1–3 times/month	88	100	103	64	192	16	72	
4 times/month	219	96	99	61	162	13	72	
>4 times/month	178	115	110	71	175	11	68	
Fatty fish								
<once/month	182	98	106	62	192	14	68	0·556
1–3 times/month	129	94	95	60	151	16	74	
4 times/month	150	108	103	71	146	7	77	
>4 times/month	135	111	105	64	170	16	67	
Shellfish								
<once/month	212	98	97	62	150	16	75	0·435
1–3 times/month	288	107	105	67	167	12	70	
>3 times/month	96	110	109	67	182	12	67	
Molluscs								
<once/month	259	102	100	62	168	14	72	0·372
1–3 times/month	242	101	102	66	158	13	71	
>3 times/month	97	110	112	78	176	10	68	
Eggs								
<twice/week	127	94	97	62	145	15	76	0·166
2 or more times/week	469	108	104	65	169	13	70	
Bread								
<once/day	132	101	105	64	169	12	73	0·354
1 time/day	244	112	106	69	162	12	70	
>1 time/day	220	96	68	61	164	16	73	

The positive association between UIC and iodine supplementation or milk intake was not confounded by gestational age, mother's weight and age, season and time of sample collection, mother's diagnosis with thyroid alterations or mother's smoking habits (Table 5). Women who consumed more than two cups of milk per day had a lower risk of having an UIC below 150 μg/l than women who consumed milk less than once per day [OR (95% CI): 0·29 (0·15–0·55)]. Moreover, iodine supplemented women also had lower risk of having UIC below 150 μg/l than nonsupplemented women [OR (95% CI): 0·44 (0·24–0·82)]. Multivariate models where repeated stratifying by type of milk (full-fat, low-fat and skimmed) (data not shown). The decreased risk of having UIC below 150 μg/l was only observed in those women who consumed mainly full-fat milk [OR (>2 cups per day) (95% CI): 0·16 (0·03–0·76)]. Nevertheless, the interaction between type of milk and frequency of milk intake was not statistically significant (*P*-value for interaction >0·10).

Discussion

Iodine levels are too low among pregnant women in Sabadell. Milk seems to be the main dietary source of iodine; however the median UIC in women with a high intake of milk (more than two cups per day) is below the WHO recommendations.[7] Fish, molluscs and shellfish are also known to be rich in iodine content; however these foods do not contribute to the variability in iodine status in this population.

Table 3. Urine Iodine concentration in pregnant women at the third trimester of pregnancy according to food intake patterns and excluding iodine-supplemented women

	n	Median (μg/l)	Geometric mean (μg/l)	PC 25 (μg/l)	PC 75 (μg/l)	% UIC <50 μg/l	% UIC <150 μg/l	Kruskal–Wallis
All sample	547	101	100	64	159	14	73	
Iodized salt								
No	489	100	99	65	152	14	74	0·497
Yes	58	109	107	62	200	13	63	
Milk (full-fat, low fat and skimmed)								
<once/day	85	76	78	55	112	19	86	0·000
1–2 times/day	210	99	97	64	153	15	74	
>2 times/day	248	111	111	72	177	12	68	
Fish (includes all kinds of fish)								
<4 times/week	148	92	98	61	169	18	72	0·613
4–7 times/week	214	103	103	68	168	13	71	
>7 times/week	181	106	97	62	146	14	77	
Lean fish								
<once/day	103	92	98	67	143	15	77	0·304
1–3 times/month	80	100	101	62	182	17	72	
4 times/month	193	94	95	60	151	15	74	
>4 times/month	167	112	106	69	169	12	70	
Fatty fish								
<once/month	163	97	102	62	186	14	70	0·761
1–3 times/month	114	93	93	57	151	19	75	
1 time/week	139	106	100	71	143	8	79	
>1 time/week	127	109	101	62	169	17	69	
Shellfish								
<once/month	197	98	96	62	149	16	76	0·460
1–3 times/month	256	100	100	65	157	13	73	
>3 times/month	90	110	109	69	177	12	67	
Molluscs								
<once/month	240	99	97	62	161	15	73	0·247
1–3 times/month	216	96	99	66	152	14	74	
>3 times/month	87	109	111	79	176	10	68	
Eggs								
<2 times/week	113	92	93	62	134	15	78	0·158
2 or more times/week	430	105	102	64	163	14	71	
Bread								
<once/day	119	101	102	63	150	13	75	0·434
1 time/day	221	111	102	67	157	14	72	
>1 time/day	203	94	95	61	159	1	73	

Table 4. Urine Iodine concentration (μg/l) in iodine supplemented pregnant women

	n	Median	Geometric mean (95% CI)
Iodine supplementation	53	141	141 (114–176)
Iodine supplementation and milk consumption			
Low (<1 time/day)	11	105	103 (60–179)
Moderate/high (≥1 time/day)	42	152	154 (122–192)
High (≥2 times/day)	18	217	199 (142–278)
Iodine supplementation and eggs consumption			
Low (<2 times/week)	14	100	132 (84–207)
Moderate/high (≥2 times/week)	39	142	145 (114–185)
Iodine supplementation and iodized salt consumption			
No iodized salt consumption	42	138	145 (114–186)
Iodized salt consumption	11	141	127 (85–191)

Only 9% of women used iodine supplements during pregnancy, either as iodine or multivitamin tablets containing between 100 μg and 200 μg of iodine each. Principally, women recruited in the latter part of the study, because of the use of iodine supplements have been promoted in this area since approximately 2006. Although women, who both used iodine supplements and had a diet rich in milk, had the median UIC above recommendations, iodine supplementation alone was not effective for reaching these recommendations.

Milk and other dairy products are important sources of iodine in numerous populations.[4,5,18–20] In a recent study in pregnant women, milk was the only variable influencing UIC in a multivariate analysis, including the use of iodized salt, iodine supplementation and different foods.[20] Dahl *et al.* found that milk and other dairy products contributed approximately 55% and 70% of the dietary iodine intake in adults and children from Norway

Table 5. Adjusted* association between different iodine sources and low urine iodine concentration

	Iodine concentration <150 (μg/l)		
Iodine source	OR	95% CI	*P*-value
Milk consumption (full-fat, low fat and skimmed)			
Less than once/day	1		0·011
1–2 times/day	0·42	0·22–0·82	
>2 times/day	0·29	0·15–0·55	0·000
Iodine supplementation			
No	1		0·009
Yes	0·44	0·24–0·82	

*adjusted by gestational age, mother's weight and age, season and time of extraction and mother's thyroid alterations diagnosed and mother's smoking habits.

respectively.[5] Similar to the present results, a study in school children from Italy found a high correlation between UIC and milk and dairy products intake, but no correlation with fish, eggs or iodized salt.[18]

It was surprising that only 11% of the women reported using iodized salt in the FFQ. Twenty years ago, the Government of Catalonia developed a public health action plan to eliminate iodine deficiency disorders. They implemented several campaigns to promote the use of iodized table salt at 60 mg of iodine, and several studies demonstrated that the prevalence of goitre decreased after the campaign.[11] Nevertheless, its use is not currently compulsory and not accompanied by a sustained educational campaign, and thus recent data show that pregnant women from Catalonia are still at risk of being iodine deficient.[12]

The consequences of iodine deficiency during pregnancy have been extensively described.[1–3,9,21] Brain damage and irreversible mental retardation in the neonate are the most important disorders induced by severe iodine deficiency during pregnancy.[2,3] Moreover, an increased perinatal mortality and lower birth weight due to severe iodine deficiency have been observed in several populations.[21] Cao *et al.* showed that to prevent these disorders in areas with iodine deficiencies, pregnant women should use iodine supplementation through the end of the second trimester, because treatment later in pregnancy or after birth is not sufficiently effective to prevent brain damage.[22]

Iodine requirements in pregnant women are higher than in general population.[1,7–9] Thus, pregnant women from an iodine-sufficient area can have a suboptimal iodine status if they do not follow a diet rich in iodine or they are not supplemented with iodine-containing tablets to increase the normal daily intake of iodine. Nevertheless, there is a need of evaluation of the iodine requirements in pregnant women from iodine-sufficient areas or from areas with mild iodine deficiency in relation to the development of the foetus and to the thyroid status of the mother. Zimmermann *et al.* recently stated that the potential adverse effects of mild-to-moderate iodine deficiency during pregnancy remain unclear.[23]

The major limitation of this study is the possible variability in iodine content in each food group. The iodine content of foods varies with geographical location and season, as it depends on the iodine content of the soil.[4] In addition, iodine content in milk is partly derived from iodine fortification of cow fodder, mainly in Northern Europe.[4,5,24] The iodine content of fish also varies across species[4], and we were unable to classify fish intakes based on iodine content, as data were collected only as lean *vs* fatty fish intakes, molluscs and shellfish. Another limitation of the study was the small number of iodine-supplemented women, who restricted the ability to study the role of combined iodine supplementation and the intake of food rich in iodine content as a way to achieve the WHO recommendations. Moreover, UIC was measured at third trimester of pregnancy, although it is known that an adequate iodine intake is mainly critical for the foetus in the first trimester of gestation.[21,25] Nevertheless, a low iodine intake during pregnancy becomes more severe with the progression of gestation to the final stages, when the intrathyroidal iodine stores become more depleted.[1]

In conclusion, milk, other dairy products and iodine supplementation are the primary sources of iodine in this population of pregnant women. However, the iodine status of this population was found to be below WHO recommendations, and only iodine-supplemented women who also had high intakes of milk and other dairy products reached the recommended UI levels. Nonetheless, further studies are needed to determine the best ways to achieve optimal iodine nutrition and the benefits or adverse effects of iodine supplementation in pregnant women, from areas without known iodine deficiency in the general population.

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