

## CLINICAL STUDY

# Iodine intake in Portuguese pregnant women: results of a countrywide study

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## Abstract

**Background:** Iodine is the key element for thyroid hormone synthesis, and its deficiency, even moderate, is harmful in pregnancy, when needs are increased, because of its potential deleterious effects on fetal brain development. In Portugal, no recent data on iodine intake exists. The objective of this countrywide study was to analyze iodine status in pregnant Portuguese women in order to propose adequate measures to the health authorities.

**Subjects and methods:** Using a fast colorimetric method, urine iodine concentration (UIC) was evaluated in 3631 pregnant women followed in 17 maternity hospitals from hinterland and coastal areas in Continental Portugal and the Portuguese islands of Açores and Madeira.

**Results:** Median UIC value was 84.9 µg/l (range 67.6–124.1) in Continental Portugal, 69.5 µg/l in Madeira, and 50.0 µg/l in Açores. The percentage of satisfactory values (>150 µg/l) was 16.8, ranging from 8.8 to 34.1 in the Continent, and being 8.2 in Madeira and 2.3 in Açores. The percentage of values below 50 µg/l was 23.7, ranging from 14.0 to 37.4 in the Continent, 33.7 in Madeira, and 50.0 in Açores.

**Conclusions:** Our results point to an inadequate iodine intake in pregnant women assisted in most Portuguese maternity hospitals. Considering the potential deleterious effects of inadequate iodine supply in pregnancy, iodine supplementation is strongly recommended in this period of life.

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## Introduction

Iodine is the key element for the synthesis of thyroid hormones. Inadequate intake of this micronutrient is the cause of endemic goiter, which has practically disappeared in western European Countries (1). However, recent studies have pointed to the existence of mild/moderate insufficient iodine intake in most European regions (2–4), which proved to be deleterious, namely in pregnancy and lactation when needs are very much increased (5–7).

Thyroid hormones are crucial for the development of the fetal and neonatal nervous system, and the mother is the only source of iodine in this period of life (8). Moreover, during the first trimester of pregnancy, the mother is the only origin of thyroxine (7, 9–11), which generates tri-iodothyronine, the active hormone that is critical in the various steps of the complex processes of fetal brain development (12–14).

Experimental work has shown that low thyroxine levels in critical phases of pregnancy are associated with irreversible alterations in fetal brain (9, 15, 16).

Epidemiological studies indicate that children born to mothers with moderate hypothyroxinemia may present neurological alterations, reduced IQ, and attention problems (17–19). Moreover, there is evidence that these neurocognitive problems may appear in children born to mothers with mild to moderate iodine-insufficient intake (20–22).

In Portugal, like in other European countries, endemic goiter is no longer a problem due to iodine prophylaxis in the previously more attained regions (23–25) and also because of silent prophylaxis, but no recent studies on iodine intake have been performed (1).

A study carried out in the eighties, showing a median urinary iodine of 70 µg/g creatinine in school children from Lisbon (25) and data from the national hypothyroidism screening program, showing a higher frequency

of congenital hypothyroidism than in most European countries (26–28), made us to consider that in Portugal iodine intake might be far from adequate.

The Thyroid Study Group of the Portuguese Endocrine Society decided to carry out a countrywide study on iodine intake, assessed by measuring urinary iodine concentrations in two study populations, pregnant women and school children, in order to recommend to the Health Authorities to undertake the appropriate measures.

We present here the results obtained from the study in pregnant women.

## Population and methods

### Population

The study was carried out in 17 maternity hospitals, 15 from Continental Portugal, 1 from Madeira, and 1 from Açores Portuguese islands; 3631 women from the 3 trimesters of pregnancy were studied. Mean age was 29.2 years, ranging from 13 to 47 years.

The study was approved by the ethics committee of Portuguese Cancer Institute in Lisbon, and informed consent was obtained from participant women.

Women were not taking iodine supplements.

### Assessment of iodine intake

Iodine status was assessed using urinary iodine determinations.

Urine samples were collected throughout the three trimesters of pregnancy. No collections were performed during delivery. Information on gestational age was obtained from 1715 women, in 8 maternities, 131 women in the first, 406 in the second, and 1178 in the third trimesters.

One random urine sample was collected from pregnant women in the morning and was preserved in frozen capped plastic tubes until use.

Urine collection was performed between January 2005 and December 2007. Urinary iodine was measured using a fast colorimetric method, appropriate for population studies (29).

Determinations were performed in the Laboratory of Endocrinology of Instituto Português de Oncologia in Lisbon and in the Laboratory of Clinical Pathology of St Antonio Hospital in Porto.

Contaminated urines due to urine test strips or iodinated pregnancy tablets were excluded.

### Statistical analyses

To describe urinary iodine concentrations, descriptive statistics were used. Urinary iodine measures were assigned to categories of an ordinal variable. Proportions, medians, and ranges by hospital were

estimated. Results were analyzed in groups relating to the islands, hinterland, and coastal regions of Portugal.

Comparison of urinary iodine proportions (below 50 µg/l and above 150 µg/l) between hinterland and coastal continental hospitals and between hinterland continental and island hospitals were performed with two-sample test of proportions.

Statistical analysis was performed using Intercooled STATA 9.2 for Windows (StataCorp, TX, USA) (30).

## Results

Table 1 presents the results of urinary iodine determinations by hospital as well as the global results in continental Portugal including and excluding the islands. Results include median values, percentage of adequate values according to the WHO criterion (> 150 µg/l), and percentage of low values (< 50 µg/l).

In continental Portugal, significantly lower urine iodine concentration (UIC) values were obtained in pregnant women from the hinterland compared with those from the coast (Table 2).

UIC values obtained in the hospitals from the islands were significantly lower than those from hinterland continent (Table 2).

Median UIC values according to gestational age were 81.1 µg/l for the first trimester ( $n=131$ ), 79.8 µg/l for the second trimester ( $n=406$ ), and 77.2 µg/l ( $n=1178$ ) for the third trimester. In these groups, the percentages of women with UIC below 50 µg/l were respectively 26.7, 26.1, and 28.2, and not statistically different. The percentages of adequate values (> 150 µg/l) in the three trimesters were respectively 16.0, 14.0, and 15.3, and not statistically different.

## Discussion

This study on iodine intake, using UIC determinations and enrolling 3631 pregnant Portuguese women from all over the country, points to a generalized, insufficient iodine intake. In continental Portugal, the median value was 84.9 µg/l. According to WHO criteria, only 16.8% of women had adequate values > 150 µg/l, and 23.7% were below 50 µg/l. Our results are in accordance with a recent publication from the University of Minho in northern Portugal enrolling 140 pregnant women (31), which refers a median UIC value of 75 µg/l and a percentage of samples with an UIC < 50 µg/l of 38, 36, and 34 respectively in the first, second, and third trimesters of pregnancy; UIC in breast milk was also below the recommended values. Studies on pregnant women conducted in Spain also point to an inadequate iodine intake: in a series of 112 pregnant women from Madrid, only 30.4% had adequate values (32); in Galicia, to the north of Portugal, in a study of 400 women, the percentage of values below 150 µg/l ranged

**Table 1** Urine iodine concentrations by hospital.

Region	City   hospital	n	Median ( $\mu\text{g/l}$ )	Urine iodine concentration			
				> 150 $\mu\text{g/l}$		< 50 $\mu\text{g/l}$	
				n	%	n	%
Coast	Almada   G Orta	341	85.8	50	14.7	63	18.5
	Aveiro   D Pedro	171	91.6	36	21.1	30	17.5
	Faro   Central	196	87.8	32	16.3	45	23.0
	Leiria   St André	203	97.2	42	20.7	35	17.2
	Lisboa   A Costa	349	88.7	65	18.6	62	17.8
	Portimão   Barlavento	209	83.5	32	15.3	50	23.9
	Porto   St António	222	77.2	26	11.7	56	25.2
Hinterland	Beja   J J Fernandes	216	76.2	27	12.5	64	29.6
	Bragança   Distrital	155	75.8	14	9.0	48	31.0
	C Branco   A Lusitano	149	75.4	21	14.1	44	29.5
	Covilhã   C Beira	203	67.6	20	9.9	76	37.4
	Vila Real   S Pedro	159	69.2	14	8.8	57	35.8
	Portalegre   J M Grande	212	95.1	47	22.2	51	24.1
	Coimbra   B Barreto	258	124.1	88	34.1	36	14.0
Midland	Coimbra   D Matos	218	82.1	35	16.1	57	26.1
	Global	3261	84.9	549	16.8	774	23.7
Continent	Açores   Ponta Delgada	174	50.0	4	2.3	87	50.0
	Madeira   Funchal	196	69.5	16	8.2	66	33.7
Islands	Global	370	60.9	20	5.4	153	41.4
Portugal	Global	3.631	82.5	569	15.7	927	25.5

from 61 to 87, according to the studied province (33); in Extremadura, Sanchez-Vega *et al.* (34) from a study enrolling 761 women concluded that six out of ten women ingested less than the recommended amount of iodine (250  $\mu\text{g/day}$ ). In Belgium, in a study of 2000 women from Brussels, Glinoeur *et al.* (35) have shown that 56% had a median UIC value below 40  $\mu\text{g/l}$  and only 10% between 81 and 160  $\mu\text{g/l}$ . A recent study from southern France, with 330 pregnant women in the third trimester of pregnancy, indicates a median UIC value of 64  $\mu\text{g/l}$  (36). Studies conducted in other European countries are also in accordance with our data (37, 38), pointing out to an inadequate iodine supply in pregnant women from different parts of Europe.

In continental Portugal, UIC values of pregnant women from hospitals in the hinterland were significantly lower than those from the coastal areas, with percentages of values above 150  $\mu\text{g/l}$  respectively 13.1 and 16.7 and percentages of values below 50  $\mu\text{g/l}$  respectively 31.1 and 20.1.

The distance from the sea with reduced fish consumption and lower socioeconomic status in the hinterland may explain, in our view, these differences. Our hinterland is mostly mountainous, and endemic goiter was a reality in some areas, 50 years ago.

In the islands of Açores and Madeira, UIC values were even lower than those obtained in the hinterland continental Portugal. The median value in the islands was 60.9  $\mu\text{g/l}$ ; the percentage of values above 150  $\mu\text{g/l}$  was 5.4 and the percentage of values below 50  $\mu\text{g/l}$  was 41.4. In Açores, UIC values were particularly low, the median being 50  $\mu\text{g/l}$ ; the percentage of values above 150  $\mu\text{g/l}$  was 2.3, and 50% of values were below 50  $\mu\text{g/l}$ . A moderately low iodine intake was also described in pregnant women from Great Britain and Ireland (39, 40). In a study conducted in school children from Açores in 1986, Oliveira *et al.* (41) found a high prevalence of goiter and a very low UIC.

In a first approach, iodine deficiency in small Atlantic islands is not easy to explain. However, according to local information, fish consumption is scarce, because of its high cost. On the other hand, soils are poor in iodine mainly because of the high precipitation rate (875  $\text{l/m}^2$  per day), which leads to a leaching effect. This is a well-known phenomenon that has been previously pointed out (41, 42). Moreover, meat, milk, and vegetables are mostly from local origin, which reduces the possibility of a silent prophyllaxis.

We had information on gestational age in 1715 pregnant women unevenly distributed by the three

**Table 2** Comparison of urine iodine concentrations from the hinterland versus coastal and hinterland versus islands hospitals.

Urine iodine concentration	Hinterland (n=1094; Median=76.1 $\mu\text{g/l}$ )		Coast (n=1691; Median=86.1 $\mu\text{g/l}$ )		Hinterland vs Coast P value	Islands (n=370; Median=60.9 $\mu\text{g/l}$ )		Hinterland vs Islands P value
	n	%	n	%		n	%	
< 50 $\mu\text{g/l}$	340	31.1	341	20.1	<0.01	153	41.4	<0.01
> 150 $\mu\text{g/l}$	143	13.1	283	16.7	<0.01	20	5.4	<0.01

trimesters of pregnancy. The size of the sample from the first trimester was small in contrast with data from the third trimester, which consequently lent more weight in the global results.

In our population with an inadequate iodine intake, UIC values tend to decrease throughout gestation (5); the progressive depletion of iodine stores due to fetoplacental use and increased renal filtration is not compensated by iodine ingestion (43).

Our data did not reveal statistical differences between UIC values in early and later stages of pregnancy, but a slight tendency for lower values in late gestation was found.

Studies on UIC values throughout gestation are not consensual. Similar to our results, one study performed in northern Portugal (31) and another from Spain (34) did not find statistical differences in UIC values between early and late pregnancy. However, other authors have referred a clear decrease (43, 44), while others have shown even an increase (45). These discrepancies are probably due to the level of iodine intake and other unclear ethnic nutritional differences in the analyzed women (44).

In the present study, UIC was consistently low all over the country. The inclusion of different women, not sequentially studied, from diverse geographical areas with a wide range of iodine intake may explain our results.

Iodine supplementation in moderately iodine-deficient pregnant women using 150–200 µg/day has no adverse effects (35, 37, 46). On the contrary, it appears to reduce thyroid volumes and thyroglobulin concentrations in the mother (35) and, above all, it improves neurodevelopment outcomes in children (20, 47). In addition, WHO, the International Council for Control of Iodine Deficiency Disorders (48, 49), as well as the American Thyroid Association and the Endocrine Society (50, 51) advise iodine supplementation during pregnancy and lactation.

Taking into account the results of this survey and the above-mentioned advantages and statements, we strongly recommend iodine supplementation in all Portuguese pregnant women and to extend this throughout lactation.

As thyroid iodine stores should be adequate before pregnancy (52), iodine prophylaxis through salt iodization should also be considered in our country.

## Declaration of interest

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

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