

ORIGINAL ARTICLE

Inadequate iodine intake in lactating women in Sweden: A pilot 1-year, prospective, observational study

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Funding information

The study was financed by grants from the Swedish research council FORMAS (Dnr 2087-398 and 2009-1504), the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBG-770691), and regional Research and Development (FOU) funds (VGFOUREG-736831 and VGFOUREG-639331).

Abstract

Introduction: Breastfed infants depend on breast-milk iodine for growth and brain development, as iodine is a trace element important for thyroid hormone production. Iodine need is higher during lactation; hence, mothers and children are at risk of iodine deficiency. We aimed to explore maternal iodine and thyroidal status during lactation.

Material and methods: Pregnant women were recruited in Gothenburg, southwest Sweden. Maternal urine and serum were collected at pregnancy week 35-37 (n = 84) and 0.5, 4, and 12 months postpartum. Seventy mothers provided breast milk at 0.5 months.

Results: Median (interquartile range) breast-milk iodine concentration was 90 (66-116) µg/L. About 58% had breast-milk iodine concentration <100 µg/L. Iodine supplement users (n = 13) had higher breast-milk iodine concentration than non-users (n = 49) (140 µg/L vs 71 µg/L, P = .001). Exclusively breastfeeding women at 4 months postpartum (n = 57) had lower median urinary iodine concentration (85 µg/L vs 133 µg/L, P = .004) and higher thyroglobulin serum concentration (22.3 µg/L vs 11.8 µg/L, P = .032) than non-exclusively breastfeeding women (n = 25). Concentrations of thyroid hormones were unaffected.

Conclusions: This pilot study suggests that lactating women in southwest Sweden present mildly inadequate iodine intake, mainly among non-iodine supplement users and exclusively breastfeeding mothers. Studies on the coverage of the iodine fortification program in breastfeeding women are warranted.

KEYWORDS

breastfeeding, human, iodine, lactation, milk, Sweden, thyroid gland, thyroglobulin, urine

Abbreviations: BMIC, breast-milk iodine concentration; eBMIE, estimated breast-milk iodine excretion; eUIE, estimated urinary iodine excretion; FT₃, free triiodothyronine; FT₄, thyroid stimulating hormone; ID, iodine deficiency; Tg, thyroglobulin; TPO, thyroperoxidase; TSH, thyroid-stimulating hormone; UIC, urinary iodine concentration.

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1 | INTRODUCTION

Iodine is essential for the production of thyroid hormones: free thyroxine (FT₄) and free triiodothyronine (FT₃) contain four and three atoms of iodine respectively, and are incorporated into thyroglobulin (Tg), which is a storage protein synthesized by the thyroid gland. Thyroid hormone production and secretion are stimulated by the pituitary, mainly through thyroid-stimulating hormone (TSH). In subclinical hypothyroidism, TSH is elevated to maintain normal levels of FT₄ and FT₃, whereas clinical hypothyroidism is defined as elevated TSH and low FT₄. The most common cause of hypothyroidism, in a global perspective, is iodine deficiency (ID).¹

In adults, severe ID may lead to hypothyroidism and goiter, whereas in mild ID, thyroid hormone levels are maintained, but with the consequence of goiter with increased levels of Tg. Elevated Tg is, in this case, the result of a TSH activation of the thyroid gland, which increases in volume as a compensatory mechanism, aiming to maintain normal thyroid production.² When it comes to pregnant women, the consequences of mild ID on infants are unclear, but mild-to-moderate gestational ID has been associated with suboptimal neuro-processing development.³ In breastfed infants, iodine intake depends on the mothers' iodine intake as this corresponds to breast-milk iodine concentration (BMIC).

BMIC is also an important marker for iodine status of lactating women.⁴ In nonlactating women, absorbed iodine is partly transported to the thyroid gland and the remainder (~90%) is cleared by passive renal glomerular filtration,⁵ measured as urinary iodine concentration (UIC). UIC is the recommended biomarker for assessing the iodine status of a given population.⁶ In lactating women, however, absorbed iodine is also transported to the mammary gland.⁵ Lactating women, living in iodine-sufficient countries, increase their fractional iodine excretion into breast milk at lower daily iodine intakes, and renal fractional iodine excretion is consequently decreased.⁴ Even nonlactating mothers present lower UIC postpartum than during pregnancy, probably as a result of higher clearance of circulating iodine to the thyroid gland for restoration of the depleted thyroid gland after the increased demands during pregnancy. BMIC is, therefore, a more reliable indicator of the iodine status of lactating mothers than maternal UIC.

Despite the importance of BMIC for mother and child, there is a huge gap in knowledge on iodine status during lactation in most Nordic countries,⁷ with the most recent Swedish data published 30 years ago.^{8,9} After the iodine fortification of table salt in Sweden,¹⁰ the general population became iodine sufficient according to a national study on schoolchildren in 2007.¹¹ However, it is questionable to extrapolate the iodine status of schoolchildren to women of reproductive age, because of possible differences in dietary iodine. Our hypothesis on possible mild ID among pregnant women in Sweden was recently confirmed in a national survey.¹² This emphasizes the need to investigate if lactating women have also become mildly iodine deficient.

As there are no current data on iodine status during lactation in Sweden and there is no recommendation by the Swedish National

Key message

Breastfeeding women in an area of Sweden presented mild iodine deficiency. Iodine supplement users (~20% of the studied population) presented breast-milk iodine concentration double that of non-supplement users. Studies on the coverage of the iodine fortification program in breastfeeding women are warranted.

Food Agency on iodine supplementation during lactation, we aimed to address these questions. (a) Are breastfeeding mothers in a south-west area of Sweden iodine deficient? (b) Do exclusively breastfeeding mothers have lower UIC and higher Tg at 4 months postpartum than non-exclusively breastfeeding postpartum mothers?

2 | MATERIAL AND METHODS

2.1 | Subjects

Pregnant women were recruited between July 2008 and July 2011, through advertisements on a webpage, on posters and in maternal healthcare centers in Gothenburg, Sweden, to participate in a study related to determinants of changes in skeletal health during lactation.¹³ Inclusion criteria were age 25-40 years and to declare oneself as healthy. Exclusion criteria were current twin pregnancy, current development of gestational diabetes or preeclampsia, recent bone fracture, intake of prescribed medicine affecting calcium and bone metabolism, pregnancy or miscarriage (later than pregnancy week 12) during the last 1.5 years before the current pregnancy, or breastfeeding during the last year before the current pregnancy. Of a total of 95 women recruited, 84 who had breast-milk sample at 0.5 month and/or urine sample at least once postpartum were selected, for the purpose of this pilot study.

2.2 | Study design

The pregnant women (n = 84) visited the Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Sweden in pregnancy weeks 35-37 (inclusion) and, thereafter, at 0.5, 4, and 12 months postpartum. The study design is shown in Figure 1. Information on age, height, weight, education level, parity, and smoking habits was collected. The women reported use of multivitamins, including information on brand, frequency of use, and number of tablets per use. Content was obtained for each brand of multivitamin from the manufacturer. In addition, women reported lactating and feeding habits (ie, whether they were breastfeeding, number and amount of formula feedings per day, date of introduction of solid foods, daily amount of solid foods given, and date of last lactation when applicable).

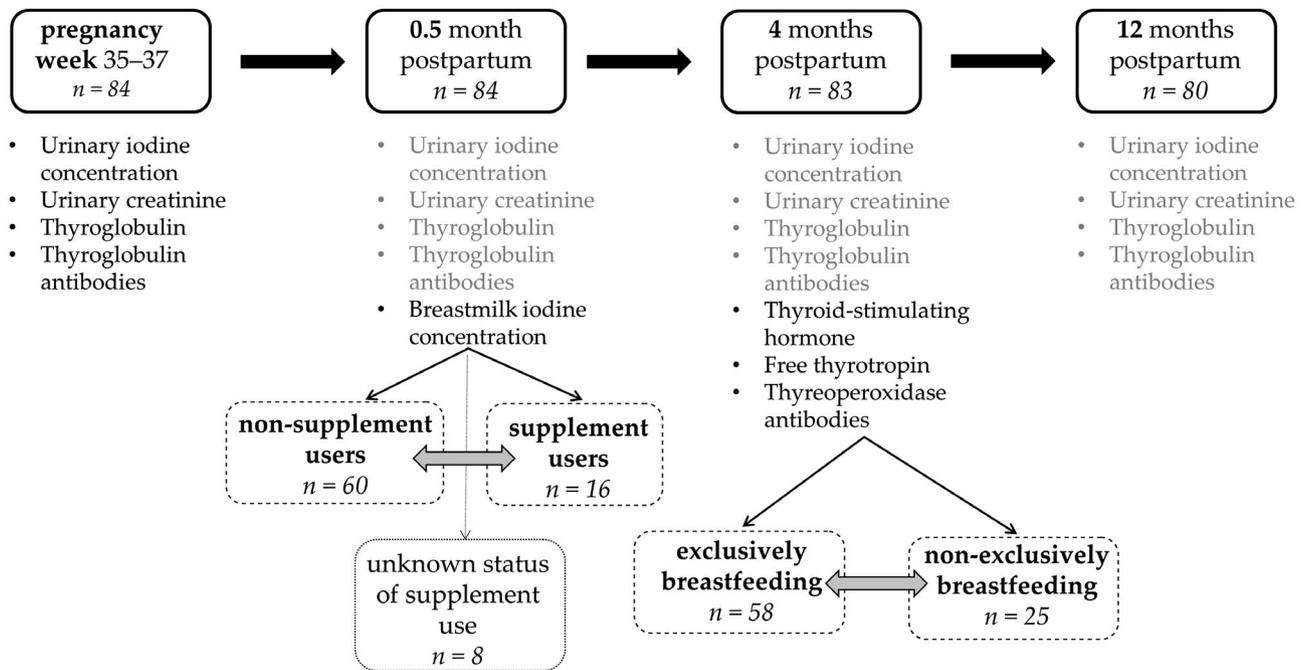


FIGURE 1 Study design and illustration of the grouping of the study population. The groups compared are marked with a gray arrow.

2.3 | Breast-milk, urinary, and serum samples

Lactating women were instructed to collect 5-10 mL breast milk in the morning, just before a breastfeeding session, and to report details on breast-milk collection; ie time of day, before or after the lactating session, left and/or right breast. The latter was of interest, because there have been observations of inconsistent, sporadic differences in the composition of breast milk from the left and right breasts, possibly due to mastitis.¹⁴ Breast-milk samples were stored at -20°C until the study visit and then at -80°C until analysis. After thawing, milk samples were homogenized. BMIC was analyzed at ETH Zurich (Zurich, Switzerland) by multicollector inductively coupled plasma mass spectrometry with the use of isotope dilution analysis using ^{129}I and tellurium for mass bias correction.¹⁵ Whole-milk powder standard reference material (National Institute of Standards and Technology) was used as an external control.

Spot urine samples of ~ 10 mL, collected in the morning on the same day as the study visit, were transported and stored at -20°C until analysis. UIC was measured by a single laboratory technician at the Department of Clinical Nutrition at Sahlgrenska Academy, University of Gothenburg (Gothenburg, Sweden) using the Pino modification of the Sandell-Kolthoff reaction.¹⁶ The laboratory successfully participates in the EQUIP network (US Centers for Disease Control and Prevention, Atlanta, GA) and was evaluated for analytical accuracy every 3 months. Urinary creatinine was measured by the Department of Clinical Chemistry, Sahlgrenska University Hospital (Gothenburg, Sweden) using a Cobas 6000/8000 analyzer (Roche Diagnostics).

Thyroglobulin, Tg antibodies, and thyreoperoxidase (TPO) antibodies were analyzed by the Department of Clinical Chemistry at Skåne University Hospital (Malmö, Sweden). In case of elevated Tg

antibodies, the Tg value was excluded from the analysis because of the risk of analytical interference. TSH and FT_4 were analyzed by the Department of Clinical Chemistry at Skåne University Hospital (Lund, Sweden). All variables were analyzed with a sandwich-type electrochemiluminescence immunoassay by Roche Cobas (Roche Diagnostics, Solna, Sweden).

Estimated breast-milk iodine excretion (eBMIE) was calculated as BMIC multiplied by the expected daily fluid intake at this age, ie, 150 mL/kg/day for children weighing <5 kg or 100 mL/kg/day for children weighing 5-10 kg.¹⁷ Estimated urinary iodine excretion (eUIE) was calculated using the formula $\text{eUIE } (\mu\text{g/day}) = \text{UIC } (\mu\text{g/L}) / (\text{urinary creatinine g/L} / 1.23 \text{ g/day})$. The expected daily creatinine excretion is 1.23 g/day for women aged 25-49 years.¹⁸

2.4 | Definitions

Exclusive breastfeeding was defined as when $\geq 90\%$ of the infant's daily energy intake came from breast milk. The group of non-exclusively breastfeeding women at 4 months included those whose infants obtained $<90\%$ of their daily energy intake through breast milk and those who were not breastfeeding at all.

Women taking at least 75 μg iodine supplementation daily were classified as iodine supplement users. This cut-off was chosen because it is half the level of iodine supplementation recommended by international thyroid associations for lactating women.^{19,20}

There is currently no consensus on a cut-off for BMIC indicating maternal iodine sufficiency and ensuring adequate iodine intake for the infant, mainly due to uncertainty regarding infant requirements. Cut-offs of 50, 75, 92, and 100 $\mu\text{g/L}$ and a range of 150-180 $\mu\text{g/L}$ have been proposed to ensure iodine sufficiency,²¹ whereas Dold

et al⁴ have proposed a broad reference range of 60-465 µg/L. In the present study, the number of women with BMIC <50 µg/L is presented, but BMIC <100 µg/L has been used as indicative of inadequate iodine intake. This cut-off was chosen because it has been supported by a recent review²² and seems to dominate among recent trials.^{23,24}

The eBMIE needed to cover the daily iodine needs of an exclusively breastfed infant at the age of 0.5 months has been estimated at 90 µg iodine/day.²⁵ UIC ≥100 µg/L indicates adequate iodine intake in lactating women.⁶

Kit-specific and laboratory-specific references were used for Tg antibodies (<115 kIE/L), TPO antibodies (<34 kIE/L), TSH (0.40-3.7 mIE/L), and FT₄ (12-22 pmol/L). TPO antibody positivity represented TPO antibodies ≥34 kIE/L. Abnormally high or low TSH represented hypo- and hyperthyroidism, respectively, classified as subclinical or clinical thyroid disease depending on whether FT₄ was within or outside the reference range, respectively.

2.5 | Statistical analyses

Data processing was performed using IBM SPSS statistics V25 (IBM). Normality was evaluated using histogram, Q-Q plots, box-plots, and the Shapiro-Wilk test. In case of non-normally distributed variables, new normality tests were performed after log-transformation. Comparisons of independent medians or means were performed with Mann-Whitney *U*-test for non-normally or *t*-test for normally distributed variables. Analysis of frequencies was performed by chi-squared test, or Fischer's exact test in case of fewer than five expected cases. To compare related samples, Wilcoxon sign rank test or paired *t*-test was used for non-normally and normally distributed

variables, respectively. All statistical significance was set as α level of 0.05.

2.6 | Ethical approval

All study participants gave written informed consent before participation. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee in Gothenburg, Sweden (Dnr 129-08 dated 25 March 2008).

3 | RESULTS

The characteristics of pregnant women at inclusion are presented in Table 1. Breastfeeding habits, iodine supplementation, and smoking habits are presented longitudinally in Table 2. When taking account of the actual intake of tablets (reported by the mothers), the daily intake of iodine through supplements was 21-150 µg/day at 0.5 months, 10-160 µg/day at 4 months, and 27-240 µg/day at 12 months postpartum. Education status, parity, and breastfeeding habits are presented longitudinally for the study population, divided by use of iodine supplement, in Table 3.

Seventy-eight percent of breast-milk samples were collected at 0.5 months postpartum as intended, ie, in the morning (at 05.00-11.00) before the breastfeeding session. Also, 78% of the mothers collected milk from one breast and the remainder from both breasts. Median BMIC (interquartile range [IQR]) was 90 (66, 116) µg/L for the whole group (*n* = 70). Iodine supplement users (*n* = 13) had median BMIC 140 µg/L compared with 71 µg/L for the rest of the group (*n* = 49) (*P* = .001, Figure 2A). BMIC was <100 µg/L

TABLE 1 Characteristics of pregnant women at baseline (third trimester of pregnancy) presented for the total and for two subgroups characterized by the breastfeeding status at 4 months postpartum. Mean ± standard deviation or percent are presented as appropriate

	Total (N = 84)	Exclusively breastfeeding (n = 58)	Not exclusively breastfeeding (n = 25)	P- value ^c
Age, y	32.9 ± 3.3	33.3 ± 3.5	31.9 ± 2.6	.07
BMI ^a , kg/m ²	22.5 ± 2.5	22.5 ± 2.4	22.3 ± 3.0	.75
Smoking status	0	0	0	–
Education status (%)				
<High school	2.4	0	8.35	.002
High school	4.8	6.8	0	
College 1-2 y	13.1	6.8	29.2	
College ≥3 y	79.8	86.4	62.5	
Parity ^b (%)				
0	52.4	44.1	70.8	.084
1	34.5	39.0	25.0	
2	13.1	16.9	4.2	

Abbreviations: BMI, body mass index; y, year.

^aBefore pregnancy.

^bPrevious live and stillbirths.

^cComparison between subgroups.

	0.5 months (N = 84)	4 months (N = 84)	12 months (N = 84)	0.5 months (n = 70)
Breastfeeding (%)				
Exclusive ^a	86.9	69.0	0	87.1
Partial	10.7	21.4	15.5	12.9
None	2.4	8.3	81.0	—
Unknown ^b	—	1.2	3.6	—
Iodine supplement^c (%)				
Yes	19.0	11.9	9.5	21.0
No	71.4	81.0	81.0	79.0
Unknown ^d	9.5	7.1	9.5	—
Smoking	—	1.2	3.6	—

TABLE 2 Breastfeeding habits, iodine supplementation, and smoking habits for all postpartum mothers at 0.5, 4, and 12 months postpartum (N = 84). The same variables are presented for the subgroup of mothers who provided breast-milk sample at 0.5 months (n = 70). Data presented as percent

^aAt least 90% of the infants' daily energy intake coming from breast milk.

^bMissing data are due to drop-out, move to other town, or new pregnancy.

^cAt least 75 µg/day.

^dMissing data are due to incomplete reports from the study participant or to unknown iodine content of the reported supplement.

TABLE 3 Education status, parity, and breastfeeding habits of all postpartum mothers divided by use of iodine supplement at 0.5, 4, and 12 months postpartum. Data presented as percent

	0.5 months			4 months			12 months		
	Suppl (n = 16)	Non-suppl (n = 60)	P	Suppl (n = 10)	Non-suppl (n = 68)	P	Suppl (n = 8)	Non-suppl (n = 68)	P
Education status (%)									
<High school	6.3	0	.81	10.0	1.5	.045	12.5	1.5	.11
High school	12.5	3.3		20.0	2.9		12.5	2.9	
College 1-2 y	18.8	13.3		10.0	14.7		0	14.7	
College ≥3 y	62.5	83.3		60.0	80.9		75.0	80.9	
Parity^b (%)									
0	50.0	51.7	.57	80.0	50.0	.18	50.0	48.5	.98
1	43.8	33.3		20.0	36.8		37.5	36.8	
2	6.3	15.0		0	13.2		12.5	14.7	
Breastfeeding (%)									
Exclusive ^a	100.0	81.7	.18	60.0	69.1	.83	0	0	.34
Partial	0	15.0		30.0	22.1		0	17.6	
None	0	3.3		10.0	8.8		100	82.4	

Abbreviations: Non-suppl, non-iodine supplement users; Suppl, iodine supplement users.

^aAt least 90% of the infants' daily energy intake coming from breast milk.

^bPrevious live and stillbirths.

in 58% and <50 µg/L in 9%. Median eBMIE (IQR) at 0.5 months postpartum was 53 (32, 73) µg/day for the whole group (n = 69). Iodine supplement users (n = 13) had median eBMIE of 80 µg/day compared with 46 µg/L for the rest of the group (n = 48) (P = .001, Figure 2B). The results on BMIC and eBMIE (both the levels and the P-values) were unaltered, when the same analyses were performed in the group of exclusively breastfeeding women (n = 60) (data not shown).

Median UIC, eUIE, and Tg for all time-points are presented in Figure 3. Non-exclusively breastfeeding women (n = 25) at 4 months

postpartum had higher median UIC than those exclusively breastfeeding (n = 57) (133 µg/L vs 85 µg/L, P = .004, Figure 4A). Non-exclusively breastfeeding women (n = 23) at 4 months postpartum had lower median Tg than exclusively breastfeeding women (n = 48) (11.8 µg/L vs 22.3 µg/L, P = .032, Figure 4B). The two groups did not differ for eUIE, TPO antibody-positivity, TSH, or FT₄ (Table 4). Thyroid morbidity was not observed in any of the study participants. As a result of the low number of supplement users and of those with <3 years at college (Table 1), no analyses were possible after stratifying for iodine supplementation or education level.

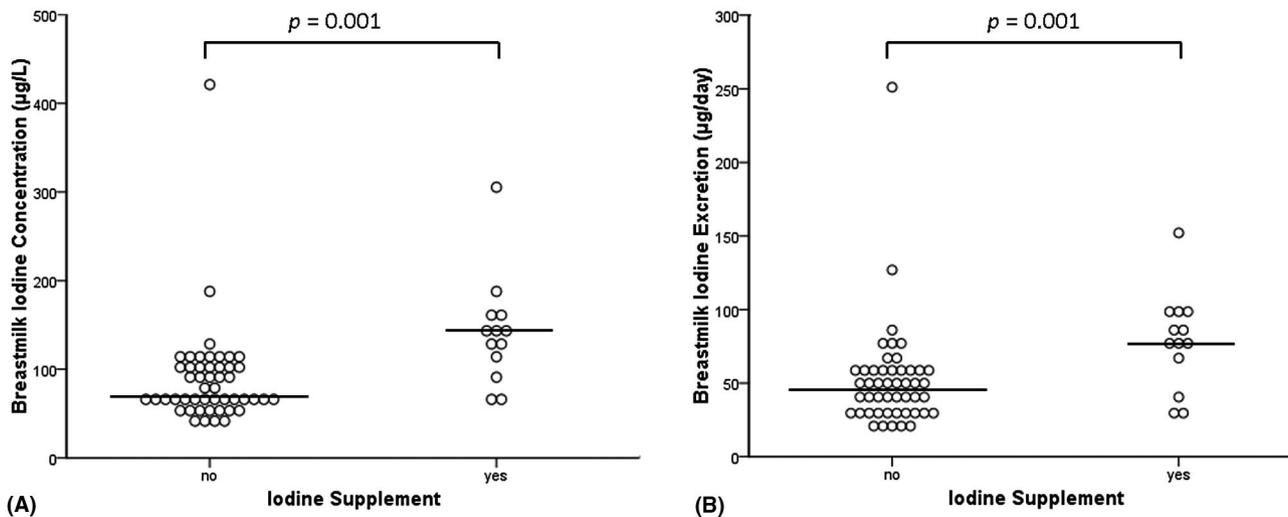


FIGURE 2 Dotplot illustrating (A) breast-milk iodine concentration of non-supplement users and supplement users, and (B) breast-milk iodine excretion of non-supplement users and supplement users at 0.5 months postpartum. The line represents the median

A subgroup was formed including women ($n = 34$) who were exclusively breastfeeding at 4 months and had ceased lactation before 10 months, at least 2 months before the last evaluation. Median UIC and eUIE were lower at 4 months compared with 12 months postpartum (UIC: $78 \mu\text{g/L}$ vs $107 \mu\text{g/L}$, $P = .005$; eUIE: $77 \mu\text{g/L}$ vs $99 \mu\text{g/L}$, $P = .014$). Tg remained unchanged. Due to the low number of supplement users ($n = 1$), analysis after stratifying for iodine supplementation was not possible.

Subanalyses between nulliparous women and the rest of the population were conducted at all time-points for UIC, eUIE and Tg and at 0.5 months for BMIC: no significant differences were revealed (data not shown).

4 | DISCUSSION

This 1-year, prospective study indicates mildly inadequate iodine intake of breastfeeding women in an area of southwest Sweden, mainly among women who did not take iodine supplements and in women who chose to exclusively breastfeed their babies.

Median BMIC at 0.5 months postpartum was $90 \mu\text{g/L}$, with 58% of women presenting BMIC $<100 \mu\text{g/L}$ and 9% with BMIC $<50 \mu\text{g/L}$. These results indicating mildly inadequate iodine nutrition are consistent with two previous local Swedish studies from the 1980s where BMIC was $92 \mu\text{g/L}$ ($n = 60$)⁸ and $90 \mu\text{g/L}$ ($n = 16$).⁹ Studies from Norway, France, Germany, Belgium, Spain, Italy, Denmark, Thailand, Zaire, and Australia have shown BMIC $<100 \mu\text{g/L}$, whereas Iran, China, the USA, and some parts of Europe have reported adequate iodine levels in breast milk.²⁶ Comparing BMIC across studies is, however, challenging because of differences in analytical methods, lack of external controls, and differences in study design. Median eBMIE in our study was $53 \mu\text{g/day}$, compared with the recommended daily iodine intake of $90 \mu\text{g}$,²⁵ but, eBMIE in our population, although calculated using a different formula, was in line with

a local Danish study.²⁷ It is important to note that iodine in breast milk in our study was measured at 0.5 months postpartum, which may overestimate overall maternal iodine status during lactation because BMIC tends to decline during the postpartum period.²⁸ BMIC is important for neuro-processing development in the child,³ which is accentuated in exclusively breastfed children. Sweden has a high prevalence of breastfeeding at 2, 4, and 6 months postpartum (85%, 74%, and 63%, respectively), with exclusive breastfeeding in 64%, 51%, and 15%, respectively,²⁹ highlighting the clinical relevance of our results.

When exclusively breastfeeding women were compared with non-exclusively breastfeeding women at 4 months postpartum, they had lower UIC, higher Tg, but similar eUIE. However, UIC is an inaccurate marker of iodine status during lactation and eUIE is even less reliable because the equation used¹⁸ is not standardized for lactating women. The parallel observation, however, of higher Tg in exclusively breastfeeding women supports the hypothesis that this group is at higher risk of ID. This is also supported by the observation that UIC and eUIE increased from 4 to 12 months postpartum after cessation of lactation, even though Tg was in this case unaltered. More research is needed to investigate lactating women's iodine status over time.

The observed ID during lactation in our study highlights the question of iodine supplementation for lactating women, as suggested by some international bodies,^{19,20} but not by the Swedish National Food Agency. Iodine supplement users (~20% of the study population) presented BMIC double that of non-supplement users. A randomized controlled trial on iodine daily supplementation, conducted in an iodine-deficient population showed BMIC 1.3 and 1.7 times higher in supplement users (75 and $150 \mu\text{g}$ iodine/day, respectively) compared with the placebo group.²⁴ A crossover study on iodine supplementation during lactation,³⁰ conducted in a generally iodine-sufficient country, revealed no difference with respect to BMIC. At the same time, the risk of iodine excess should not be ignored, as the immature thyroid gland

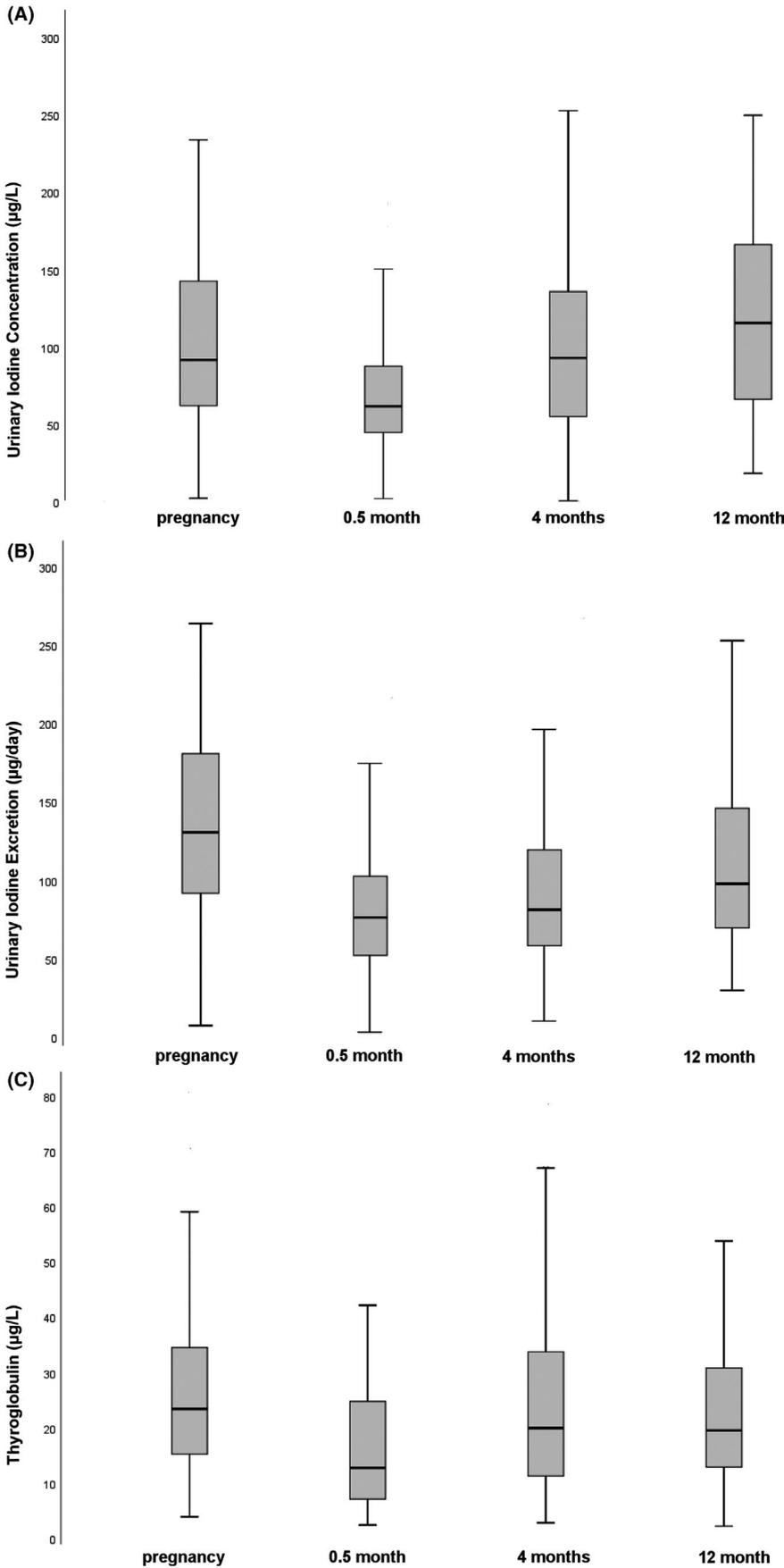


FIGURE 3 Boxplot illustrating (A) urinary iodine concentration, (B) urinary iodine excretion, and (C) thyroglobulin for the whole cohort of lactating women at baseline (third trimester of pregnancy), and 0.5, 4, and 12 months postpartum

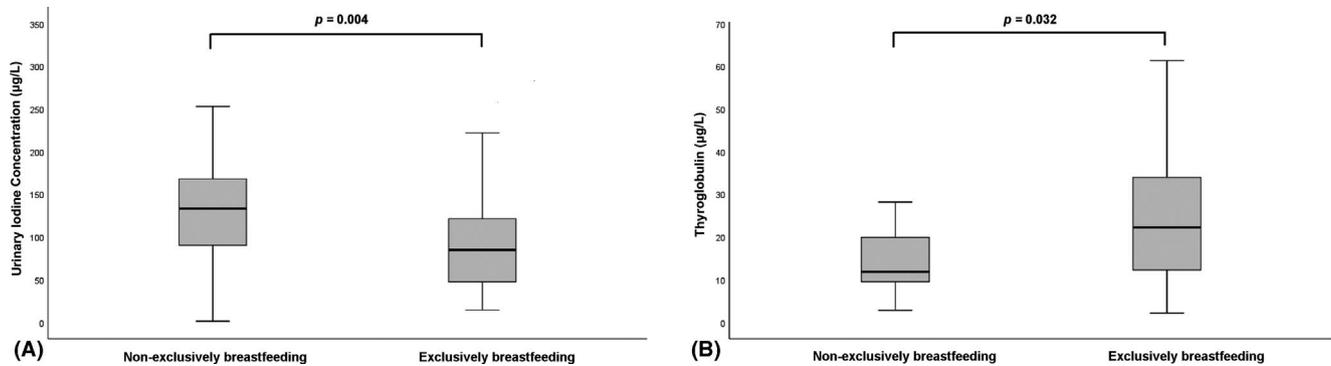


FIGURE 4 Boxplot illustrating (A) urinary iodine concentration of non-exclusively breastfeeding women vs exclusively breastfeeding women, and (B) thyroglobulin of non-exclusively breastfeeding women vs exclusively breastfeeding women at 4 months postpartum

TABLE 4 Estimated urinary iodine excretion (eUIE), thyroperoxidase (TPO) antibody positivity, thyroid stimulating hormone (TSH) and free thyrotropin (FT₄) at 4 months postpartum in non-exclusively breastfeeding women vs exclusively breastfeeding women. Data are presented as median (interquartile range) or percent

	Non-exclusively breastfeeding	Exclusively breastfeeding	P-value
eUIE	90 (64, 130)	62 (45, 103)	.07
TPO antibody positivity (%)	13.6	17.2	.75
TSH	1.60 (1.25, 2.10)	1.40 (1.00, 1.90)	.42
FT ₄	15 (14, 16)	15 (14, 17)	.91

of newborns may be more susceptible to the inhibitory effects of high iodine concentrations.³¹ Also, it is unclear whether increased iodine intake during lactation results in better outcome for the child. Taken together, there is not enough evidence supporting iodine supplementation during lactation in Sweden. Randomized controlled trials on iodine supplementation during breastfeeding in Sweden (ClinicalTrials.gov ID: NCT02378233) and on its effect on children's neuro-processing development are warranted to provide a foundation for future nutritional recommendations. An alternative to iodine supplementation is to adjust the ongoing iodine fortification program, as the World Health Organization recommends countries with salt iodine fortification to continuously evaluate their iodization program in order to meet the iodine needs of both the general population and of risk groups.

Sweden has a high level of iodization of salt at 50 mg/kg salt,¹⁰ above the recommended 20-40 mg/kg.²⁵ The fortification program in Sweden is voluntary, as it is in many countries globally.^{32,33} The USA, despite a similar iodization program³³ to Sweden, has reported adequate BMIC,³⁴ which makes the coverage of the iodization program in Sweden questionable. In the USA, ~25% of all salt consumed is estimated to be iodized,³³ which seems to be the same in Sweden (~20%) even though data are limited (personal communication with salt industry, 2017). The question is whether this statistic applies to the studied population of lactating women. The coverage of the iodization program needs to be thoroughly studied in the total population and in subgroups.

We recognize the limited sample size in our study, especially regarding supplement users. The study serves as a pilot study for an ongoing trial (ClinicalTrials.gov ID: NCT02378233). The different educational status between exclusively breastfeeding women at 4 months and the remainder of the group may be a confounding factor because of possible differences in dietary choices. It is more possible, however, that better educated mothers have higher adherence to the national recommendations for use of iodized salt during lactation,³⁵ leading to weakened significance and not the opposite. Higher educated mothers also used iodine supplement to a lesser extent, probably because supplementation during lactation is not currently recommended in Sweden. In addition, the recruitment period extends to 9-11 years ago and dietary habits in Sweden, as well as milk composition, may have changed.³⁶ The trend is however to lower dietary intake of iodine,^{10,36} which would strengthen, rather than weaken, the findings of this study. The limited number of women not breastfeeding their children at all led to the merging of non-breastfeeding women with partially breastfeeding women, which may weaken the result. Despite this risk, significant differences were shown. According to self-reporting, 22% of breast-milk samples were not collected in the intended standardized way, but several studies have failed to show variation in BMIC associated with the method of sample collection.^{26,27} The equation for calculation of eUIE is not adequate for lactating women, but the analytical method for UIC is highly validated. Another limitation is the lack of information on infant urinary iodine status and maternal dietary iodine intake. The important methodological strength of this study is the longitudinal design and that iodine status during lactation was evaluated by BMIC, the most reliable indicator for iodine status of lactating mothers,⁴ and was analyzed by multicollector inductively coupled plasma mass spectrometry, the reference standard for iodine analysis.²⁸ Moreover, eBMIE was calculated based on the infant's actual weight and not on age-based assumptions about the daily fluid intake.

5 | CONCLUSION

This pilot study suggests that lactating women in an area of southwest Sweden present mildly inadequate iodine intake,

mainly among women not taking iodine supplements and women exclusively breastfeeding their babies. Further studies are needed to understand if the coverage of the current iodine fortification program in Sweden is adequate for lactating women. Randomized controlled trials are warranted on iodine supplementation during lactation in Sweden (ClinicalTrials.gov ID: NCT02378233) and on its effect with respect to children's neuro-processing development to lay the ground for future nutritional recommendations to lactating women.

ACKNOWLEDGMENTS

We thank Petra Brembeck for contributing to recruitment and conducting the study, and Elisabeth Gramatkovski for analyzing the UIC.

CONFLICT OF INTEREST

None.

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How to cite this article: Manousou S, Augustin H, Eggertsen R, Hulthén L, Filipsson Nyström H. Inadequate iodine intake in lactating women in Sweden: A pilot 1-year, prospective, observational study. *Acta Obstet Gynecol Scand*. 2021;100:48-57. <https://doi.org/10.1111/aogs.13986>