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Iodine Status of Mother-Infant Dyads from Montréal, Canada: Secondary Analyses of a Vitamin D Supplementation Trial in Breastfed Infants

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ABSTRACT

Background: Most pregnant or lactating women in Canada will not meet iodine requirements without iodine supplementation.

Objectives: To assess the iodine status of 132 mother-infant pairs based on secondary analyses of a vitamin D supplementation trial in breastfed infants from Montréal, Canada.

Methods: Maternal iodine status was assessed using the breastmilk iodine concentration (BMIC). Singleton, term-born infants were studied from 1–36 months of age. Usual (adjusted for within-person variation) iodine intakes were estimated from urinary iodine and creatinine concentrations. Iodine status was assessed using median urinary iodine concentrations (UICs) and by estimating inadequate intakes by the cut-point method using a proposed Estimated Average Requirement for infants 0–6 months of age (72 μg/d).

Results: At 1, 3, and 6 months of age, 70%, 63%, and 3% of infants, respectively, were exclusively breastfed. From 1–36 months of age ($n = 82$–129), the median UICs were $\geq$100 μg/L (range, 246–403 μg/L), which is the cutoff for adequate intakes set by the WHO for children <2 years. Almost all (98%–99%) infants at 1 and 2 months, 2 and 3 months, and 3 and 6 months of age had usual creatinine-adjusted iodine intakes $\geq$ 72 μg/d. The median BMIC was higher ($P < 0.001$) at 1 month compared to 6 months of lactation [1 month, 198 μg/kg (IQR, 124–274; $n = 105$) and 6 months, 109 μg/kg (IQR, 67–168; $n = 78$)]. At 1 and 6 months, 96% and 79% of mothers, respectively, had a BMIC $\geq$ 60 μg/kg, the lower limit of a normal reference range. The percentages of mothers that used a multivitamin-mineral (MVM) supplement containing iodine were 90% in pregnancy and 79% and 59% at 1 and 6 months of lactation, respectively.

Conclusions: The iodine status of infants was adequate throughout infancy. These results support a recommendation that all women who could become pregnant, who are pregnant, or who are breastfeeding take a daily MVM supplement containing iodine. *J Nutr* 2022;152:1459–1466.

Keywords: breastmilk iodine concentration, estimated average requirement cut-point method, infants, urinary iodine concentration, usual creatinine-adjusted iodine intake

Introduction

Iodine is essential for the production of thyroid hormones, which are required for normal growth and brain development of the fetus and infant (1). Pregnant and breastfeeding women and infants are at risk of iodine deficiency because of high iodine requirements (2, 3). The fetus and exclusively breastfed infant are entirely reliant on the mother to meet their iodine requirements. The fetus obtains thyroid hormones from the mother via the placenta; by the second trimester, the fetal thyroid gland begins to produce thyroid hormones and maternal transfer of iodine is needed to maintain adequate fetal thyroid hormone production (4). Infants are born with limited iodine stores and must be supplied with iodine from breastmilk (or infant formula) to maintain their high rate of thyroid hormone production (4). The Estimated Average Requirement (EAR) for iodine increases from 95 μg/d for nonpregnant and nonlactating women to 160 μg/d in pregnancy and 209 μg/d during lactation (5).

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The urinary iodine concentration (UIC) is a biomarker of recent iodine intake that captures intakes from all sources (6). Most ingested iodine (∼90%) is excreted in urine within ∼24 hours (7–9). The WHO recommends using the median UIC from a spot sample for an assessment of iodine status in a population (2, 10). Reference ranges that represent insufficient to excessive iodine intakes have been established for children ≥6 years, adults, and pregnant women (2, 10). For children <2 years and lactating women, a single cutoff value of 100 μg/L for adequate intakes was set. A cross-sectional multicenter study showed that the UIC is not an accurate biomarker of iodine intakes in lactating women when intakes are near the lower end of the adequate range because of preferential partitioning of iodine into breastmilk (11). That study also suggests that the breastmilk iodine concentration (BMIC) is a more accurate biomarker of iodine status and proposes a normal reference range of 60–465 μg/kg and a target median of 171 μg/kg for exclusively breastfeeding women.

A limitation of using the median UIC to assess iodine status is that it does not provide accurate information on the prevalence of inadequate intakes. Dold et al. (12) proposed an EAR of 72 μg/d for infants 0–6 months of age based on results from an iodine balance study. Based on this EAR, thresholds were calculated of 125 μg/L for the UIC (assuming a urine volume of 0.5 L/d and urinary iodine excretion of 87%) and 92 μg/kg for the BMIC (assuming breastmilk consumption of 0.78 kg/d) (12). The prevalence of inadequate iodine intakes in infants can be determined by estimating the usual (adjusted for within-person variation) iodine intakes or usual UICs and calculating the proportion below the EAR thresholds using the cut-point method (13). Statistical procedures can be used to adjust for within-person (day-to-day) variation if ≥2 measurements are available from a representative subset of the population (14–16).

Daily iodine intakes can be calculated using an equation that estimates 24-hour urinary iodine excretion and that takes into account the rate of iodine excretion in urine. Equations that predict 24-hour urinary creatinine (Cr) excretion can be used to calculate 24-hour urinary iodine excretion from iodine and Cr concentrations in a spot sample (17, 18). We recently used this approach to estimate the prevalences of inadequate intakes in Canadian children ≥3 years, adolescents, and women of childbearing age using results from the Canadian Health Measures Survey (CHMS), cycle 5 (2016–2017) (19).

Results from the CHMS suggest that large proportions of pregnant (>50%) and lactating (>75%) women in Canada will not meet iodine requirements without iodine supplementation (19). Low BMICs from inadequate maternal iodine intakes could result in breastfed infants not meeting iodine requirements. To date, information on the iodine status of lactating women and infants in Canada is scarce (20, 21). This study reports the iodine status of mother-infant pairs based on secondary analyses of a vitamin D supplementation trial in breastfed infants from Montréal, Canada, using breastmilk and urine iodine concentrations (22).

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Supplemental Tables 1–5 and Supplemental Figure 1 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.

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Abbreviations used: BMIC, breastmilk iodine concentration; Cr, creatinine; CHMS, Canadian Health Measures Survey; EAR, Estimated Average Requirement; MVM, multivitamin-mineral; UIC, urinary iodine concentration.

Methods

Study design

This report is based on samples and data originally collected as part of a double-blinded, randomized controlled trial (registered at clinicaltrials.gov as NCT00381914) to analyze the nutrient contents of human milk and the associated infant nutritional status. The original data were collected in 132 infants randomized at 1 month of age to receive either 400 IU/d ($n = 39$), 800 IU/d ($n = 39$), 1200 IU/d ($n = 38$), or 1600 IU/d ($n = 16$) of oral cholecalciferol (vitamin D_3) for 11 months (22). Infants were then followed at 36 months of age. Infants were randomly assigned to 1 of the 4 treatment groups in a 1:1:1:1 allocation ratio, stratified by sex, in equal blocks of 4. Parents provided written informed consent prior to commencing the study. The Institutional Review Board of McGill University approved the trial (A05-M61-06A). The Health Canada and Public Health Agency of Canada Research Ethics Board (REB 2019–038H) and the Privacy Management Division (HC-PR-2019–000030) reviewed and approved the use of the data and samples in this report.

Newborns (≤1 month of age) were referred from the Lakeshore General Hospital and 5 pediatric clinics located in greater Montréal between March 2007 and August 2010. All visits at 1 (baseline), 2, 3, 6, 9, 12, and 36 months of age (±2 weeks) were conducted at the Mary Emily Clinical Nutrition Research Unit of McGill University. Infants who were healthy, term, singleton, and of appropriate size for gestational age and breastfeeding (consuming ≥80% of the total milk volume) were eligible to participate. The exclusion criteria included infants of mothers with gestational diabetes, hypertension in pregnancy, chronic alcohol use, or malabsorption syndromes. Sociodemographic information—including maternal age, race, and education and family income—were reported by the mother at the baseline visit, along with a pregnancy history, including the prepregnancy weight and smoking status.

Anthropometric measurements

At the 1-, 2-, 3-, 6-, 9-, and 12-month visits, infant nude weight (infant-scale model SB 32000, Mettler-Toledo Inc.), length (O'Leary Length Board, Ellard Instrumentation Ltd.), and head circumference (nonstretchable tape) were measured and reported as absolute units, and z-scores were calculated using the WHO growth standards (23). At the 36-month visit, weight and height were measured in light clothing and no shoes using a calibrated scale (Detecto) and stadiometer (Seca 213, Seca Medical Scales and Measuring Systems), respectively. Mothers' weight and height were measured at baseline using standard methodology to calculate the BMI. Details on anthropometric measurements have been published elsewhere (22, 24).

Breastmilk consumption and dietary records

At the 1-, 3-, 6-, 9-, and 12-month visits, for as long as the infant was still breastfeeding, total daily consumption of breastmilk was estimated using test weighing performed by the parents over a 24-hour period (25). Test weighing (Tanita Baby Scale Neonatal/Pediatric BLB) was accurate to 2 g (<6 kg) or 5 g (6–12 kg). Nutrient intakes from food or supplements were assessed for infants using 3-day dietary records completed by parents after each visit. At each visit, mothers completed a 24-hour recall, as well as a 3-day dietary record, to obtain information on maternal nutrient intakes. Nutrient intakes were estimated using the Nutritionist Pro software version 4.7.0 (Axxya Systems LLC) and the 2010b Canadian Nutrient File database (26). The iodine content of supplements used by mothers during pregnancy and lactation was obtained from the Licensed Natural Health Products Database of Health Canada (27). The start and frequency of multivitamin-mineral (MVM) supplement use by the mothers was self-reported at postnatal recruitment approximately 1 month postpartum.

Urine and breastmilk collections

Spot urine samples were collected from the infant using a urine collection bag (Pediatric U-bag, Hollister Inc.) at each visit. Mothers' breastmilk was sampled at each visit until the mother was no longer breastfeeding. Mothers were asked to pump milk using an electric breast pump (Medela). The bottle and tubing were either new or cleaned and disinfected with gas autoclave methodology at the Montréal Children's hospital. Mothers expressed 1 full feed from 1 breast, to include foremilk and hind milk. A registered nurse assisted the mothers as needed during the visit. Breastmilk samples were vortexed before storing aliquots from each visit in 20-mL plastic scintillation vials. Infant urine and breastmilk samples were stored at −80°C until 2015, then at −20°C until analysis.

Urinary iodine and creatinine

UIC was measured by the CHMS laboratory using a colorimetric microplate assay based on the Sandell-Kolthoff reaction (28). Urine samples were analyzed in duplicate, and the mean was reported. Samples were vortexed; manually diluted 1:4 with deionized, reagent-grade water; and mixed with an ammonium persulfate solution to remove interfering substances. For the colorimetric detection step, standards, controls, and samples were assayed in triplicate and the mean was used. Samples with a UIC above the assay range (25–260 μg/L) were diluted further and reanalyzed. Samples with a UIC below the assay range were reanalyzed undiluted. One undiluted sample had a UIC below the limit of detection and was reported as half the limit of detection (12.5 μg/L) (29). For each plate, results were considered acceptable if the standard curve had an $R^2 > 0.99$, the CV of the replicates was ≤ 10%, and the quality controls were within acceptable ranges. National Institute of Standards and Technology–certified reference materials (SRM2670a–Freeze-dried Urine) and additional quality controls provided by the CDC were analyzed on each plate. The CHMS laboratory subscribes to proficiency testing through the CDC's Ensuring the Quality of Urinary Iodine Procedures (EQUIP) Program (30). The urinary Cr concentration was initially measured using a kinetic modification of the Jaffe procedure and then an enzymatic method from June 2009, as previously described (31). An equation was used to correct for differences between methods with an r of 0.99.

Breastmilk iodine

Previously frozen breastmilk samples were thawed and sonicated, and a 0.5-mL aliquot was transferred to a polytetrafluoroethylene digestion tube. One mL of Indium internal standard stock solution (200 μg/L) and 0.2 mL of 25% tetramethyl ammonium hydroxide were added to the samples. The samples were diluted to a total volume of 2.5 mL with deionized water and digested by heating at 90°C overnight. After cooling, the samples were brought to a total volume of 10 mL with deionized water. Dilution factors at each step were monitored gravimetrically (accurate to 0.0001 g). Iodine-127 and Indium-115 isotopes were measured by inductively coupled plasma MS using an Agilent 8800 triple quadrupole MS. Whole-milk powder Standard Reference Material 1549a (National Institute of Standards and Technology) was reconstituted with deionized water and analyzed using the above procedure to verify analytical accuracy. The mean ± SD (n = 12) was 3.21 ± 0.17 mg/kg (CV, 5%), which is in agreement with the certified range of 3.04–3.64 mg/kg.

Calculations and statistical analyses

Descriptive statistics are presented as medians (IQRs), arithmetic means, percentiles, and proportions. The PROC SURVEYSELECT with URS method (unrestricted random sampling, selection with equal probability and with replacement) was applied to generate 10,000 replications. These replications were used to compute bootstrap SEs and bootstrap percentile CIs. Differences in the median BMICs were determined using the Mann-Whitney rank-sum test. Differences in the median UICs were determined using the Kruskal-Wallis ANOVA on ranks followed by Dunn's multiple comparison post hoc test.

TABLE 1 Characteristics of mothers and infants[1]

Characteristics	n	Values
Mothers		
Age at delivery, years	132	33 (30–35)
Prepregnancy BMI,[2] kg/m^2	129	23.2 (21.0–26.3)
Postpartum BMI,[3] kg/m^2	128	26.4 (23.2–29.9)
Children,[4] n	132	2 (1–2)
Self-reported race, %		
White	112	85
Non-White[5]	19	15
Household income,[6] %		
<75,000 CAD	52	40
≥75,000 CAD	78	60
Mothers' education, %		
High school	8	6
Vocational school or apprentice training	7	5
College or university	117	89
Smoking during pregnancy, %		
No	124	94
Yes	8	6
Use of MVM supplement containing iodine,[7] %		
During pregnancy	119	90
At 1 month of lactation[8]	103	79
At 6 months of lacation[8]	56	59
Infants		
Sex, %		
Male	76	58
Female	56	42
Gestational age at birth, weeks	131	39.7 (39.0–40.4)
Birth weight, kg	131	3.51 (3.20–3.84)
Breastfeeding,[9] %		
1 month	131	99 (70)
2 months[10]	120	99
3 months	112	97 (63)
6 months	95	88 (3)

[1]Values are medians (IQRs) unless otherwise indicated. MVM, multivitamin-mineral.
[2]Self-reported at the baseline visit.
[3]Measured at a median of 1 month (IQR, 1–1) postpartum.
[4]Determined as the number of live births.
[5]Non-White includes Black, Hispanic, First Nations, Asian, Hawaiian/Pacific Islander, and non-White mixed race.
[6]Self-reported household income.
[7]The median iodine content in MVM supplements was 220 μg/d (IQR, 150–220).
[8]Breastfeeding mothers only.
[9]The percentage of infants exclusively breastfed is shown in parentheses.
[10]Exclusively breastfed infants could not be identified.

Daily iodine intakes were calculated using the following formula:

$$Iodine\ intake\ (\mu g/d) = \frac{UIC\ (\mu g/L)}{Urinary\ Cr\ concentration\ (mg/L)} \times Predicted\ urine\ Cr\ (mg/d) \div 0.92 \quad (1)$$

Here, 0.92 represents the urinary iodine excretion rate (5, 7–9). Established equations were used to predict 24-hour urine Cr excretion (**Supplemental Table 1**) (17). Usual Cr-adjusted iodine intakes and UICs of infants were estimated from duplicate urine samples collected at 1 and 2 months, 2 and 3 months, and 3 and 6 months of age using the SAS macros MIXTRAN and DISTRID, developed at the National Cancer Institute (16, 32). The 1-part model was used for dietary components that are consumed daily. Proportions of infants with usual Cr-adjusted iodine intakes and UICs below and above EAR thresholds were calculated using the cut-point method (13). Statistical analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute Inc.) and SigmaPlot 12.5 (Systat Software Inc.).

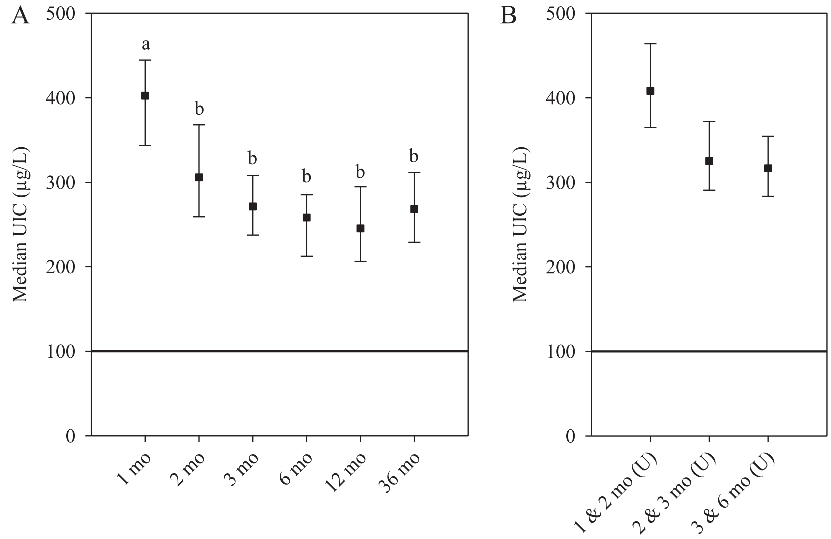

FIGURE 1 Median UICs (95% CIs) of infants (sexes combined) followed from 1 to 36 months of age. (A) Median UICs were calculated from unadjusted UICs for infants at 1 month ($n = 129$), 2 months ($n = 113$), 3 months ($n = 107$), 6 months ($n = 108$), 12 months ($n = 96$), and 36 months ($n = 82$) and (B) usual UICs were adjusted for within-person variation for infants at 1 and 2 months ($n = 131$), 2 and 3 months ($n = 116$), and 3 and 6 months ($n = 116$). Median UICs are shown in comparison with the WHO cutoff of 100 μg/L for adequate iodine intakes for children ≤2 years (solid horizontal line) (10). Unadjusted median UICs not sharing a common letter differ at a P value < 0.05. U, usual; UIC, urinary iodine concentration.

Results

Mothers and infants

Anthropometric and sociodemographic characteristics of mothers and their infants are presented in **Table 1** and **Supplemental Table 2**. Mothers were mostly of White race, highly educated, and nonsmokers. A MVM supplement containing iodine was used by 90% of the mothers in pregnancy, 79% in the first month of lactation, and 59% in the sixth month of lactation (Table 1). Of those using supplements, 39% began use before pregnancy and 61% began use after conception. Daily use of the MVM was reported by 88%. The median iodine content of the MVM supplements used by the mothers was 220 μg/d (IQR, 150–220 μg/d).

At 1 month of age, 99% of the infants were breastfed, with 70% exclusively breastfed. The percentage of infants who were breastfed decreased to 97% (63% exclusively) at 3 months of age and 88% (3% exclusively) at 6 months of age (Table 1). None of the infants ≤12 months of age consumed an iodine supplement. Five children used a MVM supplement containing iodine at 36 months of age. Body weights and weight-for-age z-scores indicated normal growth during infancy and early childhood (Supplemental Table 2). Detailed results on anthropometric measurements have been published (22, 24).

UIC

The iodine status of infants was assessed by comparing the median UIC with the WHO cutoff value for adequate intake (**Figure 1**). The median UIC for 1-month-old infants was higher ($P < 0.05$) compared to all other age groups (Figure 1A). The usual UICs, adjusted for within-person variation, were estimated for infants at 1 and 2 months, 2 and 3 months, and 3 and 6 months of age (Figure 1B; **Supplemental Table 3**). At all ages, median UICs were ≥100 μg/L for unadjusted and usual UICs, indicating overall adequate iodine intakes (Figure 1).

BMIC

The median BMIC was higher ($P < 0.001$) at 1 month compared to 6 months of lactation [1 month, 198 μg/kg (IQR, 124–274) and 6 months, 109 μg/kg (IQR, 67–168); **Figure 2**; **Supplemental Table 4**]. The target median of 171 μg/kg was exceeded at 1 month of lactation, but not at 6 months. At

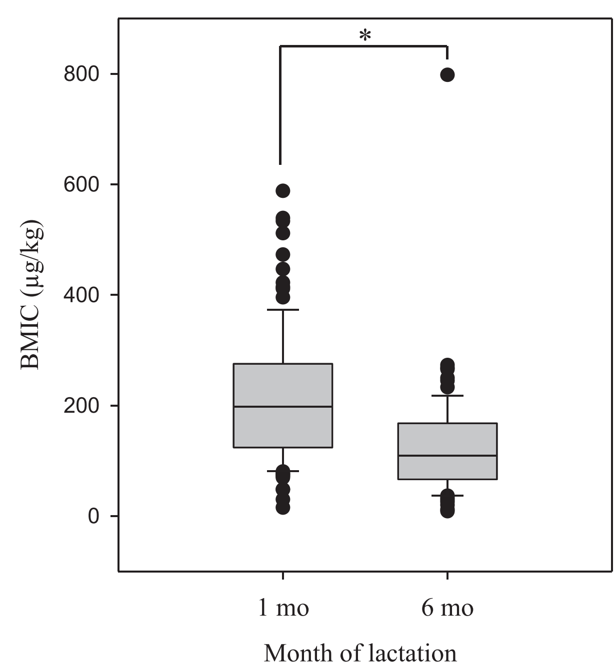

FIGURE 2 BMICs of mothers at 1 month ($n = 105$) and 6 months ($n = 78$) of lactation. Box and whisker plots show the medians and 10^{th}, 25^{th}, 75^{th}, and 90^{th} percentiles. Outliers (values <10^{th} percentile or >90^{th} percentile) are shown as solid circles. *Median BMICs at 1 and 6 months of lactation differ at a P value < 0.001. BMIC, breastmilk iodine concentration.

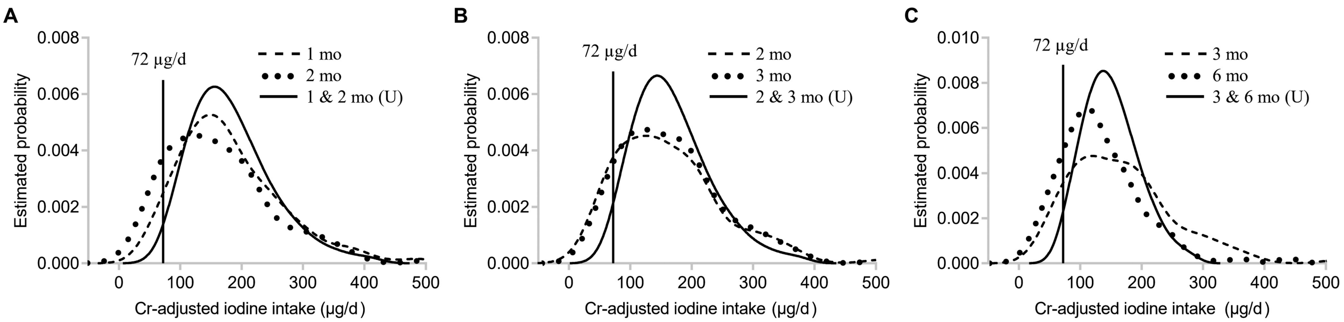

FIGURE 3 Probability distributions of Cr-adjusted iodine intakes for infants. Unadjusted iodine intakes and usual iodine intakes which were adjusted for within-person variation for infants aged (A) 1 and 2 months (n = 98–126), (B) 2 and 3 months (n = 96–110), and (C) 3 and 6 months (n = 96–114). The vertical bar corresponds to a proposed Estimated Average Requirement of 72 µg/d for infants 0–6 months of age (12). Cr, creatinine; U, usual.

1 month of lactation, 96% of mothers had a BMIC ≥ 60 µg/kg, the lower limit of the reference range (Supplemental Table 4). The corresponding value at 6 months of lactation was 79%. Almost all mothers at 1 month (95%) and 6 months (99%) of lactation had a BMIC ≤ 465 µg/kg, the upper limit of the reference range.

Iodine intakes

Probability distribution curves of Cr-adjusted iodine intakes of infants, compared with the EAR of 72 µg/d, are presented in **Figure 3**. Usual Cr-adjusted iodine intake curves were shifted to the right and had shorter tails compared with curves unadjusted for within-person variation. Almost all infants (≥98%) had usual Cr-adjusted iodine intakes ≥ 72 µg/d (**Table 2**). Probability distribution curves of UICs compared with the EAR-UIC threshold of 125 µg/L are shown in **Supplemental Figure 1**. Almost all infants (≥97%) had a usual UIC ≥ 125 µg/L (Supplemental Table 3).

Of the infants exclusively breastfed at 1 month of age, 78% had iodine intakes ≥ 72 µg/d when calculated from the BMIC and measured breastmilk consumption (**Supplemental Table 5**). At 1 and 6 months of lactation, 86% and 58% of mothers, respectively, had a BMIC ≥ 92 µg/kg, which is an EAR-BMIC threshold (Supplemental Table 4).

Discussion

Most pregnant and lactating women in Canada will not meet iodine requirements without iodine supplementation because of the large increase in iodine requirements during pregnancy and lactation and the low coverage of iodized salt (19). In Canada, only iodization of table salt is mandatory (76.5 mg/kg), but many Canadians never or rarely use salt for cooking or at the table (33). Results from the 2004 Canadian Community Health Survey–Nutrition indicate that 28% (95% CI, 25%–31%) of women 19–30 years and 31% (95% CI, 28%–34%) of women 31–50 years never add salt to food at the table (34).

Health Canada recommends that all pregnant and lactating women take a MVM supplement (35). The American Thyroid Association recommends that all pregnant and lactating women in North America take an iodine supplement of 150 µg/d (36). Most women used a MVM supplement containing iodine in pregnancy (90%), and all but 1 (87.5 µg/d) contained iodine at a level of 150 or 220 µg/d. The highest level is equivalent to the RDA for pregnant women (220 µg/d), but lower than that for lactating women (290 µg/d) (5). Most (88%) mothers reported taking the MVM supplement daily. However, the percentage of mothers that used a MVM supplement declined from pregnancy and throughout the lactation period, to 59% by the sixth month of breastfeeding.

Dietary assessment of iodine intake is challenging, because it is difficult to accurately assess discretionary consumption of iodized salt, the iodine content of similar foods can differ widely, and many national food composition databases (including the Canadian Nutrient File) do not report iodine contents in foods (1, 26). The conventional method for assessing the iodine status of populations is to use the median UIC from a single spot sample and compare it with WHO reference ranges (2, 10). The median is an appropriate measure because it is minimally affected by the typically large day-to-day variations in UIC when the sample size is large. The WHO has established a median UIC cutoff value of 100 µg/L for adequate intakes for children <2 years of age. However, there is less direct evidence on thyroid function to support this cutoff value for infants compared to school-aged children (2, 37, 38). The proposed EAR-UIC threshold of 125 µg/L suggests that 100 µg/L is too low for infants (12). Even so, median UICs at all ages were well over 100 µg/L, suggesting that overall iodine intakes throughout infancy were adequate. The median UIC at 36 months of age was 268 µg/L (95% CI, 229–312 µg/L), which is slightly higher than the median reported for children 3–5 years of age from the CHMS (19). This is consistent with the lower daily urine volume of younger children, which results in a higher UIC (39).

The median UIC does not provide accurate information on the prevalence of inadequate iodine intakes in a population. This limitation can be addressed using the EAR cut-point method (13). For infants, the National Academy of Medicine (formerly called the Institute of Medicine) has set adequate intakes for iodine that cannot be used to assess the prevalence of inadequate intakes (5). As an alternative, we used a proposed EAR derived from a rigorously conducted dose-response, crossover, iodine-balance study in infants 2–5 months of age that indicated an EAR of 72 µg/d for infants 0–6 months of age (12). Infants in that study were formula-fed, but the EAR should apply to breastfed infants since the iodine bioavailability from infant formula and breastmilk is likely comparable (12).

To calculate daily iodine intakes, Cr was used to correct for urine dilution. A study in children showed a significant correlation between Cr-estimated 24-hour urinary iodine excretion and that from 24-hour urine collections (40). The Cr prediction equations were developed for healthy infants and take into account sex and age (17). A urinary iodine excretion rate of 92% was used to calculate iodine intakes (5, 7–9).

TABLE 2 Cr-adjusted iodine intakes of infants and prevalences of inadequate intakes by the EAR cut-point method[1]

Age, months	n	Mean,[3] μg/d	Percentile distribution, μg/d									Percentage[2]	
			2.5th	5th	10th	25th	50th (median)	75th	90th	95th	97.5th	<72 μg/d	≥72 μg/d
Unadjusted													
1	116	216 (171–292)	53 (49–72)	70 (53–84)	84 (70–106)	121 (113–138)	168 (150–182)	235 (203–263)	301 (264–363)	368 (301–481)[4]	481 (360–3992)[5]	7 (3–12)[5]	93 (88–97)
2	98	173 (152–195)	50 (31–62)	56 (43–68)	64 (60–78)	94 (77–121)	148 (132–180)	214 (196–237)	306 (237–344)	355 (292–593)[4]	514 (327–621)[4]	11 (5–18)[4]	89 (82–95)
3	96	167 (150–185)	49 (43–64)	53 (45–72)	70 (57–83)	104 (83–123)	163 (129–175)	214 (189–243)	292 (243–325)	325 (285–375)	362 (299–522)	10 (5–17)[4]	90 (83–95)
6	106	134 (121–150)	28 (8–48)[5]	42 (28–58)[4]	53 (42–73)	88 (73–100)	121 (110–134)	167 (146–183)	221 (189–250)	250 (215–360)	360 (244–500)[4]	16 (9–23)[4]	84 (77–91)
Usual[6]													
1 and 2	126	185 (163–207)	85 (69–110)	94 (80–119)	107 (94–131)	135 (121–155)	173 (157–194)	221 (195–254)	278 (230–330)	317 (253–386)	357 (274–443)	1 (0–3)[5]	99 (97–100)
2 and 3	110	170 (153–186)	75 (62–93)	84 (72–103)	97 (85–115)	123 (110–140)	159 (145–176)	204 (184–227)	256 (221–290)	291 (245–338)	327 (267–386)	2 (0–5)[5]	98 (95–100)
3 and 6	114	150 (137–164)	74 (59–98)	83 (69–105)	94 (81–115)	117 (105–132)	145 (134–159)	178 (160–197)	213 (182–243)	235 (195–275)	256 (207–306)	2 (0–6)[5]	98 (94–100)

[1]Values are means, percentiles, or percentages (95% CI). Cr, creatinine; EAR, Estimated Average Requirement.
[2]Proposed EAR for infants 0–6 months of age (12).
[3]Arithmetic mean.
[4]Data with a CV from 16.6% to 33.3%;
[5]Data with a CV greater than 33.3%: interpret with caution.
[6]Adjusted for within-person variation.

This is slightly higher than the 87% reported in 1 infant study (12). Infants may have a lower excretion rate compared to older children and adults because of greater accumulation of iodine in the thyroid and, consequently, higher iodine retention. Using a lower excretion rate of 87% would have resulted in slightly higher iodine intake estimates, but this would not have changed the overall conclusions of the study. Almost all infants at all ages had usual Cr-adjusted iodine intakes above the EAR of 72 μg/d, indicating a low prevalence of inadequate iodine intakes. Notably, similar results were obtained using the EAR-UIC threshold of 125 μg/L that was derived using the lower urinary iodine excretion rate of 87% (12). It is important to mention that although proportions below and above EAR thresholds were reported for iodine intakes and UICs that were not adjusted for within-person variability, these results should not be used to assess iodine inadequacy. Extreme deviations in iodine intakes will occur for some individuals in a population on any given day, which can lead to overestimations of inadequate intakes.

The UIC in isolation is an inappropriate biomarker for assessing the iodine status in lactating women. The UIC may underestimate the iodine status in iodine-sufficient populations when intakes are near the lower end of the adequate range because of the preferential partitioning of iodine into breastmilk (11). The BMIC has been suggested as a more accurate biomarker (11). A population-based reference range of 60–465 μg/kg and a target median of 171 μg/kg (95% CI, 163–181 μg/kg) have been proposed based on data from relatively large surveys of exclusively breastfeeding women (n = 866) from iodine-sufficient regions (11). The reference range corresponds to the 2.5th and 97.5th percentiles, and thus takes into account interindividual variations in BMIC. In the first month of lactation, almost all mothers had a BMIC within this reference range and the median exceeded the target median, suggesting that maternal iodine intakes were adequate and not excessive. By the sixth month of lactation, a larger percentage of mothers (21%) had a BMIC < 60 μg/kg and the median was below the target median. The BMIC decreases gradually throughout the lactation period, and iodine supplementation during lactation increases the BMIC, with evidence of a dose-response relationship (41). The lower BMIC at 6 months of lactation is likely explained by the natural decline in BMIC during lactation and by fewer mothers using a MVM supplement containing iodine.

The proportion of exclusively breastfed infants at 1 month of age with iodine intakes ≥ 72 μg/d when calculated from BMICs and measured breastmilk consumption was lower compared with estimates based on usual Cr-adjusted iodine intakes for infants at 1 and 2 months of age (78% compared with 99%, respectively). However, estimates of inadequacy based on BMICs should be interpreted with caution, since iodine intakes were not adjusted for within-person variation and likely overestimate the prevalence of inadequacy. This is probably true even with preferential partitioning of iodine into breastmilk, because there are obligatory renal iodine losses from the turnover of maternal thyroid hormones (11).

The proportion of mothers with a BMIC ≥ 92 μg/kg, a threshold derived from the EAR and an assumed breastmilk consumption of 0.78 kg/d (5, 42), decreased from the first month of lactation (86%) to the sixth month of lactation (58%). Despite the lower BMIC at 6 months of lactation, the iodine status of 6-month-old infants appears adequate when assessed using the UIC. Only 3% of infants were exclusively breastfed at 6 months of age, and therefore these infants were obtaining iodine from other food sources (e.g., infant formula and complementary foods). These results suggest that complementary feeding was appropriate to meet iodine requirements.

This study had strengths. The collection of both mothers' breastmilk and infant urine allowed for the assessment of iodine status of mother-infant pairs. The collection of multiple urine samples per infant allowed for estimations of usual iodine intakes and prevalences of inadequate iodine intakes throughout infancy. The use of Cr-adjusted values helped reduce errors resulting from variable urine dilution. Diet records provided important information on iodine supplement use. The Sandell-Kolthoff method was used for measurement of UIC, but inductively coupled plasma MS (the gold standard) was used to measure iodine in breastmilk (6).

This study has some limitations. The EAR thresholds and BMIC reference range were adopted from 2 studies, given the absence of internationally accepted values (11, 12). The cohort was from a single geographical region and included mostly highly educated mothers and healthy, term-born infants, and therefore the results are not representative of the total Canadian population. The results are from secondary analyses of a vitamin D supplementation trial in infants and from follow-ups conducted previously (2007–2013). However, vitamin D supplementation is not expected to have influenced the results, and nutrition policies on iodine have not changed since completion of the study. Health Canada launched a sodium reduction strategy in 2010 (43), but it had little effect on iodine intakes since most sodium consumed by Canadians comes from salt added to processed foods that is not required to be iodized (19). The sample sizes were small compared to the recommended size of 500 for high-precision estimates (44), but adjusting for within-person variation decreases the sample size required. The Cr prediction equations were developed for the US population with data from a small sample of infants but should provide acceptable Cr reference values for infants in this study. The equations were from a larger set of equations that cover ages 0–92 years, which were developed using a continuity-smoothing procedure (17). Assessment of excessive iodine intakes in infants was not possible; a cutoff for the median UIC and a Tolerable Upper Intake Level are lacking.

This study contributes to the limited body of literature on iodine status of mother-infant dyads. BMICs in the first month of lactation indicated adequate maternal iodine status, but BMICs declined substantially by the sixth month of lactation, in accordance with declining supplement use. Iodine status of infants, assessed using UICs, were adequate throughout infancy, indicating sufficient iodine intakes from breastmilk during the first few months of breastfeeding and appropriate complementary feeding practices in older infants that helped meet iodine requirements. Collectively, these results reinforce Health Canada's recommendation that all women who could become pregnant, who are pregnant, or who are breastfeeding take a daily MVM supplement (35).

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Data Availability

The data described in the manuscript will not be made available because permission to share data was not requested at the time participant consent was obtained.

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