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No Difference in Urinary Iodine Concentrations Between Boston-Area Breastfed and Formula-Fed Infants

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Background: Thyroid hormone is essential for normal mental and physical development in infancy and childhood and is dependent on adequate iodine intake. During the first few months of life, infants are reliant on breastmilk and/or infant formula as their sole sources of dietary iodine. The iodine status of U.S. infants has not been well studied.

Methods: This was a cross-sectional study of 95 breastfed and/or formula-fed infants less than 3 months of age in the Boston area. We measured iodine content from infants' single spot urine samples and assessed associations with infant feeding type as well as maternal demographic data, salt and multivitamin use, smoking status, and diet.

Results: The median infant urine iodine concentration was 197.5 μg/L (range 40–897.5 μg/L). Median infant urine iodine concentrations were similar between infants who were exclusively breastfed ($n=39$, 203.5 μg/L; range 61.5–395.5 μg/L), formula-fed ($n=44$, 182.5 μg/L; range 40–897.5 μg/L), and mixed ($n=10$, 197.8 μg/L; range 123–592.5) ($p=0.88$). There were no significant correlations of infant urinary iodine with maternal salt or multivitamin use (regularly or in the past 24 hours), active or secondhand cigarette smoke exposures, infant weight, infant length, or recent maternal ingestion of common iodine-containing foods, although the correlations with iodine-containing foods are difficult to accurately determine due to the small sample sizes of these variables.

Conclusions: Both breastfed and formula-fed infants less than 3 months of age in the Boston area were generally iodine sufficient. Larger studies are needed to confirm these observations among infants nationwide and elucidate other factors that may contribute to infant iodine nutrition.

Introduction

Iodine is an essential component of the thyroid hormones, thyroxine and triiodothyronine (1). If dietary iodine intake is deficient, thyroid hormone production may be inadequate, leading to profound effects on growth and development and on the function of numerous target tissues, including the brain, lungs, heart, gastrointestinal tract, and skeleton. Unique to the fetus and neonate is the critical role of the thyroid hormones on brain development (1). Iodine deficiency is the most common preventable cause of mental retardation worldwide (2). Even mild iodine deficiency during pregnancy has been associated with deficits in neurocognitive development in the offspring (3–5).

During pregnancy and lactation, the mother is the sole source of iodine for the fetus and exclusively breastfed infant. As there is significant day-to-day and diurnal variation of iodine intake (6), dietary iodine status cannot be determined on an individual basis. Instead, median urinary iodine concentrations are used to determine the iodine sufficiency of populations, with levels ≥ 100 μg/L considered adequate in children less than 2 years old (7). Although the United States is generally considered to be iodine sufficient, recent data from the National Health and Nutrition Examination Survey have indicated that the median urinary iodine concentration for pregnant women in the United States is <150 μg/L (8), consistent with mild iodine deficiency (7). Furthermore, the prevalence of iodine deficiency varies according to poverty

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level, ethnicity, and geographic area (9), suggesting that the prevalence might be even greater in certain populations.

Young infants may be particularly vulnerable to the effects of even mild iodine deficiency because intrathyroidal iodine stores are only about 300 μg at birth, and daily thyroid hormone turnover rates per body weight in infancy are higher than at any other time of life (10). In bottle-fed infants, the only source of nutritional iodine prior to the introduction of complementary foods is infant formula. The recommendations for adequate intake levels by the U.S. Institute of Medicine for daily iodine intake are 110 μg/d for infants 0–6 months and 130 μg/d in infants 6–12 months of age (11).

Iodine nutrition among U.S. infants has not been rigorously examined. We recently reported a median urinary iodine concentration of 197.5 μg/L consistent with iodine sufficiency (7), in 64 exclusively and partially breastfed Boston-area infants less than 3 months of age (12). Among 10 banked human breastmilk samples, the mean iodine content was relatively low at 59.5 ± 28.7 μg/L (mean $\pm$ SD) (13), while the mean iodine content in eight commonly available U.S. infant formulas was 23.5 ± 13.4 μg/5 oz (158.9 ± 90.6 μg/L) (14). Eight of the 10 banked human breastmilk samples were calculated to provide less than 90 μg/d (13), the recommended daily iodine intake for a 2-month-old infant, assuming an intake of 30 oz/d (i.e., $\sim$900 mL/d) (15).

The present study measured and compared the urinary iodine concentrations as a marker of iodine nutritional status among breastfed and formula-fed infants less than 3 months of age in the Boston area.

Patients and Methods

Ninety-five healthy, full-term infants less than 3 months of age, evenly stratified by the type of primary diet (breastfed or formula-fed), at two Boston-area outpatient private pediatric clinics were recruited during routine well-baby visits. This was a pilot study, and infants were recruited consecutively on the days when a study investigator was available to enroll at the clinics. Infants or mothers who were taking any iodine-containing medication or supplements, had recent exposure to iodine-containing skin antiseptics, or had recently received iodinated contrast dyes were excluded. Informed consent was obtained from a parent of each infant, and study approval was obtained from the local Institutional Review Board.

Infants' mothers completed a questionnaire detailing maternal age, race/ethnicity, birthplace, marital status, highest level of education, gravidity, parity, smoking history, dietary history for common iodine-containing foods over the past 24 hours, and use of vitamin and mineral supplements. Infants' weight and a focused infant dietary history, including amount of breastfeeding and/or formula feeding, estimated total amount of infant formula ingested daily over the previous 3 days, and infant formula brand, were obtained by a questionnaire completed by the infants' mothers. Recent maternal dietary intake of foods naturally containing low levels of thiocyanate, a weak inhibitor of the thyroid and lactating breast sodium–iodide symporter that can reduce iodine uptake into the thyroid gland and breastmilk, was ascertained.

A single spot urine specimen was collected from each infant. Urine samples were collected using the method of Dorey and Zimmermann (16), in which an adhesive diaper pad (Newcastle sterile urine collection packs, Ontex, Corby, United Kingdom) was attached to the inside of a disposable diaper and the urine extracted using a disposable syringe. Urine specimens were stored at -20°C until assayed. Urine iodine concentrations were measured spectrophotometrically using a Technicon Autoanalyzer (Technicon Instrument, Inc., Tarrytown, NY) with a modification of the method of Benotti *et al.* (17). Iodine concentrations from all samples were measured at least twice. In cases in which the initial two measurements were not within 15% of each other (<1% of samples), a third or a fourth measurement was obtained and the average of all measurements was used. Using two controls (concentrations 50 and 485 μg/L), the interassay coefficient of variation for this assay in our laboratory ranges from 2.7% to 7%. Methodology in our laboratory has been certified using the Centers for Disease Control and Prevention EQUIP (Ensuring the Quality of Urinary Iodine Procedures) program. Descriptive statistics are reported as means, medians, ranges, standard deviations, interquartile ranges (IQRs), and frequencies. Comparisons between median urinary iodine concentrations were assessed using the Kruskal-Wallis test. Associations between infant urinary iodine concentrations and maternal and infant descriptors were assessed using Spearman's correlation coefficient, Kruskal-Wallis, and Wilcoxon rank sum tests as appropriate. Data analysis was performed using SAS 9.3 (SAS Institute, Cary, NC).

Results

Subject descriptors ($n = 95$) are shown in Tables 1 and 2. Infants' mothers were primarily Caucasian, born in the United States, married, well educated, and nonsmokers. The majority of mothers (86%) followed unrestricted diets. In the 24 hours prior to infant urine collection, 74% of mothers consumed bread, 65% consumed cheese, 59% consumed cow's milk, 37% consumed yogurt, 33% consumed eggs, 30% consumed ice cream, 9% consumed soy milk, 16% consumed saltwater fish, 14% consumed bagels, 10% consumed shellfish, 10% consumed soy sauce, and 5% consumed frozen yogurt. Mothers reported minimal recent consumption of foods naturally containing thiocyanate, including cauliflower, cabbage, and cassava. Twenty-five percent of mothers reported a family history of thyroid disease that was primarily hypothyroidism (47%). Three mothers had hypothyroidism and were taking levothyroxine.

Forty-seven percent of the infants were exclusively breastfed, 42% were exclusively formula-fed, and 11% were both breastfed and formula-fed (Table 2). Exclusively formula-fed infants ingested an average of 74.2 ± 39.4 (SD) ounces formula (2194 ± 1165 mL), while infants who consumed both formula and breastmilk ingested a mean of 27.9 ± 34.5 (SD) ounces formula (825 ± 1020 mL) over the past 3 days.

The overall median infant urine iodine concentration was 197.5 μg/L (range 40–897.5 μg/L). Median infant urine iodine concentrations were similar between infants who were breastfed (203.5 μg/L; range 61.5–395.5 μg/L), formula-fed (182.5 μg/L; range 40–897.5 μg/L), and both (197.8 μg/L; range 123–592.5) ($p = 0.88$). There were no significant associations between infant urinary iodine concentrations and maternal race/ethnicity, country of birth, marital status, highest level of education, active and secondhand cigarette smoke exposures, salt use (regularly and in the past 24 hours),

Table 1. Maternal Descriptors ($N=95$)

	n (%)
Age, years ($n=88$)	32.9 ± 5.6[a]
Race/ethnicity ($n=91$)	
Caucasian	56 (62)
Asian	9 (10)
African-American	8 (9)
Other	16 (18)
Declined	2 (2)
Birthplace ($n=90$)	
United States	61 (68)
Abroad	29 (32)
Marital status ($n=91$)	
Single, never married	13 (14)
Married	76 (84)
Divorced	2 (2)
Highest level of education ($n=91$)	
Less than high school	3 (3)
High school	13 (14)
College	19 (21)
Graduate/professional degree	51 (56)
Other	5 (5)
Gravidity ($n=93$)	2.2 ± 1.4
Parity ($n=93$)	1.8 ± 1.1
Cigarette use during pregnancy ($n=92$)	3 (3%)
Secondhand smoke exposure during pregnancy ($n=89$)	5 (6%)
Cow's milk ingestion ($n=80$)	54 (59%)
Table salt use ($n=92$)	
Regular	62 (68)
Not regular	30 (33)
Type of table salt use in the past 24 hours ($n=53$)	
Iodized	35 (66)
Noniodized	5 (9)
Do not know	13 (25)
Multivitamin use ($n=92$)	
Yes	58 (63)
No	34 (37)
Multivitamin type ($n=61$)	
Prenatal	50 (84)
Regular	8 (13)
Do not know	2 (3)
Multivitamin taken in the past 24 hours ($n=62$)	
Yes	36 (58)
No	26 (42)
Kelp or iodine use as supplements ($n=87$)	0

Number of subjects in each row may not correspond to the subject total given missing or declined questionnaire data, and percentages may not total 100 due to rounding. The median urinary iodine concentrations for each variable are unreliable and thus are not listed because of the small sample sizes.
[a]Mean ± standard deviation (SD).

Table 2. Infant Descriptors ($N=95$)

	n (%)
Infant age, months ($n=92$)	2.1 ± 0.2[a]
Sex ($n=94$)	
Female	59 (63)
Male	35 (37)
Weight, kg ($n=94$)	5.4 ± 0.7[a]
Length, cm ($n=85$)	60.5 ± 10.4[a]
Infant diet ($n=93$)	
Breastmilk only	44 (47)
Infant formula only	39 (42)
Both	10 (11)
Total formula ingested over the past 3 days ($n=40$)	64.1 ± 42.3 oz (1896 ± 1251 mL)[a]

Number of subjects in each row may not correspond to the subject total because of missing or declined questionnaire data.
[a]Mean ± SD.

multivitamin use (regularly and in the past 24 hours), infant weight, and infant length (Table 3). Among the breastfed infants, there were no significant associations between infant urinary iodine concentrations and recent maternal ingestion of common iodine-containing foods, except for milk, which was positively associated ($p<0.01$). The median urinary iodine concentrations among infants whose mothers ingested milk in the previous 24 hours were the following: breastfed infants ($n=44$; 182.5 μg/L); formula-fed infants ($n=39$; 203.5 μg/L); both infant diets ($n=10$; 197.8 μg/L) ($p<0.01$).

Discussion

Our findings provide novel data regarding the iodine status of infants in the Boston, Massachusetts, area of the United States. These data are also the first comparison of iodine nutrition in breastfed and formula-fed U.S. infants less than 3 months of age, and add to the limited data regarding the iodine status of exclusively and partially breastfed infants in the United States (12). Both breastfed and formula-fed infants had median urinary iodine concentrations above the minimal threshold of 100 μg/L, demonstrating that both groups were iodine sufficient (7).

The present findings provide a preliminary understanding of iodine nutrition among newborn U.S. infants, one of the most vulnerable subgroups at risk for mild iodine deficiency. In China, a country that is generally considered to be iodine sufficient (7), urinary iodine levels were measured in 97 infants who were either breastfed, formula-fed, or both between 2001 and 2002 (18). Exclusively formula-fed infants had a significantly lower median urinary iodine concentration than infants who were exclusively breastfed (122 vs. 183 μg/L, respectively) (18), although both groups were iodine sufficient (7). Between 2005 and 2009, Andersson *et al.* (10) studied iodine nutrition among 3- to 4-day-old and 6- to 12-month-old infants in Switzerland who were either exclusively breastfed; fed partially with breastmilk, infant formula, and/or home-prepared formula/foods; or exclusively fed with home-prepared formula/foods. Although the Swiss population is also considered iodine sufficient (7), the overall median urinary iodine concentration was 98 μg/L in the infants, consistent with mild iodine deficiency (7). Infants who ingested infant formula (exclusively or in addition to breastmilk) had significantly higher urinary iodine concentrations than those who were exclusively breastfed (109 vs. 70 μg/L; $p<0.01$) (10). These data are in contrast to our findings that show no difference in median urinary iodine concentrations of infants stratified by type of feeding. Reasons accounting for the discrepancy of the observed findings with previous studies may include the wide range for

Table 3. Associations of Infant Urinary Iodine Concentrations with Maternal and Infant Descriptors

	Breastfed		*Formula-fed*	
	n	p	n	p
Maternal race/ethnicity	43	0.13	37	0.27
Maternal country of birth	43	0.40	36	0.08
Maternal marital status	43	0.51	37	0.28
Maternal level of highest education	43	0.39	37	0.40
Maternal cigarette smoke exposure during pregnancy (active and secondhand)	44	0.70	39	0.27
Maternal milk ingestion in the past 24 hours	44	<0.01	37	0.05
Maternal table salt use in the past 24 hours	23	0.45	23	0.92
Maternal use of multivitamins regularly	44	0.61	37	0.97
Maternal multivitamin use in the past 24 hours	36	0.62	16	0.87
Infant weight	44	0.78 ($r=0.04$)	39	0.20 ($r=-0.21$)
Infant length	41	0.82 ($r=-0.041$)	33	0.20 ($r=-0.23$)

Number of subjects in each row may not correspond to the subject total because of missing or declined questionnaire data. Data for infants fed both diets are not shown because of the small size of this group.

acceptable iodine content of infant formula, the varied sources of iodine nutrition in the mothers and infants, and the relatively small sample sizes of the available studies.

Our results demonstrate no associations between infant urinary iodine concentrations and most factors related to multiple maternal and infant variables. Among the breastfed infants, the significant association between infant urine iodine concentrations and maternal consumption of milk in the previous 24 hours suggest that certain dietary factors may be particularly important during lactation. Our recent study of 64 Boston-area mother–infant pairs showed a significant positive correlation between iodine concentrations in breastmilk and infant urine iodine (12).

The recommendations for dietary iodine among infants less than 1 year old, termed adequate intake levels, are based on limited studies describing median breastmilk iodine concentrations, given the paucity of evidence for optimal iodine nutrition in this age range (11). A quantitative assessment of the exact sources of dietary iodine among young infants is lacking. In the United States, the regulations for iodine content of formula for full-term infants ranges from 5 to 75 μg/100 kcal (33.5–507.2 μg/L) (19). We previously measured the iodine content in eight U.S. infant formula brands; values ranged from 16.2 to 56.8 μg per 5 oz (148 mL) serving, which was often higher than the labeled amount (14), similar to the findings by Nichols *et al.* (20) regarding two brands of U.S. infant formula studied longitudinally between 1981 and 1997.

The current study was based on a Boston-area convenience sample, and our findings may not be representative of the larger U.S. general population. Although the iodine content of the mothers' urine and breastmilk samples and the infant formulae were not measured to support the reasons for our study samples' iodine sufficiency, the present findings demonstrate that Boston-area infants have adequate iodine nutrition. This study presents the most complete available data regarding U.S. infant iodine nutrition available.

Conclusion

As infants are reliant on adequate maternal breastmilk iodine nutrition and/or iodine-supplemented formula during the first few months following birth, our data are reassuring and demonstrate iodine sufficiency in both U.S. breastfed and formula-fed infants. Further data are needed to support the recommendations for dietary iodine intake among infants less than 1 year old. Future research should include larger nationwide population-based studies examining the iodine sufficiency of infants during this critical period of early development.

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Author Disclosure Statement

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