Original Article

Breast milk and infant iodine status during the first 12 weeks of lactation in Tianjin City, China

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Background and Objectives: The present study investigated the iodine status of breast milk and breast-fed infants during the first 12 weeks postpartum in Tianjin, China. **Methods and Study Design:** A total of 175 pregnant women were recruited before delivery. Their breastmilk and 24-h urine samples were collected at 4, 8, and 12 weeks postpartum; spot urine samples were simultaneously collected from their infants. The iodine content of the samples was measured. **Results:** The mean breast milk iodine concentrations (BMICs) at 4, 8, and 12 weeks were 221.7±103.5 µg/L, 175.2±76.2 µg/L, and 148.1±66.2 µg/L, respectively. Significant differences existed between the mean BMICs of the three sampling times (F=12.449, p<0.001). The BMIC showed a decreasing trend during the first 12 weeks postpartum. The median urinary iodine concentrations (UICs) of the mothers were 152, 112, and 109 µg/L at the different sampling times. The BMIC and UIC were not correlated in the mothers. The median UICs in the infants were 251, 183, and 164 µg/L. The infant UICs were statistically different at the three sampling times (p=0.001). Moreover, the infant UICs correlated with the BMICs (Rs=0.205, p=0.010) but not with the maternal UICs (Rs=0.131, p=0.067). **Conclusion:** The BMIC in and infant iodine intake from breast milk decreased in the first 12 weeks. Breastfed infants could receive adequate iodine from breast milk in Tianjin City.

Key Words: iodine status, breast milk, lactating women, infant, urine

INTRODUCTION

Iodine is a trace element required for biosynthesizing thyroid hormones, which are necessary for normal growth and neuro development. Iodine is obtained solely from external sources.[1] The brain grows rapidly in the first 2 years of life; therefore, an inadequate supply of iodine can limit the production of iodine-containing hormones, leading to abnormal brain development that can subsequently manifest itself in impaired cognitive and psychomotor functions.[2-5] The WHO recommends exclusive breastfeeding of infants for 6 months after birth.[6] For infants fed only with breast milk, the iodine intake solely relies on the BMIC. To ensure that breastfed infants receive adequate iodine from breast milk, mothers should have an optimal iodine status.

In 1992, China had the world's largest iodine-deficient population.[7] This situation changed when a political decision in 1993 mandated that all salt for human consumption be adequately iodized. The median UIC of school-aged children in 18 provinces exceeded 300 µg/L in 1997 and that of children in 14 provinces also exceeded 300 µg/L in 1999.[8,9] However, infants and lactation did not get enough attention in China. The current reference nutrient intake (RNI) of iodine for lactation is 250 µg/d, established by the WHO, International Council for Control of Iodine Deficiency Disorders (ICCIDD), and UNICEF; in China, the RNI of iodine is 240 µg/d for mothers and 85 µg/d for infants younger than 6 months.[10] The BMIC in countries with an optimal iodine status typically ranges from 150 to 180 µg/L;[11,12] however, the BMIC in countries with a suboptimal iodine status is often as low as 50 g/L and is unlikely to supply infants with an adequate iodine dose.[13]

The present study determined the BMIC and 24-h UIC in mothers and the UIC in their infants during the first 12 weeks postpartum as well as the correlation between these factors. This study provides additional information on changes in the BMIC and UIC during lactation, which may optimize diet for lactation and reduce the risk of io-

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dine deficiency happening to lactation or infants.

PARTICIPANTS AND METHODS

Participants

This study analyzed data from the KNHANES VI (2013–2014), a cross-sectional and nationally representative survey conducted between 2007 and 2014 by the Korea Centers for Disease Control and Prevention (KCDC). This study complied with the provision of the Helsinki declaration and was approved by KCDC (Institutional Review Board numbers: 2013–07CON-03-4C and 2013-12EXP-03-5C). Signed Informed consent was obtained from all individual participants included in this study. Participants who completed 24-h dietary recall interviews were included; of them, individuals with daily energy intake of <500 or >5,000 kcal were excluded.

Sample collection

We collected 24-h urine samples from all mothers and spot urine samples from the infants at 4, 8, and 12 weeks postpartum; breast milk samples were collected from the mothers at 4, 8, and 12, weeks postpartum. Foremilk samples were collected through manual expression from both breasts and were stored in deiodinated glass vials. Before collection, the mothers' nipples were cleaned with deionized water. After collection, the mothers were requested to store the samples in their home freezer until collection by a research assistant. Furthermore, 24-h urine samples were collected in polyethylene bottles, which were cleaned with deionized water; subsequently, the urine volume was carefully measured. Two aliquots were taken from each sample and preserved in 5-mL centrifuge tubes. The used polyethylene bottles were cleaned with deionized water again and returned to the mothers for the next collection. In addition, 24-h urine samples reported to be complete or to have a single missed void were considered acceptable. Urine volumes of the samples were carefully measured, and two aliquots were extracted from each sample. Urine samples from the infants were collected in an adhesive pediatric urine bag or directly into a specimen container. Urine and milk samples were stored at 4°C and −20°C, respectively, until laboratory analysis.

Laboratory analysis

The BMIC was measured in duplicate through inductively coupled plasma mass spectrometry (ICP-MS, PerkinElmer Inc., Hopkinton, MA, USA), as previously reported by Sturup and Buchert.[14] Briefly, 3-g breast milk samples were digested with 1.5 mL of tetramethylammonium hydroxide and 0.4 mL of hydrogen peroxide by using an ultrasonic method at 60°C for 3 h. After cooling, the digestion solution was diluted with 25 mL of deionized water and subjected to ultracentrifugation. The supernatant liquid was filtered with 45-μm filter membranes and analyzed through ICP-MS, with internal standard calibration. The average recovery rate was 99%, and the coefficient of variation was 3.1% (n=95). The UIC was determined at the Key Laboratory of Hormone and Development (Ministry of Health), Metabolic Diseases Hospital and the Tianjin Institute of Endocrinology, Tianjin Medical University. Ammonium per sulfate digestion with spectrophotometric detection of the Sandell–Kolthoff reaction was performed for measuring the UICs.

Statistical analysis

Normally distributed data are expressed as means [mean±standard deviation (SD)]; nonnormally distributed data are expressed as medians (25th–75th percentiles).The Kolmogorov–Smirnov test was performed to assess sample normality. Differences in normally distributed data were compared by performing one-way ANOVA. The least significant digit posthoc comparison test was used to examine different mean pairs. Furthermore, the Kruskal–Wallis test was used for comparing on normally distributional sample values, namely the maternal and infant UICs. The Mann–Whitney rank test was used for pairwise comparisons. The maternal urinary iodine excretion (UIE) was calculated by multiplying the maternal 24-h UIC with the urine volume for the samples that were considered complete.

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, Version 21.0 for Mac, IBM Corp., Armonk, NY, USA) and Graph Prism (Version 6.0c for Mac, Graph Pad Software, La Jolla California USA, www.graphpad.com.). The significance level was set at a two-tailed p value of <0.05.

RESULTS

Among the 175 pregnant women who participated in the current study, 106 were successfully followed up at the three sampling times. No significant differences existed between the participants who were enrolled and those who withdrew from this study. Table 1 presents the demographic characteristics of the mothers and their infants.

The mean±SD of BMICs at 4, 8, and 12 weeks were 221.7±103.5 μg/L, 175.2±76.2 μg/L, and 148.1±66.2 μg/L, respectively. The mean BMIC sat the three sampling times were significantly different (F=12.449, p<0.001). There were 4, 8, and 14 values of BMIC less than 100 μg/L, at the three sampling times, respectively (Table 2).

At 4, 8, and 12 weeks, the median (25th–75th percentiles) UICs of the mothers were 152 μg/L (118–203 μg/L), 112 μg/L (83–160 μg/L), and 109 μg/L (71–169 μg/L), respectively. Hence, the entire population was considered marginally iodine sufficient. However, considerable variation existed among all maternal UICs, ranging from 24 μg/L to 489 μg/L (Table 3). No significant differences existed between the complete and incomplete samples at week 8 (114 μg/L vs 112 μg/L; p=0.716) and week 12 (115 μg/L vs 107 μg/L; p=0.894), but a significant difference was observed at week 4 (176 μg/L vs 136 μg/L;

Table 1. Subject characteristics

	Value (mean±SD)
Mothers (n=106)	
Age(year)	27.2±3.0
Height (cm)	163.9±3.5
Weight (kg)	67.5±17.9
Infants (n=84)	
Male, n (%)	45 (42.5)
Birth weight (g)	3559±656
Birth Length (cm)	50.7±2.2

Table 2. Distribution of the breast milk iodine concentration at three sampling times†

	wk 4			wk 8			wk 12		
(μg/L)	BMIC (*n*=87)	Maternal UIC (*n*=88)	Infant UIC (*n*=77)	BMIC (*n*=60)	Maternal UIC (*n*=75)	Infant UIC (*n*=56)	BMIC (*n*=51)	Maternal UIC (*n*=68)	Infant UIC (*n*=61)
<100	4 (4.6)	9 (10.2)‡	4 (5.2)	8 (13.3)§	28 (37.3)¶	6 (10.7)	14 (27.5)‡	30 (44.1)††	8 (13.1)
100~200	44 (50.6)	56 (63.6)	19 (24.7)	33 (55.0)	39 (52.0)	25 (44.6)	28 (54.9)	23 (33.8)	30 (49.2)
>200	39 (44.8)	23 (26.1)	54 (70.1)	19 (31.7)	8 (10.7)	25 (44.6)	9 (17.6)	15 (22.1)	23 (37.7)

wk: week; BMIC: breast-milk iodine concentration; UIC: urinary iodine concentration.
†Data were represented as real number (percentage).
‡Four values less than 50 μg/L.
§One value less than 50 μg/L.
¶Five values less than 50 μg/L.
††Eight values less than 50 μg/L.

Table 3. Iodine nutritional status of lactation and infants at three sampling times

	wk 4		wk 8		wk 12		*p*
	n	Value†	n	Value†	n	Value†	
BMIC (μg/L)‡	87	221.7±103.5	60	175.2±76.2	51	148.1±66.2	<0.001*
Maternal UIC(μg/L)§	88	152 (118–203)	75	112 (83–160)	68	109 (71–169)	0.000*
Maternal UV (mL)‡	44	1042.2±385.1	32	1313.0±467.5	25	1124.6±473.8	0.393
Maternal UIE(μg/d)‡	44	171±124	32	135±94	25	132±90	0.225
Infant UIC (μg/L)§	77	251 (183–323)	56	183 (134–242)	61	164 (116–221)	0.001*

wk: week; BMIC: breast-milk iodine concentration; UIC: urinary iodine concentration; UV: urinary volume; UIE: urinary iodine excretion.
†Data were represented as mean±SD or median (25th–75th percentiles);
‡Calculated using a one-way ANOVA. LSD was used for post hoc comparison;
§Calculated using a Kruskal-Wallis one-way ANOVA on ranks test in groups. Mann-Whitney rank test was performed for pairwise comparisons;
*Differences were between week 4 and the other two sampling time points.

p=0.043). The maternal UICs at the three sampling times between weeks 4 and 8 (p=0.001) as well as weeks 4 and 12 (p=0.010) significantly varied; however, no statistical difference existed between weeks 8 and 12 (p=0.597). The mean 24-h UIE was 171±124 μg/L (n=44), 135±94 μg/L (n=32), and 132±90 μg/L (n=25) at 4, 8, and 12 weeks, respectively. The mean 24-h UIEs were not significantly different (F=1.514, p=0.225).

A moderate correlation existed between the BMICs and maternal UICs at week 4 (r=0.313, p=0.007), but not at week 8 (r=0.154, p=0.261) or week 12 (r=0.093, p=0.552). The distribution of the 24-h urine volume values at the three sampling times conforms to the normal distribution law. The mean 24-h urine volumes at the three sampling times were 1042.2±385.1 mL (n=44), 1313.0±467.5 mL (n=32), and 1124.6±473.8 mL (n=25).

The median (25th–75th percentiles) UICs of the infants at the three sampling times were 251 μg/L (183–323 μg/L), 183 μg/L (134–242 μg/L), and 164 μg/L (116–221 μg/L); these UICs were significantly different (p=0.001). The infant UICs showed a significant positive correlation with the BMICs at week 4 (r=0.363, p=0.003), week 8 (r=0.387, p=0.010), and week 12 (r=0.383, p=0.009; Figure 1). However, no correlation existed between the infant and maternal UICs. Data combinations on the scatter diagram revealed that 18 (11.6%) pairs had BMICs lower than 100 μg/L, but the infant UICs were not lower than 100 μg/L; 11 (7.1%) pairs had BMICs not lower than 100 μg/L, but the infant UICs were lower than 100 μg/L. Only three pairs of combined data were lower than 100 μg/L.

DISCUSSION

For breastfeeding infants, breast milk is the sole source of iodine intake. Therefore, an optimal iodine status of breast milk is essential for infants to synthesize adequate thyroid hormones for normal neurodevelopment. Despite increasing numbers of studies examining BMICs, no consistent recommendations have been established for an optimal iodine content of breast milk. The iodine concentration of 100–200 μg/L in breast milk has been considered as the optimallevel.[15,16] The mean iodine concentrations of 221.7, 175.2, and 148.1 μg/L at the three sampling times in our study, which meet or exceed the level, indicate the iodine content of breast milk could meet the requirement of infants. Liu et al conducted a cross-sectional study and stated that in areas of China with varying water iodine concentrations, the BMIC was 346 μg/L (n=91, 25th–75th percentiles: 208.7–449.5 μg/L)in iodine-sufficient areas, such as Fenyang City in Shanxi Province.[17] Moreover, the median UIC of mothers was 427 μg/L, higher than that determined in our study. However, the results obtained from Beihai City in Guangxi Province, an iodine-deficient counterpart of the city mentioned in the aforementioned study, showed an iodine content of 41.5 μg/L (25th–75th percentiles: 26.4–64.4 μg/L) in breast milk and 51.3μg/L (25th–75th percentiles: 28.1–73.7 μg/L) in maternal urine samples. BMICs of 100–200 μg/L have been reported in studies on mothers living in Western China, Thailand, Iran, and the United States.[18-21] Moreover, BMICs lower than 100 μg/L were reported in studies conducted in New Zealand, the United

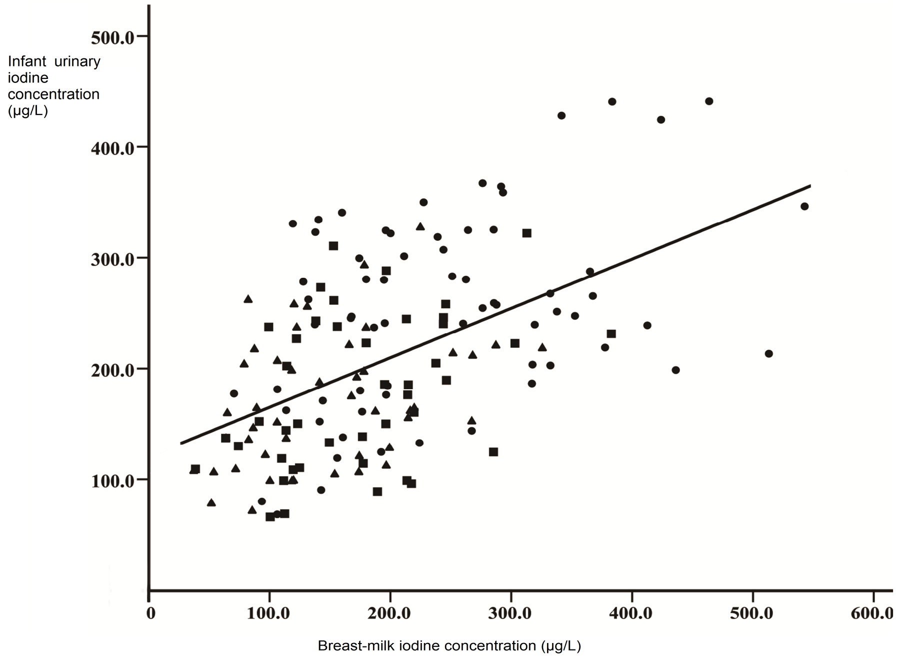

Figure 1. Breast-milk iodine concentration plotted against infant urinary iodine concentration (n=155 pairs) wk4 (●r=0.363, p=0.003), wk8 (■r=0.387, p=0.010), wk12 (▲r=0.383, p=0.009) and total (r=0.518, p<0.001). The prediction line was drawn on (y=0.445x + 120.6; R^2=0.2684, p<0.0001).

States, and Azerbaijan in the past decade.[21-23] Yan et al suggested various reasons for insufficient and sufficient iodine in breast milk, whereas most researchers have considered the consumption of iodized salt as one of the main reasons for a sufficient BMIC.[18,19,22] China has implemented universal salt iodization since 1993. A study reported that the median BMIC doubled after 2 years of mandatory consumption of 20 μg/g potassium iodide.[24]

In the present study, the BMICs significantly decreased in the postpartum period (F=12.449, p<0.001). Table 2 shows that the BMIC decreased by almost 50% at week 12. Furthermore, some researchers have reported a decrease in the BMIC in the first 6 months postpartum.[21] The breast milk volume increases in the postpartum period.[25] During lactation, the sodium iodide symporter mediates the active transport of iodide in the mammary gland; therefore, dietary iodine is secreted into breast milk rather than into urine.[26,27] Anther possible factor might be the practice of "sitting the month". During the first month postpartum, mothers tend to eat highly nutritious food, such as seafood with a high iodine content, to enhance breast milk secretion.

In our study, the maternal urinary iodine concentrations were slightly higher than the recommended standard of 100 μg/L established by the WHO, ICCIDD, and UNICEF for the three trimesters (152, 112, and 109 μg/L).[28] As shown in Table 2, the maternal UIC at week 4 was significantly higher than that at weeks 8 and 12. The main explanation for this phenomenon might be differences in the proportions of complete urine samples. More complete urine samples were collected at week 4(n=44, 50%) than at week 8 (n=32, 42.7%) and week 12 (n=25, 36.8%). Another reason for these differences may be the unique Chinese custom of sitting the month, which is practiced in the first month after delivery. Women are typically served by their family members and offered rich dishes.

The median UICs of 251, 183, and 164 μg/L at 4, 8, and 12 weeks postpartum in the infants were higher than the 100 μg/L cut off value, indicating an adequate iodine status.[28] In this study, no infants showed an UIC below this value (data not shown), clearly indicating that the iodine status of infants within the first 12 weeks is optimal in Tianjin.

The BMICs and infant UICs were significantly associated during the lactation period in the current study. Researchers from Azerbaijan (r=0.414, p=0.000) and China (r=0.526, p=0.000) have reported similar correlations between BMICs and infant UICs.[23,29] The infant daily iodine intake certainly depends on the maternal BMIC, for exclusively breastfeeding infants, because of the relatively fixed consumption of milk.[30] Therefore, the BMIC reflects the infant iodine status.

The BMICs and maternal UICs were significantly correlated at the first sampling time (r=0.313, p=0.007), but not at the second or third sampling times. In studies conducted in Iran and Azerbaijan, a moderate correlation existed between the BMICs and maternal UICs (Iran: r=0.44, p<0.0001 and Azerbaijan: r=0.414, p=0.000);[20,23] however, no 24-h urine samples were obtained nor were data analysed at different times in both the studies. Therefore, it is questioned whether the maternal urinary iodine level can be used to indicate the breastfed infant iodine status, regardless of the clear correlation between BMICs and maternal UICs. In addition, in the present study, the maternal and infant UICs were not significantly correlated; these results additionally reveal that the iodine status of mothers cannot reflect the status of infants. In a study conducted by Azizi, although the maternal UIC indicated sufficient iodine consumption, the BMIC remained lower than the cut off value. Therefore, their infants were at risk of iodine malnutrition.[31]

The study had limitations. Firstly, not all urine samples were completely collected at 24 h. The median UIC of spot urine samples is typically used to evaluate the iodine status of a population, whereas the 24-h UIE more efficiently reflects the individual situation.[32,33] Secondly, the sample size was relatively small, hindering us in providing a persuasive conclusion. Nevertheless, only a few studies have reported similar results in the postpartum stages in China. Due to difference in regions, and living condition, all the results and conclusions in this paper are applicable to the same population in Tianjin City, and to where lifestyle and diets and ethnic mixes are quite similar to Tianjin City. We have reviewed the researches between 2012 and 2016, and few studies have reported similar data about breast milk and infant iodine status for Tianjin City. Future studies should explore a more definitive breast milk iodine range for an optimal infant iodine status because the recommended range of 100–200 µg/L is considered too broad.

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AUTHOR DISCLOSURES
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