

ORIGINAL ARTICLE

Breastfeeding and maternal and infant iodine nutrition

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Summary

Objective The aim of this review is to explore information available regarding iodine secretion in milk, both mothers and infants iodine nutrition during breastfeeding and to make recommendations for appropriate iodine supplementation during lactation.

Design MEDLINE was queried for studies between 1960 and 2007 that included lactation and breastfeeding with iodine and iodine deficiency. Studies were selected if they studied (i) Secretion of iodine in breast milk; (ii) breastfeeding and iodine nutrition; (iii) factors affecting maternal iodine metabolism and (iv) recommendations for iodine supplementation during breastfeeding.

Results Thirty-six articles met the selection criteria. The iodine content of breast milk varies with dietary iodine intake, being lowest in areas of iodine deficiency with high prevalence of goitre. Milk iodine levels are correspondingly higher when programs of iodine prophylaxis such as salt iodization or administration of iodized oil have been introduced. The small iodine pool of the neonatal thyroid turns over very rapidly and is highly sensitive to variations in dietary iodine intake. Expression of the sodium iodide symporter is up-regulated in the lactating mammary gland which results in preferential uptake of iodide. In areas of iodine sufficiency breast milk iodine concentration should be in the range of 100–150 µg/dl. Studies from France, Germany, Belgium, Sweden, Spain, Italy, Denmark, Thailand and Zaire have shown breast milk concentrations of < 100 µg/l. Adequate levels of iodine in breast milk have been reported from Iran, China, USA and some parts of Europe.

Conclusions Adequate concentration of iodine in breast milk is essential to provide for optimal neonatal thyroid hormone stores and to prevent impaired neurological development in breast-fed neonates. In many countries of the world, low iodine content of the breast milk indicates less than optimum maternal and infant iodine nutrition. The current WHO/ICCIDD/UNICEF recommendation for daily iodine intake (250 µg for lactating mothers) has been selected to ensure that iodine deficiency does not occur in the postpartum period and that the iodine content of the milk is sufficient for the infant's iodine requirement.

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Introduction

The main changes in thyroid function associated with pregnancy are due to an increase in hormone requirements which begins in the first trimester of gestation, a transfer of T₄ and iodide from the mother to the foetus, and an increased loss of iodide due to increased renal clearance.^{1–3}

Following delivery, there is decrease in maternal and infant hormone requirements and transfer of T₄ and iodine from mother to foetus is no longer required.⁴ However, loss of iodide in breast milk occurs during lactation, causing an increase in dietary iodine requirement in the lactating mother.⁵ The infant also needs a supply of iodine for normal thyroid activity, vital for brain development in the first 2 years of life. The neonatal full-term thyroid gland contains about 100 µg of iodine under conditions of iodine sufficiency.⁶ The supply of iodine to the neonate and infant comes exclusively from breast or formula milk in the first 6 months of life and from milk/formula and complementary foods thereafter. The iodine demand of newborns is partly supported by thyroid-iodine storage during intrauterine life. At birth, an infant's thyroid gland, weighs approximately 1.8 g and can store 180 µg iodine/mg DNA.⁷

In this article we review iodine secretion in human milk, maternal and infant iodine nutrition during breastfeeding, and constitutional and environmental factors affecting maternal iodine metabolism during lactation, and we encompass recommendations for appropriate iodine supplementation during lactation.

Data source

The terms 'iodine and breastfeeding', 'iodine and lactation', 'iodine and human milk', both separately and in conjunction with the terms 'nutrition', 'maternal', and the terms 'breast milk iodine and urinary iodine', 'iodine deficiency, and iodine supplementation and lactation' were used to search MEDLINE for articles published between 1960 and June 2007. All abstracts were reviewed; studies published in English, French and German were included if appropriately designed. The articles of abstracts meeting criteria were then reviewed to identify details of materials related to breast iodine secretion,

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breastfeeding and iodine nutrition, factors affecting iodine metabolism and recommendations for iodine supplementation during breastfeeding. Recent unpublished recommendations of WHO were also included. The strategy used to search for articles was developed with the assistance of a research librarian at the Research Institute for Endocrine Sciences of Shaheed Beheshti University of Medical Sciences.

Study selection

The following criteria were considered essential to qualify an article for inclusion in this review:

1 Proper study design of survey, case control, cohort studies and clinical trials.

2 Review articles of prominent scholars.

Reviewers were not blinded to the study authors' names; this was done because we wished to include all pertinent studies. A deliberate strategy to limit bias was therefore employed. All articles were initially potential candidates for inclusion. Failure to provide appropriate study design resulted in exclusion of the article.

Of 89 articles identified, 66 articles (74%) were published between 1998 and 2007 and half of all 89 articles were published between 2003 and 2007. The above criteria resulted in the exclusion of 41 articles. Review of the remaining 48 articles led to identification of 36 articles with appropriate information and design, 3 reviews and 1 WHO recommendation.

Results

Maternal iodine nutrition

During pregnancy and lactation, the mammary gland's iodide concentrating mechanism appears to ensure an adequate supply of iodine to the newborn.⁸ Concentration of iodine in human milk is 20–50 times higher than that of plasma. Iodide transport is a sodium-dependent process mediated via the sodium iodide symporter (NIS) that can be blocked by perchlorate and thiocyanate.⁹ The NIS appears to control iodide uptake by the mammary gland, and its expression increases during lactation.¹⁰ Fig. 1 shows iodine secretion in human milk. NIS mediates iodide transport from blood of mother into the breast, and iodine appears in the breast milk, which is secreted upon influence of various hormones.

Following delivery, iodine concentration in human milk is approximately 200–400 µg/l in colostrum, but decreases during the next few weeks and remains steady in mature milk.⁶ The uptake of iodine by the mammary gland during lactation may reduce the maternal iodine pool in case of inadequate iodine status.¹¹ In the USA, the reported mean values for increased use of iodine by the bread and dairy industries have caused an increase in consumption of iodine and iodine concentration in mature human milk has varied considerably over the last 50 years.^{12,13} Therefore, mean iodine concentration in human milk had increased from 70 µg/l in the 1950s and 1960s¹⁴ to 110 µg/l in 1985.¹⁵ However a decline in urinary iodine excretion has recently been reported from the USA,¹⁶ later shown to have stabilized at a median of 167 µg/l.¹⁷ Therefore iodine intake may be borderline for a proportion of pregnant mothers

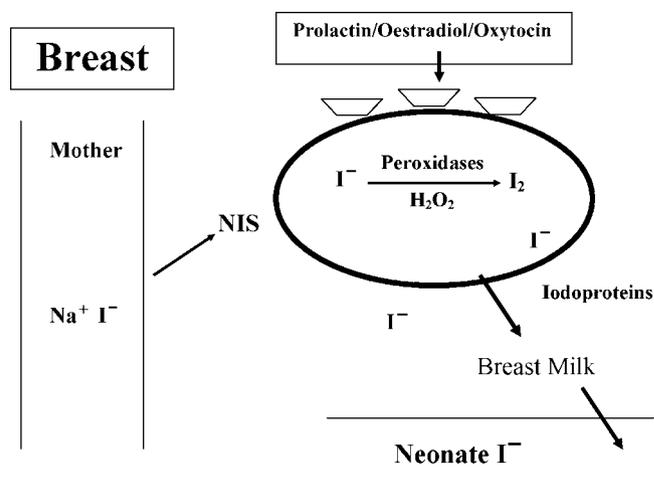


Fig. 1 Iodine secretion in human milk and the role of sodium iodide symporter (NIS). Mammary gland is controlled by NIS and its expression increases during lactation.

according to the recent WHO recommendations of 250 µg iodine intake per day for pregnant women.¹⁸

Iodine content of breast milk. Despite the importance of iodine to infant health, there are only few studies related to the iodine content of human milk in the scientific literature. These studies have shown that the mean iodine content of human milk is relatively low (9–32 µg/l) in women from areas with a high prevalence of goitre. However in areas where salt iodization programs have been implemented, iodine content of milk has increased. Table 1 shows iodine content of breast milk in studies with a minimum of 40 samples.

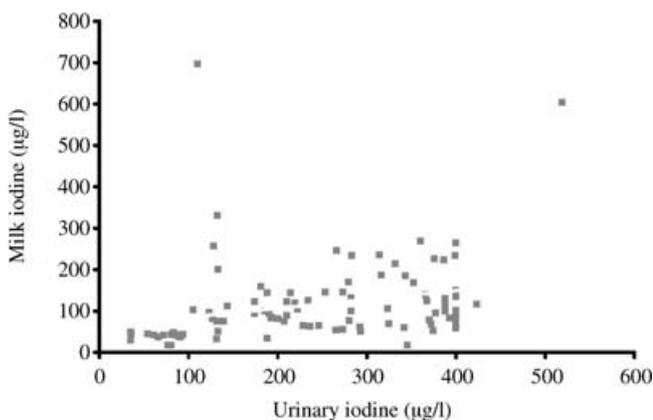
Effect of salt iodization. Breast milk iodine concentrations are higher in areas where iodized salt is consumed. Median concentrations of 146, 121, 92 and 146 µg/l have been reported from the USA, Iran, Sweden and China, respectively.^{13,19–21} It has been shown that 2 years of supplementation of 10–20 µg/potassium iodide per kilogram with salt doubled the median iodine concentration in breast milk.²² In Germany, breast milk iodine increased from 14 µg/l, in 1982, to 95 µg/l in 1996 as a result of maternal iodine prophylaxis.²³ However in Saudi Arabia, mothers consuming iodized salt showed a significant increase in urine iodine, whereas the increase in milk iodine was not significant.²⁴

Effect of iodized oil. A faster increase has been reported in urine iodine elevation rate from iodized fatty acid in ethyl-esters than from iodized fatty acids in triacylglycerol.²⁵ Iodine radiotracer studies have shown differences in iodine secretion due to the iodinated fatty acid,²⁶ indicating that the mobilization of fatty acid increases within saturation for a given chain length, and decreases with increasing chain length for a given unsaturation. Sharp increases in milk iodine after iodized oil administration was not affected by maternal intestinal parasites.²⁷

Effect of supplements. Median breast milk iodine concentrations were found to be higher among women who received supplements

Table 1. Iodine content of breast milk in studies with minimum of 40 samples

| First author | Year | Location | Number of samples | Mean or median breast milk iodine ($\mu\text{g/l}$) | Remarks | No. of reference |
|-------------------------|------|------------|-------------------|---|---|------------------|
| Etling and Gehin-Fouque | 1984 | Paris | 68 | 82 | | 67 |
| Heidemann | 1984 | Germany | 50 | 18 | Mothers with goitre | 37 |
| Biernaux | 1986 | Brussels | 91 | 95 | 5 days after delivery | 65 |
| Heidemann | 1986 | Gottingen | 41 | 25 | Recent salt iodization | 20 |
| | | Eskilstuna | 60 | 92 | Salt iodization present | |
| Delange | 1988 | Zaire | 143 | 13 | Severe goitre, not therapy | 64 |
| | | | 123 | 146 | Severe goitre, after iodized oil | |
| | | Jena | 55 | 12 | Endemic goitre | |
| Delange and Burgi | 1989 | Brussels | 91 | 95 | | 66 |
| | | Paris | 68 | 82 | | |
| | | Stockholm | 60 | 93 | | |
| | | Madrid | 69 | 77 | | |
| | | Freiburg | 41 | 25 | Area with endemic goitre | |
| | | Sicily | 59 | 27 | Area with endemic goitre | |
| Johnson | 1990 | Wellington | 57 | 126 | < 30 days after delivery | 32 |
| Nohr | 1994 | Denmark | 95 | 34 | No iodine supplements | 28 |
| | | | 53 | 57 | Iodine supplements | |
| Pongpaew | 1999 | Thailand | 75 | 51 | Rural northeast Thailand | 61 |
| Seibold-Weiger | 1999 | Germany | 40 | 55 | Without iodine supplements | 30 |
| Bazrafah | 2005 | Iran | 100 | 117 | Salt-iodization program, city of Gorgan | 19 |
| Yan Y.Q. | 2005 | China | 710 | 146 | Salt iodization program | 21 |
| Pearce | 2007 | Boston | 57 | 155 | Salt iodization | 62 |
| Ordookhani | 2007 | Iran | 48 | 148 | Salt iodization program, Tehran | 63 |

**Fig. 2** Scatter plot showing moderate correlation between urinary iodine and milk iodine values in 142 lactating mothers from Iran ($r = 0.40$, $P < 0.01$), unpublished data.

containing iodine compared with women controls;²⁸ however, another study showed no impact of iodine supplementation upon milk iodine in well-nourished women.²⁹ None of these studies were randomized controlled clinical trials of iodine supplements, but rather, milk iodine concentrations were measured in women who reported use or no use of iodine supplements during pregnancy. Higher breast milk iodine concentration was reported among mothers who took 200 μg iodine daily during pregnancy, but compliance and duration of supplementation were not described.³⁰

Factors affecting breast milk iodine

Maternal constitutional factors. Some studies have shown no significant correlation between breast milk iodide and the infant's age,¹³ and no significant differences due to stage of lactation,^{24,31} but others have found a significant decrease in 60- and 90 day milk iodine.^{32,33} No significant differences were observed for term and preterm,^{5,31} maternal age or for the length of lactation studied.³⁰ In addition, no significant differences have been observed due to the sampling time of the day,³² between individuals,¹³ between right and left breast or between fore- and hind milk.³⁴ However, substantial diurnal and day to day variation in breast milk iodine concentration has recently been reported.³⁵

In areas of iodine deficiency, there was no significant difference in milk iodine between treated and untreated goitrous mothers³⁵ and breast milk iodine in goitrous mothers may or may not show a significant decrease compared with controls.^{20,36} Therefore, it is reasonable to assume that a compensatory mechanism enhances iodine uptake by the mammary gland of iodine deficient mothers.

Environmental factors. Higher values of iodine concentrations in non-endemic goitre regions as compared to regions endemic for goitre have been reported in many studies.³⁷⁻³⁹ In areas of iodine sufficiency breast milk iodine concentration correlates with urinary iodine level¹⁷ (Fig. 2). It has been reported that in areas of high prevalence of goitre in children, breast milk iodine was also low. However, multicentre studies have shown that breast milk iodine

concentrations vary in many countries with the same degree of iodine sufficiency or iodine deficiency;⁴⁰ therefore environmental factors other than iodine depleted soil where crops are grown, may influence breast milk iodine concentration.

It has been shown that in an area of mild iodine deficiency, smoking was associated with decreased iodine content in breast milk and in the infant's urine, 5 days after delivery.⁴¹ This finding is consistent with thiocyanate inhibition of the function of NIS in the lactating mammary gland in smokers.

No seasonal variation has been noted in iodine concentrations in human milk.⁴² However, in the plains of Nepal with mild to moderate iodine deficiency, median urinary iodine in lactating women was higher in April–June and dropped to levels of moderate iodine deficiency during other seasons of the year.⁴³

Iodine status of breast-fed infant

The human infant is sensitive to maternal iodine nutrition during foetal and neonatal development. This is reflected in a strong and positive correlation between both iodine in urine and thyroid volume in neonates, with breast milk concentration.^{28,44}

Many factors may influence iodine nutrition of infants in the first year of life. In breast-fed infants breast milk iodine concentration and in bottle-fed infants iodine supplementation are the key elements in infants' iodine nutrition.^{44–47} In countries with the lowest breast milk iodine concentration, urinary iodine values are low in breast-fed infants⁴⁵ and the greatest reduction is seen in exclusively breast-fed, as compared to formula or partially bottle-fed infants.⁴⁴ Infants fed with formula supplemented by iodine, showed higher urinary iodine concentration than breast-fed infants at 3 months of life.⁴⁷ In iodine deficient regions, median urinary iodine from breast feeding infants was significantly greater than in formula fed infants with non-supplemented iodine.^{3,48} Children who consume infant formula, enriched with iodine, have better iodine status than breast-fed infants.⁴⁹ In addition, serum T4 and T3 concentrations are significantly higher in breast-fed as compared to formula-fed term and preterm infants.^{50,51}

It is noteworthy that even if iodine has not been stored in the thyroid during foetal development, the newborns demand is quite sufficiently provided by breast milk. Iodine and thyroid hormones in breast milk are well-absorbed and may prevent impaired neurological development in the euthyroid infant.⁵² Therefore, even in circumstances of low total iodine concentration in breast milk, its metabolic effect is superior to cow milk based formulas.

Requirements for iodine

In conditions of iodine sufficiency, iodine content of breast milk is 150–180 µg/l.^{5,53} Considering that milk production ranges from 0.5 to 1.1 l/day up to 6 months postpartum, the daily loss of iodine in a lactating woman is estimated to be approximately 75–200 µg/day. Therefore, the iodine requirement during lactation is 225–350 µg/day.¹

The requirement of iodine in neonates has been estimated by the value, which resulted from a status of positive balance to ensure a progressively increased intrathyroidal iodine pool in the growing young infant. This amount is calculated to be at least 15 µg/kg in

Table 2. Recommended iodine intake (µg/day) for pregnant and lactating women and infants in the first year of life*

| Subjects | Institute of medicine | World Health Organization | |
|---------------------|------------------------|---------------------------|------|
| | | 2001 | 2005 |
| Pregnant women | 160 (EAR) 220 (RDA) | 200 | 250 |
| Lactating women | 209 (EAR) 290 (RDA) | 200 | 250 |
| Infants 0–6 months | 110 (AI) | 90 | 90 |
| Infants 7–12 months | 130 (AI) | 90 | 90 |

*Revised and completed from Semba and Delange, 2001. EAR, estimated average requirement; RDA, recommended dietary allowance; AI, average intake.

Table 3. The median urinary iodine concentration for classification of the iodine status of pregnant and lactating women and children*

| Population group | Median urinary iodine concentration (µg/l) | Category of iodine intake |
|------------------------|--|---------------------------|
| Pregnant women | < 150 | Insufficient |
| | 150–249 | Adequate |
| | 250–499 | More than adequate |
| | ≥ 500 | Excessive |
| Lactating women | < 100 | Insufficient |
| | ≥ 100 | Adequate |
| Children < 2 years old | < 100 | Insufficient |
| | ≥ 100 | Adequate |

*Adopted from WHO, 2007.¹⁸

full term and 30 µg/kg in preterm infants per day, corresponding to 90 µg/day.¹ Table 2 shows recommendations for iodine intake for pregnant and lactating women and infants.

Assessment of iodine status

In their latest recommendation,¹⁸ WHO/ICCIDD/UNICEF proposed that a median level of more than 150, 100 and 100 µg/l urinary iodine should be considered for iodine sufficiency of pregnant, lactating women and children < 2 years (Table 3). In lactating women, the figures for urinary iodine are lower than daily iodine requirements because of iodine loss from breast milk. The exact cut-off for concentration of iodine in human milk has not been specified; however, values above 75 µg/l of milk may be considered as an index of sufficient iodine intake.

Iodine excess

Iodine-induced thyrotoxicosis and hypothyroidism may occur following excess iodine consumption.^{54,55} It has been shown that

iodine-induced thyrotoxicosis is rare in a well-executed IDD control program.⁵⁶ In rare circumstances, high milk iodine concentrations may pose risk of thyrotoxicosis to the breast-fed infant of mothers exposed to excess iodide in medications. Mothers consuming iodine-rich foods can concentrate even larger quantities of iodine in milk than in cases of iodine contamination from iodophors in antiseptic solutions. Consumption of iodine-rich seaweed is known to be associated with thyroid dysfunction and has been linked with increased prevalence of sub-clinical hypothyroidism.⁵⁷ However, there are no reports of adverse effects to the breast-fed infants, as is the case in the breast-fed infant with maternal supplementation with iodized salt or iodolipids supplementation. In fact, in underdeveloped countries with a high prevalence of IDD, maternal supplementation with iodized oil protected breast-fed infants from hypothyroidism for 3 years and could also decrease the mortality rate in such children.⁵⁸

Recommendations

In order to recommend suitable iodine intake for pregnant and lactating women and infants under 2 years of age, WHO/ICCIDD/UNICEF have divided all countries into three groups.¹⁸

Group 1. Countries with effective and sustained salt iodization. In this first group of countries, the population is considered iodine sufficient and therefore pregnant and lactating women have no need for iodine supplements. Children 0–24 months old do not require any iodine supplements either. Indeed the amount of iodine stored in the thyroid of the child at birth, when added to the iodine intake from mother's breast milk, is likely to be sufficient to meet the child's need for iodine for the first 6 months of life and even up to 24 months of age.

Group 2. Countries with uneven or lapsed iodized salt distribution. In this second group of countries iodine intakes are generally insufficient to meet iodine requirements and to protect the foetus and young child against the adverse effects of iodine deficiency, especially on brain development. Therefore, while measures should be taken to ensure that effective universal salt iodization is implemented in conjunction with a programme of public education, iodine supplementation is still needed for pregnant and lactating women and for young children. Supplements are also needed by women of child-bearing age to allow them to start pregnancy with enough stored iodine to meet both their own needs and the needs of their foetus. The following measures are recommended:

- Women of childbearing age should be given a daily oral dose of 150 µg of iodine as potassium iodide OR a single annual oral dose of 400 mg of iodine as iodized oil. At the same time, measures should be taken to educate this group about why and how to prevent iodine deficiency.
- Pregnant and lactating women should be given a daily oral dose of 250 µg of iodine as potassium iodide, either alone or in combination with other minerals and vitamins OR a single annual oral dose of 400 mg of iodine as oral iodized oil.
- Children aged 0–6 months should be given iodine supplements only if the mother was not supplemented during pregnancy or if the

child is not being breast-fed. The supplements should be given as soon after birth as possible. In this age group, iodine can be given as a daily oral dose of 90 µg iodine as potassium iodine OR as a single oral dose of 100 mg of iodine as iodized oil.

Group 3. Countries with weak or negligible iodized salt distribution. In this third group of countries, despite their poor iodine nutrition, populations do not receive any additional iodine in the form of supplements or in fortified foods. Such populations should be given supplements, focusing on pregnant women, lactating women, women of childbearing age, and children < 2 years old. Because such people may live in remote areas or may have suffered an emergency, it may not be possible to deliver a daily iodine supplement, and giving iodized oil may therefore be a better option. While giving such supplements, strong efforts should be made to establish or reinstate universal salt iodization and to ensure that iodized salt is distributed widely. The recommendations for this group are almost similar to those for group 2 countries.

It is interesting to note that the American Thyroid Association (ATA) recommends that women receive 150 µg iodine supplements daily during pregnancy and lactation. Although the median urinary iodine in the USA was 168 µg/l in 2001–2002, this recommendation is based on the fact that the lower 95% CI in this study was < 150 µg/l.⁵⁹

Conclusion

Breast milk is the single source of iodine for breast fed infants in many countries during the critical period of brain development and the concentration of iodine in breast milk constitutes another index of iodine nutrition. The current WHO/ICCIDD/UNICEF recommendation for daily iodine intake of 250 µg for lactating mothers has been estimated to ensure that iodine deficiency does not occur in the postpartum period and that the iodine content of the milk is sufficient for the infant's iodine requirement. In countries with effective and sustainable salt iodization programs, there is no need for iodine supplementation for pregnant and lactating women; However, further studies are still needed in this regard.⁶⁰ In countries with insufficient iodine intake, iodine supplementation should be given to pregnant and lactating women to protect the foetus and infants against the adverse effects of iodine deficiency, in particular on brain development. The optimum protective effect to ensure adequate iodine intake for pregnant and lactating women is the implementation and sustainability of universal salt iodization. Iodized oil may be used temporarily in areas with iodine deficiency, where iodized salt is not available or the program has failed.

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