views
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The Micronutrient Composition of Human Milk

Current knowledge and information gaps

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There is no doubt that breast milk is the optimum food for the infant; evidence continues to accumulate about its protective and development-promoting properties, especially now that analytical techniques, such as mass spectrometry, are revealing human milk constituents that support healthy gut microbiota.[1] However, surprisingly little attention has been paid to the micronutrient content of breast milk, even though it is recommended that infants should depend on it as their sole source of micronutrients for six months, and as an important source for two years or beyond.[2]

There are several reasons for this lack of scrutiny: Lactating women often receive relatively little attention from the health care system, which focuses on pregnancy but shifts postpartum to the infant and not the mother; there is little interest in questioning whether human milk is the perfect food in all situations; poor growth or micronutrient status of infants during the first six months of life tends to be attributed to factors such as the premature introduction of other fluids or foods, infections, or *in utero* deprivation; and there is considerable uncertainty about the appropriate methods for breast milk collection, including timing during a feed, time postpartum, and circadian changes in composition. The human milk matrix also poses challenges for valid laboratory analyses.

Information on nutrient concentrations in human milk is useful for several purposes. One of the most important is to set recommended nutrient intakes for breastfeeding infants and young children. For those exclusively breastfeeding during the first six months postpartum, Adequate Intake (AI) recommendations by the Institute of Medicine, for example, are based on reported average or median concentrations of each micronutrient as reported in the literature, and an estimated milk consumption of 0.78 L/day.[3] During the second six months, the intake of milk is assumed to be 0.6 L/day, and most AIs are based on the average amount of each micronutrient consumed in milk plus the average amounts provided by complementary foods. The formulation of complementary foods is often based on the need to fill the gap between requirements and estimated intakes from breast milk while the child is still breastfeeding. The additional micronutrient requirements of lactating women are also based on the estimated amounts of each nutrient they secrete in milk.

> "Information on nutrient concentrations in human milk helps set recommended nutrient intakes for breastfeeding infants and young children, as well as lactating women"

It is important to know whether the amounts of micronutrients are inadequate in the milk of women with poor micronutrient status or low intake, and to what extent this can affect infant micronutrient status and development. Maternal requirements for most micronutrients are higher in lactation than they are during pregnancy. Some 10 years ago, we defined two groups of micronutrients in the context of lactation.[4] The concentrations of Group I nutrients in milk – and subsequently the status of the infant – are affected by maternal status or intake; maternal inadequacy of these nutrients could result in infant depletion, but maternal supplementation or food fortification could increase milk levels. Based on updated information and as shown in **Table 1**, Group I nutrients include thiamin, riboflavin, niacin;

TABLE 1: Micronutrient groups during lactation[a]

Group I	Group II
Thiamin (B_1), riboflavin (B_2),	Folate
pyridoxine (B_6), cobalamin (B_{12})	Vitamin E
Vitamins A, D and K	Calcium
Choline	Iron, copper, zinc
Iodine	
Selenium	

[a]Group I micronutrients share the following characteristics in lactation: Their concentration in breast milk is affected by maternal status and/or intake so that the infant can become depleted if the status of the mother is inadequate. Supplements or fortification are likely to increase the levels in milk. Group II micronutrients in milk are relatively unaffected by maternal status or intake, and will be unaffected by maternal supplementation or fortification.

Washing red blood cells as part of the Diet-Mother-Milk-Infant (DMMI) project in Guatemala

vitamins B_{12}, A, D, and K; choline, iodine and selenium. Group II micronutrients include folate, probably vitamin E, and calcium, iron, copper and zinc. Amounts of these nutrients in milk will be independent of maternal status or intake, and increasing the mother's intake is unlikely to affect milk concentrations.

Status of current information

Our laboratory recently conducted a systematic review of micronutrients in human milk,[5] which revealed that the available data are sparse and often inadequate. Values from the literature used to estimate the AIs for infants and recommended intakes for their mothers have some major limitations. They were typically based on small numbers of milk samples collected at various times during lactation and at different times during a feed. It was not always clear whether mothers were well nourished or supplemented during pregnancy and/or lactation, and some laboratory methods of milk analysis were invalid.

"We need guidance on the collection and measurement of micronutrients in human milk in order to improve our data on its composition"

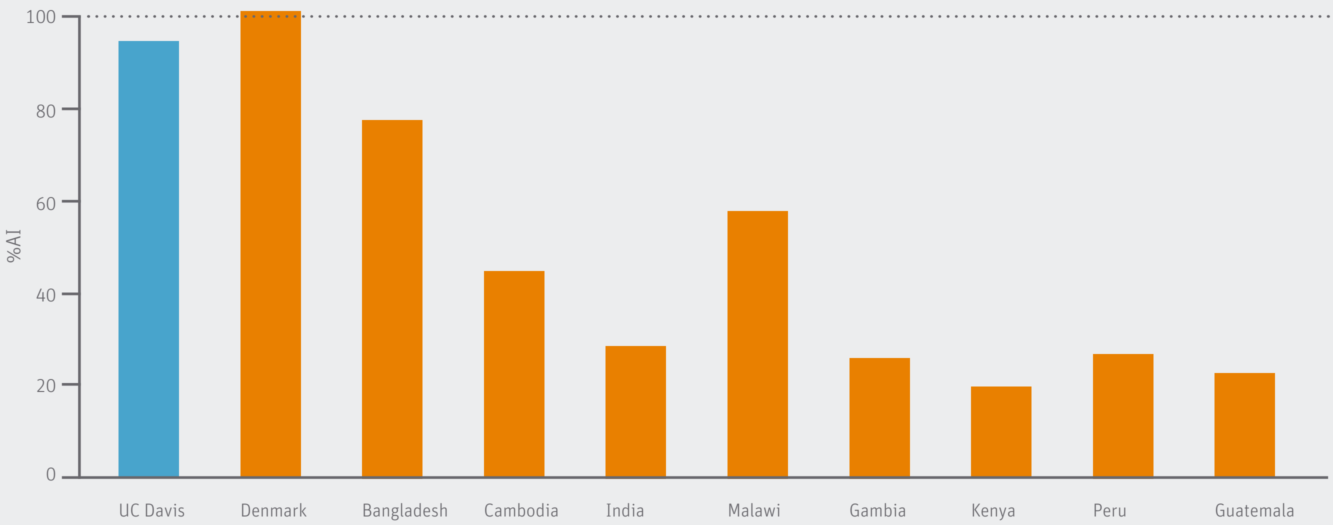
These factors typically contribute to the wide range in reported concentrations within and among studies. FAO/WHO used many of the same milk concentrations as the Institute of Medicine (e.g., for all B vitamins except niacin and folate, and for vitamins C and A) to set their Recommended Nutrient Intakes (RNI) for infants and lactating women, and the source of data for several others is unclear. A European report on infant nutrient intakes concluded that we need guidance on the collection and measurement of micronutrients in human milk in order to improve our data on its composition.

There are several likely explanations for this unsatisfactory situation. It has been very tedious and costly to analyze all the individual micronutrients in a milk sample, and this also deters investigators from conducting systematic studies of the effects of differences in sample collection methods (such as time within a feed vs. a complete breast emptying, time of day, acute effects of mothers taking a supplement, etc.) on the concentrations of all micronutrients in milk. There are large changes in micronutrient concentrations, especially from colostrum through the first 1–2 months postpartum. Not all milk analysis methods were valid. We have recently conducted a more systematic study of the effects of collection method, time of day, and acute supplementation on micronutrients in milk.[6]

As an example, our systematic review of vitamin B_{12} in breast milk found 26 relevant studies, but half were in low- or middle-income countries or in vitamin B_{12} deficient population groups.[5] Seven of the 26 studies used an invalid method of analysis, and samples were collected at very different stages of lactation. The review demonstrated substantial differences among studies in reported values, a fall in milk vitamin B_{12} from colostrum to ≈4 months postpartum, and the already established influence of maternal status on milk vitamin B_{12} concentrations.

Our own laboratory has used a recently validated method for vitamin B_{12} in milk[7] to show that concentrations in samples from India, The Gambia, Kenya, a remote region of Peru, and Guatemala are only 20–25% of the values estimated for setting the AIs (**Figure 1**). These were convenience samples, however, and

FIGURE 1: Concentrations of vitamin B_{12} in human milk samples from different countries[b]



[b] Samples are not necessarily representative of the overall population concentration in each country.

unlikely to be representative of the overall population in those countries. In Guatemalan infants aged seven months, vitamin B_{12} concentrations were lowest in those consuming breast milk and highest in those consuming some dried cow milk.[8] Some maternal and infant plasma vitamin B_{12} concentrations at 12 months postpartum were as low as those reported in clinical case studies of infant vitamin B_{12} deficiency.

Our review also indicated that low concentrations of retinol, iodine and several other B vitamins are found where mothers have poor status or low intakes of these nutrients. We recently published a mass spectrometry method for the simultaneous analysis of vitamers of thiamin, riboflavin, niacin, vitamin B_6 and pantothenic acid,[8] and compared concentrations with those used to set the AIs. While these data are provided with the caution that the samples may not be representative of the countries, at around 3–4 months postpartum we found concentrations of B vitamins to be much lower than values used to set the AIs, especially for riboflavin (10–25% of AI values in Bangladesh, Malawi, Peru, The Gambia, Philippines and Kenya), niacin (< 10% of AI values in most countries), vitamin B_6 (10–20% in The Gambia and Philippines) and thiamin (50–70% in India, Peru, The Gambia and Cambodia).

A milk sample is collected from a participant in the Diet-Mother-Milk-Infant (DMMI) project in Guatemala

The need for reference values

All we know at this time is that micronutrient concentrations in milk samples from poorer countries can be much lower than those used for setting the AIs for breastfeeding infants and lactating women by the Institute of Medicine and FAO/WHO. A big caveat, however, is that the quality and amount of data available for setting the AIs was poor, and that we don't really know how to define a concentration as 'low' or 'inadequate'. Samples obtained from women and/or infants identified with clinical or biochemical signs of deficiency are somewhat useful for this purpose[9] but suffer from many of the same usual limitations in data quality (invalid analytical methods, various collection protocols, etc.).

Moving forward, during the next few years we will be conducting a study to obtain reference values based on milk collected from well-nourished but unsupplemented women in four

Anthropometric indices are measured in one of the participating infants

countries, during the first nine months of lactation. The micronutrient status of mothers and infants will be assessed, as will milk volume. The reference values will be published as percentile curves, in a similar way to infant growth data. They can then be used to express milk concentrations of each micronutrient among and across populations, and to evaluate the need for, and effects of, maternal supplementation or food fortification.

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Summary

Based on the importance of exclusive breastfeeding and the need to optimize the quality of human milk, more attention should be directed at ensuring adequate maternal micronutrient status during lactation; it has been a relatively neglected concern. Data on milk micronutrient concentrations is currently inadequate, and while few carefully collected, representative data are available, the weight of current evidence suggests that we should pay more attention to maternal micronutrient status in lactation. The concentrations of most micronutrients in breast milk are affected by maternal status and/or intake, which implies that multiple micronutrient supplementation during pregnancy, rather than folic acid and iron supplements which have no effects on milk, as well as during lactation, may help protect milk micronutrients. However, this is as yet unproven. An additional consideration is that the poor quality of current data on milk composition probably means that our estimates of some nutrient requirements for young infants and lactating women are inaccurate. Milk micronutrient concentrations may also be a useful marker of population status, and a tool for evaluating the need for, and effectiveness of, fortification and maternal supplementation.

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