CHAPTER

5

Antioxidants in Breast Milk of Lactating Mothers with HIV

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OUTLINE

Abstract

Antioxidants play important roles in growth, development, detoxification, and effective immune responses. It is reported that the serum concentrations of antioxidants are altered in people living with human immunodeficiency virus (HIV). However, there is the dearth of information on the effects of HIV on the quality of breast milk, especially its antioxidants components. The breast milk of lactating mothers with HIV contains all the antioxidants that are normally found in human milk, although there are slight alterations. Breast milk concentrations of copper, iron, total antioxidant potential, riboflavin, vitamin B_6, vitamin C, and folate are lower in lactating mothers with HIV compared with HIV-negative mothers. Other antioxidant trace elements and vitamins are in comparable concentrations. It appears that shedding of HIV is not only the problem with breastfeeding but also a reduction in breast milk concentrations of certain antioxidants that are vital for infant growth and survival.

Keywords: Antioxidants; Breast milk; Essential trace metals; Lactating mothers with HIV; Vitamins.

List of Abbreviations

Cu Copper
DDT Dichloro-diphenyl-trichloroethane
DHA Dehydroascorbic acid

HIV/AIDS
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DNA Deoxyribonucleic acid
EGF Epidermal growth factor
Fe Iron
FIL Feedback inhibitor of lactation
FRAP Ferric reducing ability of plasma
HIV Human immunodeficiency virus
Ig Immunoglobulin
IGF Insulin-like growth factor
IL Interleukin
Mn Manganese
NADPH Nicotinamide adenine dinucleotide phosphate (reduced)
NF-kB Nuclear factor kappa B
NGF Nerve growth factor
PCBs Polychlorinated biphenyls
RNA Ribonucleic acid
Se Selenium
sIgA Secretory immunoglobulin A
SOD Superoxide dismutase
TAC Total antioxidant capacity
TGF Transforming growth factor
TNF-α Tumor necrosis factor-alpha
TRAP Total radical trapping antioxidant parameter
UNICEF United Nations Children's Fund
WHO World Health Organization
Zn T-4 Zinc transporter-4
Zn Zinc

INTRODUCTION

Breast milk is a dynamic fluid containing numerous bioactive compounds that are necessary for the survival of the newborn.[1] Its unique significance to the growth and overall health of newborn, especially in the first 6 months of life, is well established. In 1989, the World Health Organization and the United Nations Children's Fund[2] made a joint declaration that the ideal food for infants is breast milk and cannot be equaled by artificial alternatives. This declaration was predicated on the unique properties of breast milk, which protect infants from morbidity and mortality that could result from infection and chronic diseases at a critical time when the immune system is still naïve.

COMPOSITION OF HUMAN MILK

The normal constituents of human breast milk are numerous (Table 5.1). The first bioactive compounds recognized in human milk were antibodies as transfer of immunity from mother to infant through breast milk was reported as early as 1892.[3] Other components include lactobacilli (*Bifidobacterium bifidum*), secretory immunoglobulin A, and other immunoglobulin classes, leucocytes, lactoferrin, lysozyme, haptocorrin, triglyceride, α-lactalbumin, soluble tumor necrosis factor-alpha receptors, interleukin (IL)-1 receptor antagonist, IL-10 transforming growth factor β, protease inhibitors, hormones, complement factors, antitrypsin, adiponectin, and glycans among others.[4–7] In addition, there are numerous nutritional factors in the breast milk. These factors include macronutrients such as protein and fat, essential trace elements such as selenium (Se), zinc (Zn), copper (Cu), iron (Fe), and vitamins such as vitamins A, B, C, D, E, and K (Table 5.2).

There are myriad of factors that influence the concentration of breast milk constituents. These include stage of lactation (colostral, transitional, mature, and involutional), time of the day, breastfeeding routine, parity, age, regional differences, season of the year, time since last meal, gestational age of the newborn, and other maternal factors such as nutrition. This shows that the composition of breast milk is not uniform, and hence, the daily intake of milk constituents by the breastfed infant is dependent on the differences in the breast milk composition. It is of importance to note that variations in concentration of breast milk constituents are not inversely related to the breast milk volume.

TABLE 5.1 Some Nonnutritional Components of Breast Milk

Components With Antimicrobial Activity	Components With Inflammatory Functions
Immunoglobulins (secretory IgA, IgG, IgM)	Interleukins 1, 6, 8, and 10
Lactoferrin	Tumor necrosis factor-alpha
Lysozyme	Tumor growth factor-beta
Lactoperoxidase	Alpha-1-antitrypsin
Alpha-lactalbumin	
Complement factors	
Components With Transport and Absorption Activities	**Digestive Enzymes**
Beta-casein	Lipase
Folate-binding protein	Amylase
Insulin-like growth factor–binding protein	Esterase
Alpha-lactalbumin	
Growth Factors	**Other Possible Components**
Insulin-like growth factors	Viruses
Epidermal growth factor	Polychlorinated biphenyls,
Nerve growth factors	Dichloro-diphenyl-trichloroethane
Transforming growth factor	DNA, RNA
	Drugs

DNA, deoxyribonucleic acid; *RNA*, ribonucleic acid.
This Table was adapted from the reports of Prentice A. Constituents of human milk. Food Nutr Bull *1996;***17***(4); Lönnerdal B. Nutritional and physiologic significance of human milk proteins.* Am J Clin Nutr *2003;***77***(6):1537S–43S.*

TABLE 5.2 Some Nutritional Factors in Human Milk

Macronutrients	Micronutrients
Carbohydrate (mainly lactose)	***Vitamins***
Energy	Water-soluble vitamins
Protein	(vitamin C, riboflavin, niacin,
Fat	and pantothenic acid)
Total fat	Fat-soluble vitamins
Saturated fatty acids	(vitamins A, D, E, and K)
Monounsaturated fatty acids	***Essential trace elements***
Polyunsaturated fatty acids	Copper (Cu)
Linoleic acid	Iron (Fe)
Alpha-linolenic acid	Zinc (Zn)
Arachidonic acid	Selenium (Se)
Docosahexaenoic acid	Manganese (Mn)
Trans fatty acids	

HUMAN IMMUNODEFICIENCY VIRUS SHEDDING INTO BREAST MILK

It is well known that shedding of human immunodeficiency virus (HIV) into breast milk is a feature in mothers with HIV. Approximately 40% of milk samples from HIV-infected mothers contain HIV RNA, but it is likely that only a small percentage of the HIV RNA in breast milk represents infective virions.[8] Postnatal transmission of the virus is thus possible via breastfeeding. Although several attempts, such as flash-heating and pasteurization, are made to eliminate HIV from breast milk, it is still apparent that breastfeeding by mothers living with HIV is unsafe for the newborn. This prompted the advice that HIV-infected mothers who have uninterrupted access to safe breast milk substitutes should avoid breastfeeding. In developing countries, however, this advice against breastfeeding is met with numerous challenges. First, there is a general cultural belief that a child who is not breastfed will not be kind to the mother when he/she grows up. Second, the usual problem of discrimination against people living with HIV is that most mothers, especially the younger and the less educated ones, find it difficult to cope with the discrimination specifically in public places when the need to feed their babies arises. Third, the widespread poverty in the developing countries is another concern. Usually, artificial substitutes are given free of charge to the mothers living with HIV in most health centers; some mothers still find it difficult to transport themselves to the health centers when they exhaust the formula given to them. This compels some mothers to breastfeed their babies pending when they will be able to access the formula again. This mixed-feeding system increases the chance of HIV transmission to the child.

Based on these aforementioned challenges, one would have expected that there will be heightened research on the quality of breast milk in mothers living with HIV, but hitherto, studies on the impact of HIV infection on components of breast milk, especially the antioxidants, are relatively scarce.[9] Efforts in this line are probably militated against by the assumption that all babies breastfed by mothers living with HIV have the risk of being infected. Also, the inaccessibility of formula by mothers living with HIV appears to affect mothers in the developing countries, where often time little attention is given to quality research more than their counterpart in the developed world.

ANTIOXIDANTS AND HUMAN IMMUNODEFICIENCY VIRUS INFECTION

To achieve effective breastfeeding, breast milk is expected to provide adequate amounts of vital micronutrients, including the vitamins and essential trace elements with antioxidants properties. Generally, antioxidants are substances that prevent the damaging effects of free radicals emanating from aerobic metabolism and/or the actions of xenobiotics among others. They play important roles in growth, development, detoxification, and effective immune responses. It is known that micronutrients are extremely essential in maintaining quality health and development; their need, however, increases when there is trauma or infection such as HIV. Up until now, there is still the dearth in knowledge on the effects of infection on these micronutrients as against the general knowledge on optimal requirements.[10]

Although there are important factors determining the antioxidants component of breast milk and plasma, alteration in plasma levels of antioxidants in people living with HIV is usually attributed to increases in nutrient expenditure, loss of appetite, nutrient malabsorption, urinary loss, redistribution from plasma to tissues, and complex metabolic alterations that result in weight loss and wasting.[11,12] Therefore, deficiencies of vitamins and minerals such as vitamins A, B, C, and E and essential trace metals such as Se, Fe, manganese (Mn), Cu, and Zn have been reported as common observations in people living with HIV.[12,13] Since there is a cross-talk between the blood and the breast milk, a similar deficiency pattern cannot be ruled out in the breast milk of mothers living with HIV. However, very little is known about the mechanisms that control the secretion of micronutrients into human milk.

BREAST MILK LEVELS OF CU AND FE

Copper (Cu) is an essential trace element that is usually bound to caeruloplasmin and to a lesser extent amino acid and low-molecular chelators. Its concentration in human breast milk is about 20%–25% of that in the serum.[14] Usually, the amount of Cu provided by the breast milk is insignificant with regard to meeting the Cu requirement of the newborn. Hence, newborn term infants have ample stores of Cu primarily in the liver, and these are mobilized in early life.[15] In humans, breast milk Cu concentration declines during lactation. In mature breast milk of mothers living with HIV, Cu level has been reported to be lower compared with mothers not living with HIV.[16] This reduction is thought to be due to low prolactin as a result of poor/nonsuckling. Suckling increases milk Cu secretion due to its direct relationship with circulating prolactin level.[17] In contrast, caeruloplasmin, a Cu transport protein, is higher in the breast milk of lactating mothers with HIV compared with HIV-negative mothers.[9]

The concentration of iron (Fe) in breast milk is low in relation to serum Fe and to estimated Fe requirements of infants. Its concentration in breast milk is about 20%–30% of serum Fe;[14] this relatively low concentration of Fe in human milk is thought to be a form of protection for the infants against Fe toxicity since term infants are born with ample stores that can be utilized in the first 6 months of life.

Serum Fe is almost exclusively bound to transferrin, but the major Fe-binding protein in human milk is lactoferrin and to a lesser extent xanthine oxidase. Usually, Fe is shielded from the body fluids and stored by ferritin to prevent ionic Fe from producing oxidative damage. In infection, there is an acute phase response that increases synthesis of ferritin, thereby causing uptake of Fe with a resultant fall in plasma Fe level.[18]

During lactation, breast milk Fe level declines as lactation progresses. This decline is usually functional as it parallels decrease in transferrin receptor and ferroportin expression, and not due to tissue depletion.[19] In mothers living with HIV, breast milk Fe level is reported to be lower than that in the breast milk of HIV-negative mothers (Table 5.3). In contrast, breast milk transferrin level was found to be elevated in mothers living with HIV compared with HIV-negative mothers.[9] If it were to be in the serum, this picture is that of Fe deficiency anemia. Usually, Fe deficiency anemia is indicated when there is low Fe concentration with elevated transferrin concentration.

TABLE 5.3 Breast Milk Concentrations of Antioxidant Trace Elements and Total Antioxidant Potential in Human Immunodeficiency Virus–Lactating Mothers and Human Immunodeficiency Virus–Negative Mothers[16]

Trace Elements	HIM	HNM
Zn (μg/dL)	146 ± 20	148 ± 16
Cu (μg/dL)	68 ± 5[a]	71 ± 5
Fe (μg/dL)	66 ± 6[a]	71 ± 6
Se (μg/L)	64 ± 6	65 ± 3
Mn (μg/dL)	61 ± 7	64 ± 5

Cu, copper; *Fe*, iron; *HIM, HIV*-infected mothers; *HNM, HIV*-negative mothers; *Mn*, manganese; *Se*, selenium; *Zn*, zinc.
[a]*Significantly different at* P < *.05.*

TABLE 5.4 Correlation Between Plasma and Breast Milk Concentrations of Antioxidant Trace Elements and TAP in Human Immunodeficiency Virus–Lactating Mothers and Human Immunodeficiency Virus–Negative Mothers[16]

	HIM		HNM	
Trace Elements	r-values	*P*-values	r-values	*P*-values
Cu (μg/dL)	−0.355	0.135	−0.093	0.626
Zn (μg/dL)	0.042	0.866	−0.249	0.184
Se (μg/L)	−0.112	0.647	0.299	0.108
Fe (μg/dL)	−0.022	0.928	0.233	0.215
Mn (μg/dL)	0.496	0.043[a]	−0.157	0.406
TAP (μmolTE/L)	−0.111	0.651	0.000	0.999

Cu, copper; *Fe*, iron; *HIM, HIV*-infected mothers; *HNM, HIV*-negative mothers; *Mn*, manganese; *Se*, selenium; *TAP*, total antioxidant potential; *TE*, trolox equivalent; *Zn*, zinc.
[a]*Significantly different at* P < *.05.*

Therefore, aside from the danger of shedding HIV in the breast milk, there is even a nutritional danger of Fe deficiency in breastfed infants of lactating mothers with HIV. Unfortunately, infants fed with formula usually have poor Fe status, in spite of the fact that formula contains up to three times more Fe than does breast milk.[20] Thus, infants depend more on breast milk Fe to meet their needs.

Domelleof et al.[21] reported that no correlation exists between human milk Fe and iron-status variables in the serum. This is not different in mothers living with HIV as no significant correlation was observed between the plasma Fe level and that of the breast milk (Table 5.4).[16] This thus indicates that there is a need to ensure optimal Fe supplement in infants (and not maternal Fe supplementation) of mothers living with HIV who are breastfed or those fed with treated (flash-heated or pasteurized) breast milk.

BREAST MILK LEVEL OF ZN

During infection, there is increased synthesis of metallothionein, leading to the uptake of Zn into the liver, thereby causing a fall in plasma Zn level. Similarly, plasma albumin usually falls during acute phase response, thereby causing a fall in plasma Zn level since albumin is its binding protein.[10]

Unlike Fe and Cu, serum Zn concentration is considerably lower than that in the breast milk.[14] There is an indication that mechanisms ensuring mammary gland Zn uptake as well as subsequent secretion into the breast milk are so effective that the increased level of Zn persists for the first several months of lactation.[14] Every day, more than 0.5–1.0 mg of Zn is taken up by the mammary gland and secreted into the breast milk. This amount is almost twice that of Zn transferred across the placenta to the fetus during late pregnancy; this illustrates the remarkable capacity of the mammary gland to transport Zn.[21] It has been shown that breast milk Zn concentration is similar in women with low Zn status and those who receive daily supplements, thereby showing that homeostasis of breast milk Zn transfer is tightly regulated.[22]

During human lactation, the concentration of breast milk Zn reduces, whereas plasma Zn level increases.[23] This has been attributed to relocalization of Zn transporter-4. No difference has been reported between the concentrations of Zn in the breast milk of mothers living with HIV and mothers without HIV. Rahamon et al.[16] showed that the breast milk Zn levels are similar in both groups and there was no correlation between breast milk and plasma Zn levels. Also, albumin, a Zn carrier, which was lower in plasma of the mothers living with HIV, was not affected in the breast milk. This indicates that metabolic changes associated with HIV might not affect the mammary gland Zn uptake as well as its secretion into the breast milk in mothers living with HIV. However, some women, irrespective of HIV status, are known to have abnormally low breast milk Zn level, hence, placing their infants at the risk of transient neonatal Zn deficiency. Infants of such women who are breastfed without any form of Zn supplementation usually experience severe eczema and decreased growth by 2–3 months of age. This is even exacerbated in premature infants due to their lower Zn stores at birth. In this group of women, breast milk Zn concentration cannot be increased by maternal Zn supplementation.[24]

BREAST MILK LEVELS OF SE AND MN

Selenium (Se) is an essential component of about 25 selenoproteins, which are involved in protection against oxidative damage. It plays a vital role in a number of physiological processes such as immune response and viral suppression. In HIV, there is Se deficiency, which is related to faster disease progression and to mortality, especially in children. Its supplementation has been shown to stimulate glutathione peroxidase activity, thereby reducing nuclear factor kappa B activation in HIV-1–infected cell lines.[25]

In infant nutrition, there is a particular emphasis on Se because breast milk is its only source during this most rapid period of growth.[26] Breast milk Se level is dependent on maternal intake, which depends on where she lives, the soil on which what she consumes are grown, and supplementation. During lactation, Se level in the breast milk decreases significantly through the phases of lactation.

Like other essential trace elements, there is presently little information on the impact of HIV infection on human breast milk Se concentration. Rahamon et al.[16] reported that the breast milk Se level, as well as plasma Se level, of lactating mothers living with HIV was not different from that of HIV-negative mothers. This probably indicates that Se concentration in the breast milk of mothers living with HIV might be optimal when there is adequate plasma concentration.

Manganese (Mn) is present in minute quantity in the body. It is a component of the antioxidant enzyme superoxide dismutase, which is the principal antioxidant enzyme in the mitochondria. Neonates have been found to be in negative Mn balance after birth. Interestingly, human breast milk also contains a very low level of Mn. This might be a physiological measure as early life exposure to elevated Mn level is associated with poor neurodevelopment and cognitive performance resulting from the ability of developing nerve cells to highly express receptors for manganese transport protein and the immaturity of the liver, which impedes its bile elimination system. Although there is higher Mn content in most formula, Mn from human breast milk is still believed to be more available than that from the formula.[27]

Similar to Se and Zn, breast milk concentration of Mn does not appear to be affected by HIV infection. The Mn concentration in the breast milk of mothers living with HIV is similar to that of mothers without HIV. However, there seems to be a positive correlation between plasma and breast milk levels of Mn in mothers living with HIV.[16] This suggests that their plasma Mn level probably dictates the quantity that is found in the breast milk.

VITAMINS IN HUMAN MILK

Other vital micronutrients required for health and growth are vitamins. They are organic compounds required in minute quantities in the body, especially for their catalytic functions. All of the types of vitamins are present in human milk in nutritionally significant concentration except vitamin K.

Adequate amount of vitamins in the breast milk is essential for infant's health. Generally, the type and concentrations of vitamins in the breast milk is dependent on the maternal type and concentrations. This underscores the simple fact that adequate intake by mothers is a prerequisite for adequate concentration in the breast milk. As with the essential trace elements in the breast milk, there is lack of information on the effect of infections such as HIV on the quality and quantity of vitamins in the breast milk of mothers living with HIV.

VITAMINS A AND B IN HUMAN MILK

Vitamin A is a micronutrient that is usually obtained from animal-derived foods as preformed vitamin A or as provitamin A carotenoids, which is converted to retinol after absorption. It is required for growth, immune function, and bone remodeling among others. Due to its numerous functions, its excess or deficiency impacts negatively on human health, especially in children. For example, vitamin A deficiency is associated with childhood blindness, diarrhea, respiratory illnesses, depressed immune function, and increased risk of mortality. In contrast, excess intake, resulting from acute intoxication or chronic ingestion, can cause hypervitaminosis A.[28]

Vitamin A in the breast milk is well absorbed by children as breast milk also contains lipase that helps in vitamin A digestion. Adequate transfer of vitamin A from mother to child is very essential for child survival. Usually, mother-to-child transfer of vitamin A occurs during gestation and lactation. After birth, infants of well-nourished mothers have small vitamin A reserve, which gets augmented as soon as lactation begins. Although vitamin A belongs to the group of breast milk components that are affected by maternal concentration, its concentration varies during the phase of lactation with colostrum having the highest concentration. Mother's milk continues to be the best delivery source of vitamin A to the infants, and hence, diseases such as xerophthalmia are practically not found in fully breastfed infants.[29]

The B vitamins are water-soluble vitamins performing myriads of important functions such as carboxylation, decarboxylation, transamination, acylation, oxidation, reduction, methyl group transfer, and energy utilization among others. They are made up of eight vitamins consisting thiamine (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_7), folate (B_9), and cobalamin (B_{12}). Although B vitamins are usually grouped together, each of the various types performs unique but synergistic functions. Depending on the type, B vitamins are commonly found in cereals and foods of animal and plant origins. Their deficiencies are associated with a number of diseases mainly due to the resulting impairment in their numerous functions.

All B vitamins are found in the breast milk and their concentration, except folate, largely depends on maternal status as maternal depletion can rapidly and substantially reduce their secretion into the breast milk.[30] This explains why diseases such as beriberi and epileptiform convulsions are found in exclusively breastfed infants of mothers with certain B vitamins deficiency. During postpartum period, the concentrations of B vitamins in the breast milk change. However, exclusively breastfed infants between 0 and 6 months derive adequate B vitamins from breast milk alone.

VITAMINS C AND D IN HUMAN MILK

Vitamin C are molecules with antiscorbutic properties. These include ascorbic acid and its oxidized form, dehydroascorbic acid. It is a water-soluble vitamin found in many fruits and vegetables. Many of the biologic properties of vitamin C are linked to its antioxidant properties as it can donate a hydrogen atom to form a radical that is reduced back to ascorbate by glutathione or reduced nicotinamide adenine dinucleotide phosphate. Vitamin C is essential to the health and development of infants due to its role in the synthesis of collagen, tendons, and bone with its deficiency usually manifesting as scurvy. To prevent scurvy, therefore, it is necessary to consume vitamin C regularly since it is water soluble and cannot be stored in the body.[31]

Vitamin C is an essential nutrient in human milk, which is dependent on maternal dietary intake. At birth, vitamin C concentration in infant's blood is higher than that in the maternal blood.[32] Its concentration in breast milk is also higher than in maternal blood, but the breast milk concentration declines progressively as the lactation progresses. Irrespective of the lactation phase, breastfed infants of vitamin C-replete mothers are still able to meet the recommended daily intake during the first 6 months of life.

Vitamin D, a fat-soluble vitamin, can be obtained from diets and can be synthesized endogenously. It performs an essential function in bone metabolism as its deficiency results in impaired bone metabolism manifesting as rickets in children and osteomalacia in adults. Its deficiency in children has also been associated with increased risk of respiratory tract infections.

During gestation, there is placental transfer of vitamin D to the fetus. This transfer is dependent on maternal vitamin D status as maternal supplementation increases the breast milk concentration. The concentration of vitamin D in breast milk of healthy lactating mothers is low and insufficient to prevent vitamin D deficiency in exclusively breastfed infants. Therefore, intake of vitamin D from breast milk and adequate sunlight exposure are required to maintain optimal concentration to avoid rickets after birth.[33]

VITAMINS E AND K IN HUMAN MILK

Vitamin E is a fat-soluble vitamin with established roles in antioxidant defense system and cellular respiration. It is mainly obtained from oils and fats while meats, fruits, and vegetables contribute little quantity of vitamin E. There is a synergistic interaction between vitamins C and E in lipoperoxidation reduction as they help regenerate the reduced forms of each other.

Breast milk continues to be the most important source of vitamin E to newborn as placental transfer of vitamin E is usually limited. It becomes even more important in premature and low-birth-weight infants who are characterized by poor placenta transfer and limited adipose tissue.

Breast milk concentration of vitamin E decreases as the milk becomes mature. This change in concentration is independent of parity, anthropometric nutritional status, socioeconomic status, and habitual dietary intake of vitamin E by the mother.[34] Pockets of report have, however, shown that maternal plasma level of vitamin E determines its content in the transitional milk but not the colostrum. This, thus, suggests that vitamin E uptake by the mammary gland involves distinct transfer mechanisms.[35]

Vitamin K is another member of the fat-soluble vitamins family. It plays important roles in blood clotting and bone metabolism. Margarines, plant oils, milk products, vegetables, and eggs are common sources of vitamin K. There is limited placenta transfer of vitamin K during gestation and haemorrhagic disease of the newborn manifests when there is poor placenta transfer.

Concentration of vitamin K in breast milk tends to decrease over the lactation period. Early breast milk and mature milk have low vitamin K contents, which cannot meet the recommended intake for infants especially in the first 6 months of life.[10] Unfortunately, supplementation with vitamin K is usually not recommended in exclusively breast-fed infants as their liver is still immature and very high doses of vitamin K can elevate serum bilirubin concentration.[36]

Reduced plasma concentrations of vitamins, especially the fat-soluble class, are found in pregnant women living with HIV. This necessitated the strong suggestion for multivitamin supplementation in this group of people. Even with supplementation, however, HIV disease especially at the advanced stage can suppress vitamin release from their stores. For example, vitamin A release from the liver is suppressed by HIV, thereby leading to its low plasma level despite adequate liver stores.[37] Adequate maternal vitamin pool as well as multivitamin supplementation especially with vitamins B, C, and E reduces adverse pregnancy outcomes and possibly mother-to-child transfer of HIV.

VITAMINS IN THE BREAST MILK OF HUMAN IMMUNODEFICIENCY VIRUS–LACTATING MOTHERS

Presently, there is little information on the concentrations of vitamins in the breast milk of mothers living with HIV. A South African study showed that lactating mothers with HIV have low serum concentrations of retinol, folate cobalamin, and alpha-tocopherol.[38] In addition, serum alpha-tocopherol reduces progressively during the first 6 months after delivery. This indicates that the breast milk concentrations of these vitamins could also be low since the breast milk concentration of most vitamins, especially the water-soluble vitamins, largely depend on maternal status. As in serum, there is the dearth of information on vitamin concentrations in the breast milk of lactating HIV mothers. In a study assessing the effects of flash-heat treatment on vitamin concentrations in the breast milk of lactating mothers with HIV in South Africa, it was observed that the median concentrations of riboflavin, B_6, vitamin C, and folate in unheated breast milk were lower compared with concentrations in well-nourished women (Table 5.5).[30,39,40] Vitamin A was, however, an exception as its median concentration was higher in the breast milk of lactating mothers with HIV compared with the reported concentration in well-nourished women.[39,40] This single report is not enough to conclude on the vitamin concentrations in the breast milk of lactating mothers with HIV, and hence, more studies are suggested.

TOTAL ANTIOXIDANT CAPACITY IN BREAST MILK OF HUMAN IMMUNODEFICIENCY VIRUS–LACTATING MOTHERS

The practical impossibility of measuring all antioxidants in samples of interest leads to the concept of total antioxidant capacity (TAC). This concept assesses the reductant properties of antioxidants against free radicals or the delayed production of a measurable free radical. There are two common methods for assessing TAC; these include the total radical trapping antioxidant parameter assay or ferric reducing ability of plasma assay.[10] As interesting as

TABLE 5.5 Breast Milk Concentrations of Vitamins in Human Immunodeficiency Virus–Lactating Mothers and Human Immunodeficiency Virus–Negative Well-Nourished Mothers

Vitamins	HIM[a39]	Well-Nourished Women[40]
Riboflavin	0.01 mg/L	0.35 mg/L
B_6	0.04 mg/L	0.13 mg/L
A	637.00 µg/L	485.00 µg/L
C	27.00 mg/L	50.00 mg/L
Folate	19.45 µg/L	81.00 µg/L[30]

HIM, HIV-infected mothers.
[a]*Median concentration.*
This Table was adapted, with slight modification, from the reports of Allen LH. B vitamins in breast milk: relative importance of maternal status and intake, and effects on infant status and function. Adv Nutr *2012;3(3):362–69; Allen LH. Multiple micronutrients in pregnancy and lactation: an overview.* Am J Clin Nutr *2005;81(5):1206–12S; Israel-Ballard KA, Abrams BF, Coutsoudis A, Sibeko LN, Cheryk LA, Chantry CJ. Vitamin content of breast milk from HIV-1-infected mothers before and after flash-heat treatment.* J Acquir Immune Defic Syndr *2008;48(4):444–49.*

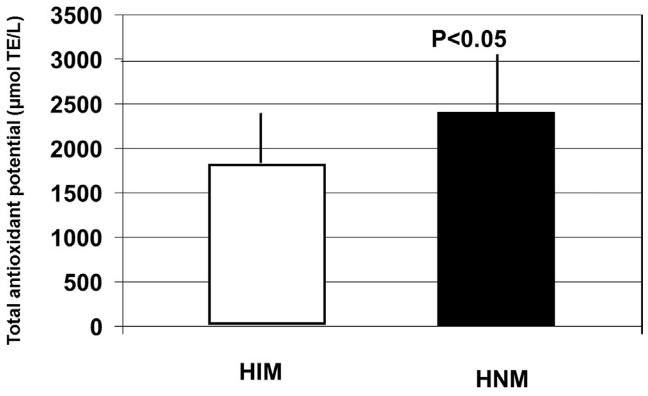

FIGURE 5.1 Breast milk concentrations of total antioxidant potential (µmolTE/L) in human immunodeficiency virus–lactating mothers and human immunodeficiency virus–negative mothers.[16] *HIM, HIV*-infected mothers; *HNM, HIV*-negative mothers.

this concept might be, it is usually affected by endogenous antioxidants such as albumin and uric acid whose levels are affected by the prevailing clinical condition. For example, acute phase response or change in renal function can alter TAC result without reflecting the changes in antioxidant vitamins and trace elements concentration. However, this problem can be overcome by calculating the antioxidant gap.

Effect of HIV infection on the TAC in breast milk is poorly understood. A Nigerian study showed that TAC was significantly lower in the breast milk of lactating mothers with HIV compared with HIV-negative mothers (Fig. 5.1). A similar, but insignificant, reduction was observed in the maternal plasma. This reduction in the total antioxidants concentration in the breast milk of lactating mothers with HIV is thought to be due to low concentrations of antioxidant trace metals such as Cu and Fe in their milk.

CONCLUSION

From the few available reports on antioxidants in breast milk of lactating mothers with HIV, it appears that shedding of HIV is not only the problem with breastfeeding but also a reduction in breast milk concentrations of certain antioxidants that are vital for infant growth and survival. Therefore, multiantioxidants supplementation could be beneficial in infants of lactating mothers with HIV who are exclusively breastfed or fed with flash-heated or pasteurized breast milk.

SUMMARY POINTS

- The breast milk of lactating mothers with HIV contains all the dietary antioxidants that are normally found in human milk.
- Breast milk concentrations of copper (Cu), iron (Fe), total antioxidant potential, riboflavin, vitamin B_6, vitamin C, and folate are lower in lactating mothers with HIV compared with HIV-negative mothers.
- Other antioxidant trace elements and vitamins are in comparable concentrations in lactating mothers with HIV and HIV-negative mothers.
- Shedding of HIV might not only be the problem with breastfeeding but also a reduction in breast milk concentrations of certain antioxidants that are vital for infant growth and survival.
- Multiantioxidants supplementation could be beneficial in infants of lactating mothers with HIV who are exclusively breastfed or fed with flash-heated or pasteurized breast milk.
- Due to the little available information, there is an urgent need for more information on breast milk concentrations of antioxidants in lactating mothers with HIV.

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