Nutritional Interventions in HIV-Infected Breastfeeding Women

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Abstract

Breastfeeding is the international gold standard for infant feeding, as it is known to reduce the risk of infant morbidity and mortality and foster improvements in child growth and development. However, in the context of HIV, breastfeeding significantly increases the risk of mother-to-child transmission (MTCT) of HIV, and this risk is proportional to the duration of breastfeeding. As a result, the World Health Organization recommends avoidance of breastfeeding among HIV-infected mothers when replacement feeding is acceptable, feasible, affordable, sustainable, and safe. Unfortunately, the adoption of formula feeding is not widespread in developing regions such as sub-Saharan Africa, partly due to its high cost and partly due to the social stigma associated with not breastfeeding. Further, in settings where access to adequate hygienic conditions is limited, formula feeding may lead to increased infant morbidity and mortality. Consequently, breastfeeding continues to account for a substantial proportion of pediatric HIV infections in developing regions of the world. Some observational studies examining the role of nutritional status in vertical HIV transmission found that low serum levels of vitamin A were associated with higher risk of MTCT. However, in two trials in Malawi and South Africa, vitamin A had no significant effect on MTCT,

while trials in Tanzania and Zimbabwe found that maternal vitamin A supplementation significantly increased the risk of MTCT of HIV. In Tanzania, maternal multivitamin (vitamins B, C, and E) supplementation reduced the risk of HIV transmission via breastfeeding among women who were nutritionally and immunologically compromised, and had additional health benefits such as a decreased incidence of fetal loss and a reduced rate of maternal disease progression. Overall, there is no evidence to support vitamin A supplementation for HIV-infected pregnant mothers. However, multivitamin supplementation including vitamins B, C, and E is strongly recommended. Further research is warranted to investigate the role of other nutrients in vertical HIV transmission via breastfeeding and overall maternal and infant health among HIV-infected breastfeeding women and their children. In settings where alternatives to breastfeeding are not viable, exclusive breastfeeding is recommended for 6 months for children born to HIV-infected women together with rapid weaning and replacement feeding that is optimal for infant health.

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Introduction

Worldwide an estimated 1,800 children become infected with HIV each day, with approximately 650,000 new pediatric infections and 500,000 AIDS-related deaths

annually [1, 2]. Sub-Saharan Africa accounts for the majority of the global pediatric HIV/AIDS disease burden, comprising more than 85% of the new HIV infections among children worldwide. In 2003, AIDS was responsible for 6.5% of deaths among children under five in Africa, an increase from 2% in 1990 [2]. The majority of pediatric HIV infections are acquired through mother-to-child transmission (MTCT) via in utero, intrapartum, or breastfeeding routes.

In developed nations, strategies such as antiretroviral therapy (ART) and exclusive formula feeding have successfully reduced the rates of vertical HIV transmission to less than 2% [3]. However, in the absence of ART and nutritional interventions in developing regions, children have a 25–48% risk of acquiring HIV infection from their HIV-infected mothers [4]. In fact, breastfeeding continues to account for 300,000 new pediatric infections annually in developing countries, or approximately 40% of all MTCT of HIV [5].

As a result, the World Health Organization recommends avoidance of breastfeeding among HIV-infected mothers ‘when replacement feeding is acceptable, feasible, affordable, sustainable, and safe’ [6]. However, exclusive replacement feeding is generally not viable in less developed areas, due to the lack of potable water, inadequate hygienic conditions, high cost of formula, social stigma, and the increased risk of infant morbidity and mortality [7–9]. Additionally, developing regions face a paucity of antenatal care services, including HIV voluntary counseling and testing, and access to ART. For example, although HIV seroprevalence estimates range from 15 to 30% at antenatal clinics in many sub-Saharan African countries, the average prevention of MTCT service coverage is estimated to be less than 6% [2]. In this context, preventive health interventions, including infant feeding and nutritional counseling, and provision of ART, become increasingly important to reduce MTCT of HIV and foster improvements in maternal and child health.

In this article, we examine the role of nutrition among HIV-infected breastfeeding women and their children. We begin with a brief review of the benefits of breastfeeding and overall nutritional requirements during lactation. The relationship between nutrition, HIV, and breastfeeding is explored in detail by reviewing the available evidence from observational studies and randomized trials. Finally, we conclude with a discussion of the implications of findings on clinical and public health practice.

Breastfeeding by HIV-Uninfected Women

Benefits of Breastfeeding

Breastfeeding is well established as the international gold standard for infant feeding, due to its benefits for both the mother and infant. Benefits to the mother include child spacing, psychological comfort, a more timely return to pre-pregnancy weight, a reduced risk of postpartum hemorrhage, and decreased rates of premenopausal breast and ovarian cancer [10].

Breastfeeding confers nutritional and immunological benefits to the nursing infant, including reduced morbidity and mortality due to diarrhea and acute respiratory infections [11]. For example, in developing countries, formula-fed infants experience a three- to tenfold increase in mortality due to diarrhea and pneumonia, compared to exclusively breastfed infants [12, 13]. In fact, according to a recent review, breastfeeding promotion programs alone could directly prevent an estimated 1.3 million child deaths annually worldwide [14]. This increased risk of morbidity and mortality due to infectious diseases associated with formula feeding has been shown to persist even in the context of modest access to potable water and sanitation [15]. A potential explanation for this observation is that formula feeding may deprive the infant of the protective immunological benefits of breastfeeding, including delivery of cytokines and antibodies [16–18]. Breastfeeding also confers benefits to infant growth and development, including enhanced neurocognitive functioning among preterm neonates with very low birth weight [19], likely attributable to the polyunsaturated fatty acid content in breast milk [20]. Additionally, breastfeeding reduces the risk of otitis media and urinary tract infections in the infant [10, 13, 21].

Nutritional Requirements during Breastfeeding

In order to support maternal metabolism and infant growth and development, the nutritional needs of the mother are increased during lactation compared to the prenatal period. For example, infants double their weight at birth in their first 4–6 months of life [22]. Maternal macronutrient requirements are also greater during lactation, and are directly proportional to the intensity and duration of breastfeeding. Current guidelines recommend an additional 500 kcal/day during the initial 6 months of lactation, and 400 kcal/day thereafter [22, 23].

Maternal and infant micronutrient requirements are also increased during the lactation period. In the context of inadequate caloric intake, maternal ingestion of calcium, magnesium, zinc, folate, and vitamins B₆, B₁₂, and D may be reduced [24]. In particular, maternal supplementation with vitamins B₁₂ and D may be required during the lactation period, particularly when the maternal diet excludes animal products [22, 24]. Research to date has primarily focused on the role of vitamins B₁₂ and folate, due to their association with overt congenital deficiency diseases. However, the effects of micronutrient deficiencies on maternal and infant health during the lactation period have been largely unexamined.

Breastfeeding by HIV-Infected Women

MTCT of HIV via Breastfeeding

Vertical HIV transmission via breast milk was initially postulated when nursing infants acquired HIV infection from women who seroconverted after delivery by sexual exposure or blood transfusion [25, 26]. This assertion was supported by subsequent reports of HIV transmission via wet-nursing and pooled breast milk methods among infants with no other known source of HIV exposure [27].

As previously mentioned, interventions such as ART and exclusive formula feeding have reduced the MTCT of HIV rates to less than 2% in developed countries such as the United States [3]. However, in developing countries, where breastfeeding and HIV are widely prevalent, the proportional contribution of MTCT to the burden of HIV disease is considerably greater.

Maternal and infant factors influence the risk of MTCT of HIV via breastfeeding. For example, maternal characteristics, such as high HIV RNA levels in plasma and breast milk, compromised immune status (e.g., low CD4 cell counts), advanced clinical disease, and poor nutritional status, increase the likelihood of vertical HIV transmission [28–30]. Viral characteristics may also affect the risk of MTCT of HIV. For example, in a study of HIV-infected mother–infant pairs, only viruses which were non-syncytium-inducing and exhibited greater tropism for macrophages were transmitted to breastfeeding infants [31, 32]. The presence of inflammatory conditions such as maternal mastitis and breast abscesses also contribute to the risk of infant viral exposure and subsequent HIV transmission [33, 34]. Infant factors such as oral candidiasis and ulcers [33, 34], and the epi-

thelial integrity of the gastrointestinal tract [35] also affect the risk of exposure to HIV and transmission risk [33, 34].

Infant feeding practices also modulate the risk of MTCT of HIV. Several studies have demonstrated that the rate of HIV transmission increases cumulatively with the duration of breastfeeding throughout the postnatal period [36, 37]. This finding is likely attributable to increased infant exposure to the virus. For example, in the multi-site Breastfeeding and HIV International Transmission Study, among infants who were HIV-negative at 4 weeks of age, the rate of HIV transmission via breastfeeding was 0.74% per month, or a 4% risk per 6-month duration of breastfeeding [5].

Timing of maternal seroconversion may also affect the risk of vertical HIV transmission. For example, in a prospective cohort study in Rwanda, investigators observed an 80% HIV transmission rate among infants born to women who seroconverted within 3 months after delivery, compared to a 40% transmission rate among infants whose mothers became infected between 4 and 21 months postpartum [38]. However, breastfeeding transmission of HIV has been reported to occur as late as 36 months postpartum [39].

Infant feeding mode also affects the likelihood of MTCT of HIV; for example, mixed breastfeeding has demonstrated the greatest risk of HIV transmission, compared to exclusive short-course breastfeeding and formula feeding in several studies [40–42]. These studies, along with others that related maternal and infant factors to the risk of vertical HIV transmission via lactation, have been reviewed in detail by Downs and Cooper [43].

Effects of Breastfeeding on Nutritional Status and Mortality in HIV-Infected Women

Several observational studies and randomized trials have been conducted to examine the effects of breastfeeding on maternal health among HIV-infected women. For example, an observational study in South Africa compared nutritional status and body composition between 44 HIV-negative and 17 HIV-positive breastfeeding women. There were no significant differences observed on measures of weight, body mass index, mid-upper arm circumference, or triceps skin-fold thickness between HIV-negative and HIV-positive breastfeeding women [44].

In a randomized clinical trial in Kenya, 425 HIV-infected women were randomized to breastfeeding or formula-feeding arms. Investigators compared maternal weight at baseline (i.e., 2 weeks to 3 months postpartum) and follow-up (i.e., 5–9 months postpartum), and assessed mortality throughout the follow-up period. Breastfeeding mothers lost an average of 0.17 kg/month, whereas women in the formula-feeding group did not lose any weight on average ($p = 0.03$) [45]. There was also a three-fold increase in the risk of mortality among breastfeeding women, compared to women in the formula-feeding group. Investigators postulated that the observed increase in mortality in the breastfeeding group was likely due to a depletion in maternal nutrients. However, low levels of adherence may attenuate the observed association between infant-feeding status and subsequent risk of maternal mortality, and constrain interpretability of findings. For example, 4% of women assigned to the breastfeeding group did not provide any breast milk to their infants, and 29% of women assigned to the formula-feeding group also breastfed their infants. There were also significant differences on baseline characteristics between breastfeeding and formula-feeding groups, including a higher median plasma viral load in the women randomized to breastfeeding, which would be expected to increase the risk of MTCT of HIV in the breastfeeding arm. Further, the rate of intrauterine HIV transmission was higher in the breastfeeding group, which may be attributable to advanced disease among the breastfeeding women. However, the authors did not provide any information on clinical disease progression in the two groups [46]. Additionally, there is a lack of plausible biological mechanisms to account for an effect of breastfeeding on maternal mortality [47].

The association between breastfeeding and risk of mortality has not been replicated in other field studies among HIV-positive breastfeeding women. For example, in a study of 566 HIV-infected women in South Africa, breastfeeding status did not affect the risk of maternal mortality: 2 of 410 (0.49%) women who had ever breastfed died, compared to 3 of 156 (1.92%) who had never breastfed [47]. Similarly, in a cohort of Tanzanian women, breastfeeding status or duration were not related to the risk of maternal mortality, weight loss, anemia, or changes in CD4 cell counts [48]. Further, no association was observed between breastfeeding status and maternal mortality risk in studies in Zambia [49], Malawi [50], or in a multi-site study conducted by the Breastfeeding and HIV International Transmission Study Group [51].

Role of Nutrition in HIV-Infected Breastfeeding Women

The benefits of improved maternal nutrition are expected to be twofold. Firstly, it may reduce MTCT of HIV via breastfeeding, either as an adjunct intervention in women who are already receiving ART, or as a stand-alone strategy for women who are at a pre-ART disease stage. Secondly, nutritional interventions are likely to improve maternal health and quality of life, and infant growth and development. For example, controlled trials among HIV-infected men and women in Canada [52], Thailand [53], and Tanzania [54] and several well-designed observational studies [55] have demonstrated the benefit of micronutrient supplementation on clinical progression of HIV disease. Nutritional interventions such as micronutrient supplementation may therefore be a useful adjunct to ART or stand-alone strategies among HIV-infected breastfeeding women, in order to foster improvements in maternal and child health.

There are several potential mechanisms by which maternal nutrient supplementation may confer benefits to both the mother and infant, including improved health and reduced risk of vertical HIV transmission. For example, micronutrients are important in the promotion of epithelial integrity of maternal breast tissue, which affects infant viral exposure and risk of HIV transmission. In particular, several studies have demonstrated that vitamin A deficiency in mammary epithelial cells results in irregularly shaped cell colonies with abnormal polarity or cell–cell junction proteins [56–58]. Similarly, micronutrient supplementation may strengthen the mucosal integrity of the infant gastrointestinal tract and affect the functioning of maternal and infant T and B cells [59–61]; such effects may subsequently reduce the susceptibility to HIV infection. For example, in a South African study among children born to HIV-infected mothers, the presence of T-helper cell responses to HIV envelope proteins in umbilical cord blood was protective against HIV transmission via intrapartum and breastfeeding routes [62]. Human breast milk also confers nutritional and immunological benefits to the nursing infant, including factors which may be protective against HIV infection, such as immunoglobulins, lactoferrin, lysozyme, oligosaccharides, and glycosaminoglycans. The benefits of these immunological factors in breast milk may be further augmented by improvements in maternal nutritional status via micronutrient supplementation [59, 63].

Effect of Maternal Nutritional Status on MTCT of HIV via Breastfeeding

Observational Studies

There is a paucity of research investigating the role of nutrition as a determinant of health outcomes among HIV-positive breastfeeding women and their children. Observational studies have predominantly examined the role of micronutrients in overall MTCT of HIV, with a focus on vitamin A. For the purposes of this article, we reviewed observational studies that investigated the overall MTCT of HIV, which includes in utero, intrapartum, and breastfeeding routes. Although these studies were not designed to specifically examine HIV transmission via breastfeeding, selected outcomes were assessed at 6 weeks postpartum, which would include some contribution of HIV breastfeeding transmission.

An observational study in Kenya was conducted in order to evaluate the relationship between maternal vitamin A status and the risk of vertical HIV transmission. Investigators examined a total of 212 breast milk samples from 107 HIV-infected lactating women. There was no association between maternal vitamin A status and the presence of HIV DNA in breast milk in the overall sample; however, low serum vitamin A levels ($<20 \mu\text{g/dl}$) were associated with a 20-fold increase in the risk of detectable HIV DNA in breast milk in a sub-sample of women who were immunocompromised (i.e., CD4 cell counts of $<400/\text{mm}^3$; odds ratio = 19.7, 95% confidence interval [95% CI] 2.1, 188.5) [64].

A study in Malawi was conducted to examine the relationship between maternal vitamin A status and vertical HIV transmission. Among 338 HIV-infected pregnant women, the cumulative rate of MTCT of HIV was 21.9% at 12 months postpartum. The observed rates of vertical HIV transmission were highest among women with the lowest levels of serum vitamin A [65].

The observed association between maternal vitamin A status and the risk of vertical HIV transmission may be attributable to alternate confounding factors. For example, an infection may contribute to decreased mobilization of vitamin A liver stores, and therefore reduced serum levels [66, 67]. Therefore, low vitamin A levels may be a marker of advanced HIV disease stage, and account for the observed increase in the risk of HIV transmission. There may also be residual confounding due to additional factors that were not controlled for in these observational studies, including other nutritional deficiencies, opportunistic infections, and limited access to health care. Another limitation of these observational studies is

the lack of examination of vertical HIV transmission route or timing, which constrains interpretation of findings regarding the specific contribution of breastfeeding to MTCT of HIV.

Supplementation Studies

The findings and limitations of the aforementioned observational studies prompted the undertaking of randomized controlled trials to further investigate the relationship between nutritional supplementation and maternal and infant health outcomes among HIV-positive women.

In a trial in South Africa, 728 HIV-infected pregnant women were randomized to daily supplementation of either vitamin A or placebo throughout the prenatal period. Vitamin A supplementation consisted of daily administration of 5,000 IU of vitamin A (1.67 mg retinol equivalent) and 30 mg of β -carotene (5 mg retinol equivalent) throughout the third trimester of pregnancy, and 200,000 IU of vitamin A administered at delivery. There were no differences in the risk of HIV infection or the rate of fetal or infant mortality between the two groups at 3 months postpartum [68]. Among a sub-sample of 551 HIV-infected pregnant women who were followed through 15 months postpartum or until breastfeeding cessation, prenatal vitamin A supplementation did not reduce the risk of HIV transmission via breastfeeding [42]. In an analysis of HIV RNA levels in breast milk samples among a subset of 79 HIV-infected women, viral load was found to be strongly associated with the risk of MTCT of HIV. However, maternal vitamin A supplementation did not significantly reduce the risk of vertical HIV transmission [69].

In a trial in Malawi, 697 HIV-infected pregnant women were randomized to daily administration of iron and folate throughout pregnancy until delivery, either alone or in combination with vitamin A (3 mg retinol). All women also received 30 mg of retinol at 6 weeks postpartum as part of standard of care. There were no differences between the two groups on overall rates of MTCT of HIV at 6 weeks (vitamin A 26.6%, placebo 27.8%; $p = 0.76$) or 24 months postpartum (vitamin A 27.7%, placebo 32.8%; $p = 0.21$). However, maternal vitamin A supplementation was associated with a reduced rate of MTCT of HIV among a subgroup of infants who were HIV-negative by polymerase chain reaction (PCR) at 6 weeks. This observed effect was presumably attributable to a reduction in HIV transmission via breastfeeding (2.8 vs. 7.7% at 24 months; $p = 0.04$). However, breastfeeding status was not specifically examined in this trial, which con-

strains interpretation of findings [70]. Additionally, the authors found that maternal vitamin A supplementation during pregnancy did not significantly affect the levels of breast milk HIV viral load in a subset of these women [33].

In the ZVITAMBO trial in Zimbabwe, HIV-infected mothers and their infants were randomized to daily administration of a single high-dose of vitamin A and/or placebo supplement within 96 h of delivery in a two-by-two factorial design. The four intervention arms were: vitamin A to both mother and infant; vitamin A to mother and placebo to infant; placebo to mother and vitamin A to infant, and placebo to both mother and infant. A total of 2,060 HIV-negative infants were followed throughout the postpartum period, in order to evaluate the rate of postnatal HIV transmission (i.e., seroconversion among infants who were HIV-negative at 6 weeks postpartum). During the follow-up period, 12.1% of the infants seroconverted; single high-dose vitamin A supplementation did not reduce the risk of postnatal HIV transmission [71]. Vitamin A also had no effect on mortality among infants who were PCR-positive for HIV at baseline. Among infants who were PCR-negative at baseline but PCR-positive at 6 weeks, neonatal vitamin A supplementation reduced infant mortality by 28% ($p = 0.01$) although maternal supplementation had no effect on mortality in these infants. In contrast, among infants who were PCR-negative at 6 weeks, maternal and infant vitamin A supplementation resulted in a significant two-fold increase in mortality ($p \leq 0.05$).

In the Trial of Vitamins (TOV) study in Dar es Salaam, Tanzania, 1,078 HIV-infected pregnant women were randomized at 12–27 weeks gestation to receive daily administration, in a two-by-two factorial design, of vitamin A, multivitamins, combined vitamin A and multivitamins, or placebo supplements. The vitamin A supplement consisted of 30 mg of β -carotene (5 mg retinol equivalent) and 5,000 IU of preformed vitamin A (1.667 mg retinol equivalent); the multivitamin supplement included vitamin B complex, C, and E (20 mg thiamine, 20 mg riboflavin, 25 mg vitamin B₆, 100 mg niacin, 50 μ g vitamin B₁₂, 500 mg vitamin C, 30 mg vitamin E, and 0.8 mg folic acid). Women in the vitamin A-supplemented groups also received an oral dose of vitamin A (200,000 IU) at delivery, whereas women in the multivitamin and placebo groups received a placebo supplement. As part of standard of care, all women also received 120 mg of ferrous iron and 5 mg of folate tablets daily, and 300 mg of chloroquine as malaria prophylaxis weekly. Neither multivitamin (relative risk [RR] = 0.95, 95% CI 0.73, 1.24) nor

vitamin A (RR = 1.06, 95% CI 0.81, 1.39) supplements affected the risk of HIV transmission or infant survival up to 6 weeks postpartum. Maternal multivitamin supplementation, but not vitamin A, increased infant birth weight [72] and resulted in significant reductions of approximately 40% in the risks of fetal death, low birth weight (<2,500 g), severe preterm birth (<34 weeks gestation), and small size for gestational age [73]. Multivitamins, but not vitamin A, also resulted in a significant increase in maternal CD4, CD8, and CD3 cell counts [73].

In the TOV trial, maternal vitamin A supplementation resulted in a significant 38% increase in the risk of overall vertical HIV transmission, whereas multivitamins did not demonstrate a similar effect [74]. Multivitamin supplementation also significantly reduced the risk of HIV transmission via breastfeeding and improved HIV-free survival among children who were born to women who were nutritionally or immunologically compromised (i.e., lowest quartile of total lymphocyte count) at baseline, and remained HIV-negative at 6 weeks.

In the TOV study, the investigators also examined various clinical and immunological markers of disease progression among HIV-infected women throughout the follow-up postpartum period. Multivitamin supplementation reduced the risk of progression to WHO stage IV and of AIDS-related death by approximately 30% (RR = 0.71, 95% CI 0.51, 0.98) [54]. Multivitamins also significantly reduced the incidence of maternal oral and gastrointestinal manifestations of HIV disease, reported fatigue, rash, and acute upper respiratory infections. Multivitamin supplements significantly increased maternal CD4 and CD8 cell counts, reduced the level of viral load [54], and demonstrated a protective effect against wasting among HIV-infected women [75]. Vitamin A supplementation alone did not result in similar improvements on these outcomes [73].

The adverse effects observed in the vitamin A arm of the Tanzania trial may be attributable to the β -carotene component of the regimen. Although β -carotene has been found to be relatively safe for short periods of time among HIV-infected individuals, the safety of prolonged supplementation has not been investigated [76, 77]. Some recent insight into the long-term safety, as well as therapeutic efficacy, of carotenes has come from an intervention trial in adult patients with advanced AIDS in Canada, the CTN 091/CRIT Carotenoids Study Group [78]. Investigators in the latter study randomized 166 patients in the control group to a standard micronutrient supplement (including vitamin A and trace elements) and 163

patients in the treatment group to the standard micronutrient supplement plus mixed carotenoids (equivalent to 72 mg of β -carotene) daily for 18 months. No adverse effect of carotenoids was observed; in fact, a statistically nonsignificant increase in mortality was found in the participants who did not receive carotenoids compared with those who did. This increase became significant on adjustment for baseline CD4 counts and serum carotene concentrations (hazard ratio of time to death = 3.15, 95% CI 1.10, 8.98). One major limitation of this study, however, was the markedly reduced potency of the dose of the supplement administered; the authors reported that the daily dose of the study medication was equivalent to only 9.2 mg of β -carotene during the course of the study instead of the 72 mg proposed.

The observed adverse effects of vitamin A on vertical HIV transmission in the trials in Tanzania and Zimbabwe may also be due to the effect of vitamin A on the HIV genome; vitamin A could potentially modulate HIV replication via a retinoic acid response element in the viral genome [79]. Vitamin A may also lead to an increased density of CCR5 receptors by increasing the multiplication and differentiation of lymphoid and myeloid cells; these CCR5 receptors are critical for the attachment of the virus to the lymphocytes, and subsequent viral replication [71, 80]. Additionally, vitamin A may increase the risk of HIV transmission by accelerating the rate of maternal HIV disease progression. For example, in a large observational cohort study in the United States, investigators observed a U-shaped relationship between dietary and supplemented vitamin A intake and the risk of progression to clinical AIDS and death [81, 82]. Specifically, the lowest and highest quartiles of vitamin A intake were associated with significantly increased progression to AIDS, compared to the middle two quartiles.

There are two notable distinctions between the TOV study in Tanzania and the other aforementioned studies. Firstly, in the Tanzanian trial, maternal supplementation continued beyond the antenatal period, which increases the relevance of findings for HIV-infected breastfeeding women and their infants. Secondly, investigators examined the effects of micronutrient supplements on specific vertical transmission routes, including intrauterine, intrapartum, and breastfeeding modes. Findings demonstrated the beneficial effects of multivitamin supplementation on three aspects: maternal nutritional and immune status; MTCT of HIV via breastfeeding, and infant growth and development, morbidity, and mortality outcomes.

Conclusions

Breastfeeding confers benefits to both the mother and nursing infant, including improved maternal and child health and improved infant growth and development. However, in the context of HIV/AIDS, breastfeeding also increases the risk of MTCT of HIV, and this is proportional to the duration of breastfeeding. Additional factors exacerbate the risk of vertical HIV transmission, including the mode and pattern of infant feeding, maternal nutritional and immunological status, and maternal HIV disease stage.

The World Health Organization guidelines recommend avoidance of breastfeeding among HIV-infected mothers when replacement feeding is acceptable, feasible, affordable, sustainable, and safe. In developing countries where these conditions are not present, the WHO recommends exclusive breastfeeding for the first 6 months followed by abrupt cessation.

There is a paucity of research investigating the role of nutrition among HIV-infected breastfeeding women and their children. Current evidence does not support supplementation with vitamin A for HIV-infected pregnant or breastfeeding women, based on the increased risk of vertical HIV transmission from trials in Tanzania and Zimbabwe. However, daily maternal multivitamin supplementation, including vitamins B, C, and E, is strongly recommended throughout the prenatal and postpartum periods in order to reduce vertical HIV transmission, delay maternal HIV disease progression, and improve maternal and child health. This is likely to be particularly beneficial among women who are earlier in their HIV disease and not yet eligible for ART; the efficacy and safety of multivitamin supplementation among individuals who are on ART have yet to be ascertained.

Research Gaps and Future Directions

Further research is warranted to examine the role of nutrition in maternal and child health among HIV-positive breastfeeding women and their children. Specifically, additional research is needed to elicit the exact mechanism of HIV transmission via breastfeeding; this would help to identify nutritional and other factors that may be the most relevant to reducing MTCT of HIV. The impact of nutritional factors on conditions that promote HIV transmission risk, such as mastitis, also needs to be defined.

Additional research is therefore needed to determine the appropriate micronutrient supplementation for HIV-infected lactating women and their infants. In particular, the interaction between ART and nutritional factors including micronutrient supplementation needs to be elucidated.

Further research is also warranted in the development of viable alternate feeding plans for infants. This becomes particularly important in light of recent findings that

demonstrate the contribution of inadequate complementary or replacement feeding to the increased risk of growth failure and stunting in infants born to HIV-infected women [83]. Provision of nutritional and infant feeding counseling to nursing mothers is therefore urgently needed to ensure early breastfeeding cessation and adequate feeding practices thereafter among HIV-infected women who choose to breastfeed.

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