Full Length Research Paper

Does infant feeding modality have an impact on the health of mothers infected with human immunodeficiency virus in sub-Saharan Africa? A systematic literature review

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Concerns for perinatal HIV transmission and health of infants have led to calls for a religious adoption of WHO recommendations on HIV and infant feeding. That which is not established is how this impacts on the health of mothers. While the dilemma of breastfeeding and risk of transmitting the virus to the infant is fast becoming history, the impact infant feeding choices may have on the health of mothers is not well characterized. This review provides current knowledge on how infant feeding choices of HIV-positive mothers affect their own health. A computer-aided systematic search of literature for articles published between 1985 and 2010 was done. Two independent literature searches were conducted using PubMed and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Ten eligible articles, most of which reported no adverse effect of breastfeeding on health of HIV-positive mothers. One study presented findings attributing increased maternal mortality to breastfeeding. Another study concluded that breastfeeding was associated with reduced CD4 counts and lower body mass index, although these effects were not clinically relevant. Several others attributed maternal morbidity and mortality to high levels of plasma HIV viral load. This review does not support the belief that HIV-positive mothers are exposed to an increased risk of adverse conditions when breastfeeding.

Key words: Infant feeding modality, sub-Saharan Africa, HIV-positive mothers, breastfeeding, mixed feeding, formula feeding.

INTRODUCTION

In sub-Saharan Africa, breastfeeding is largely the culturally acceptable mode of infant feeding, with over 95% of infants in the region being breastfed (Dop, 2002). However, particularly in West Africa, the rate of exclusive breast-feeding is low; giving water and other liquids to breastfed infants is a widespread practice (Abiona et al., 2006; Becquet et al., 2008; Dop, 2002; Engebretsen et al., 2007) and the rate of bottle-feeding is high in some

countries exceeding 30% in Tunisia, Nigeria, Namibia and Sudan (Abiona et al., 2006; Dop, 2002). Nevertheless, prolonged breastfeeding is common, and median breastfeeding duration has been reported to be about 16 to 28 months.

Before the advent of HIV, breastfeeding was unquestionably the international gold standard for infant feeding, as it is known to reduce the risk of infant morbidity and mortality as well as foster improvements in child growth and development. However, the recognition that HIV could be transmitted through breastfeeding precipitated a public health dilemma. The strong preferences by health professionals for either breastfeeding or

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replacement feeding for HIV-positive mothers have often resulted in heated debates about the subject (Coovadia and Coutsoudis, 2007; Coovadia et al., 2007). The key arguments in resource-limited settings are whether the multiple benefits of breastfeeding outweigh its disadvantage in increasing the risk of transmission of the virus, versus the zero risk of transmission through formula feeding countered by exposure to the increased risks of mortality and morbidity from common childhood diseases.

As a result of these new concerns, the effect of infant feeding modality on the health of infants of mothers infected with HIV has been the central subject of HIV research over the past three decades (Chisenga et al., 2005; Engebratsen et al., 2007; Becquet et al., 2008; Abiona et al., 2006). This without a doubt has resulted in making infant feeding safer for children born to HIVpositive women. Ironically, the impact of infant feeding type on the health of the HIV-positive mother, whose health invariably affects the health of the infant, has not received as much attention. Of note is the fact that when a mother is sick, care of her child is compromised, and when she dies, the risk of her child dying also is more than tripled (Nduati et al., 2001; Taha et al., 1996). The dearth of data regarding the impact of infant feeding modality on the health of HIV-positive mothers has been echoed by a number of eminent researchers in this field (Coutsoudis et al., 2001; Lawrence, 1994; Nduati et al., 2001; Taha et al., 2006).

Thanks to the enormous amount of research done on some aspects of this problem, the dilemma of breastfeeding and risk transmitting the virus to the infant through their milk, or to do replacement feeding and risk losing them to diarrhea-related infectious morbidities, is fast becoming history. That which is still uncertain is the impact infant feeding choices has on the health of mothers. To breastfeed or to replacement feed is thus one of the dilemmas that pregnant women infected with HIV and living in resource-constrained settings contends with. These dilemmas are not constructs based solely on the survival of infants but also on their (the mothers' own) health. This review therefore seeks to bridge this evidence gap by providing the current state of knowledge on the impact on health of mothers of their infant feeding modality.

METHODOLOGY

Search strategy

A computer-aided search of online data bases was performed. Different strategies relating to mode of feeding (breastfeeding, mixed feeding, formula feeding) and health of HIV mothers were used to search the literature for articles on health impacts of feeding modes on HIV-positive mothers.

In order to prevent selection bias, by capturing as many relevant studies as possible, two independent literature searches were conducted: one using MEDLINE/PUBMED and another in Cumulative Index to Nursing and Allied Health Literature (CINAHL). Additional

relevant references cited in retrieved articles and related articles were subsequently obtained. In addition to the electronic search, the reference lists of the articles initially identified were searched.

Selection criteria for studies

Studies were selected for reviews if they were published in English, were examining the effects of infant feeding modality (breastfeeding, mixed feeding, formula feeding) on the health of HIV-positive mother. Studies, which met the above criteria, were selected regardless of duration of breastfeeding in HIV-positive mothers.

Criteria for including articles

Only peer-reviewed articles (in English) published between 1985 and 2010 were included. Only articles of studies conducted in Sub Saharan Africa were included; articles must have included information about breastfeeding and/or mixed feeding and/or formula feeding and health of HIV-positive women concurrently.

Studies restricted to outcome measures in infants were excluded from the analysis. Articles were also excluded if they were literature reviews or commentaries, or patient/sample were not HIV-positive women.

A matrix was developed for extracting data and included Author and Date of publication; Study design; Study publication; Type of infant feeding investigated; Outcome measures; and Results/Findings.

Detailed appraisals of articles were done not only of their titles and abstracts but also the methodological quality of the study. Examination for potential biases was done by qualitatively assessing the study design, blinding, premature discontinuation rates, and loss to follow-up rates where applicable.

RESULTS

The primary literature search yielded 456 articles. Of these, 436 were excluded, since they were irrelevant to the topic being researched. A search of other metanalyses and reference lists yielded 8 additional studies, which were included in the review process. From the 28 publications, 18 were eliminated based on the inclusion criteria. Ten articles were selected for the final review.

The studies included in the review are shown in Table 1. All 10 studies were conducted in sub-Saharan Africa: Malawi (n=2), Kenya (n=2), Tanzania (n=1), Zambia (n=1), Botswana (n=1), South Africa (n=2) and one study which covered different regions of Africa was conducted Breastfeeding and HIV the International Transmission Study Group. Two of the 10 reviewed studies are randomized control trials (Kuhn et al., 2005; Nduati et al., 2001). 1 an individual metanalysis of clinical trials in the BHITS database (Breastfeeding and HIV International Transmission Study Group, 2005), 5 prospective observational studies; nested in ongoing clinical trials (Bland et al., 2007; Coutsoudis et al., 2004; Otieno et al., 2007; Sedgh et al., 2004; Taha et al., 2006), 1 formative study (Bentley et al., 2005) and 1 cross

Table 1. Summary of characteristics of reviewed articles.

Author/Date/ Location	Aims	Study design	Type of Infant feeding	Outcome measures	Results/Findings
(Coutsoudis et al., 2001) Durban, South Africa	Are HIV-infected women who breastfeed at increased risk of mortality and morbidity?	Observational	*Ever breast feed *Never breastfeed	*Maternal mortality *Maternal morbidity	*No increase in mortality rates among breast feeders *No increased risk of morbidity in breastfed compared to formula feeding (never breastfed) group
(Nduati et al., 2001) Nairobi, Kenya	Determine effects of breastfeeding on maternal death rates 2 years after delivery	Clinical trial	*Breastfeed *Formula feed	*Maternal mortality	*Mortality among mothers was higher in the breastfeeding group than in the formula feeding group
(Sedgh et al., 2004) Tanzania	*To examine association between breastfeeding and maternal HIV disease progression	Observational	*Exclusive Breastfeeding (duration, frequency)	*Mortality *Disease progression markers like CD4 cell count, anemia and weight loss	*No significant associations in the risks of adverse outcome with durations of breastfeeding. These associations did not change over time * Regardless of baseline health status, No significant associations between breast feeding and mortality/ adverse outcomes for disease progression markers
(Bentley et al., 2005) Lilongwe, Malawi	*To find out the perceived ability for HIV + women to exclusively breastfeed for 6months *Secondarily, to find out perceived relationship between maternal health and exclusive breastfeeding by HIV-positive women	Formative research (semistructured interviews)	*Exclusive breastfeeding *Exclusive formula feeding	*Maternal health	Women perceived breastfeeding may increase the progression of HIV Also women perceived high cost of formula a barrier to replacement feeding
(BHITS- Breastfeeding and HIV International Transmission Study Group , 2005)	* Estimate the risk and timing of mortality among HIV +mothers (18 months after delivery) according to their children's feeding modality * To identify factors associated with mothers' mortality.	Clinical trials (Metanalysis)	*Ever Breastfed *Never Breastfed	*Mortality *CD4 counts	*Maternal mortality did not differ according to infant's feeding modality with/without adjustment for maternal CD4 counts. *Of women who initiated breastfeeding, lower mortality risk in women still breastfeeding compared with those not breastfeeding is likely due to better overall maternal health *Factors associated with mothers' mortality include adverse events in infants like HIV infection, low birth weight and mortality

Table 1. Contd.

(Eide et al., 2006) Botswana	*To find out about social consequences for women participating in PMTCT projects- choice of infant feeding mode	Cross sectional study (structured interviews)	*choice of exclusively breastfeeding * choice to formula feed	Social consequences	Interrogation, judgement, stigmatization from the community for both choices, depending on expectations of the community
(Kuhn et al., 2005) Lusaka, Zambia	*Determine if mortality (up to 2 years post partum) increases with longer duration of breast feeding	Intervention trials	*Prolonged breastfeeding *Abrupt cessation of breastfeeding after 4 months	Mortality	No difference in mortality between long breast feeding and short breastfeeding group
(Otieno et al., 2007) Nairobi, Kenya	*Compare risk of mortality in breastfeeding and formula feeding women * Compare markers of HIV disease progression in breastfeeding and formula feeding women	Observational- prospective	*Breastfeeding *Formula feeding	*Maternal mortality *BMI *HIV-1 RNA levels * CD4 counts	* Breastfeeding not associated with increase in HIV-1 RNA levels and mortality *Breastfeeding associated with significant decreases in CD4 cell counts and BMI
(Taha et al., 2006) Malawi	*Determine impact of breastfeeding on risk of mortality and morbidity of HIV + women *Determine impact of breastfeeding on mortality of their children	Longitudinal study	*Breastfeeding *Mixed feeding *No breastfeeding	*Maternal mortality and morbidity *Infant mortality and morbidity	*Breastfeeding significantly not associated with mortality or morbidity *Breastfeeding significantly associated with reduced infant mortality
(Bland et al., 2007) South Africa	*To compare occurrence of breast health problems in HIV infected and HIV uninfected women	Observational (prospective)	Exclusive breastfeeding	Breast health problems	No differences in HIV infected and HIV uninfected women for the breast health problems investigated

sectional study using structured interviews (Eide et al., 2006).

DISCUSSION

This systematic review provides evidence that to a large extent breastfeeding does not have an adverse effect on health of HIV-positive mothers. Additionally, anemia and breast health problems have no significant association with breastfeeding in HIV-positive mothers. The major risk factor associated with mortality in mothers was the level of plasma viral load. These findings support the revised WHO recommendations, in late 2009, to provide mothers known to be HIV-infected with lifelong anti-retroviral treatment, in order to reduce HIV transmission through breastfeeding (WHO, 2010).

The reviewed articles gave insight into the associations

of infant feeding type to maternal mortality, Acquired Immune Deficiency Syndrome (AIDS), CD4 counts/Viral Loads, maternal health and the perceptions of HIV-positive mothers on breastfeeding. These are discussed.

Mortality

The weight of evidence supports the findings that breastfeeding in HIV-positive women is not associated with increased mortality. Out of 6 studies, that investigated association between breastfeeding and mortality in HIV-positive women, all but one (Nduati et al., 2001) found no association.

In the clinical trial conducted by Nduati et al. (2001), although women randomized to breast feed were similar to those randomized to formula feed in terms of their baseline CD4 cell counts and HIV-1 viral load, women in

the breastfeeding arm had a 3.2- fold increased risk of mortality in the 2 year postpartum period (95% CI 1.3,8.1). These women also had a significantly greater decline in weight compared to the formula feeding women (mean 0.17 versus 0.00 kg/month; p=0.03). The authors concluded that breastfeeding might lead to adverse effects on an HIV-infected mother. This study has a number of limitations that must be noted. Chief among them according to Otieno et al. (2009) was the fact tat, the study was primarily designed to determine infant feeding choices on vertical transmission of HIV; the maternal outcomes published were assessed as a secondary analysis. Thus, data were not available for other indicators of maternal disease progression such as CD4 counts, BMI, viral levels or even cause of death (Otieno et al., 2009). There was no record of adherence to random assignment, making it difficult to ascertain if women randomized to the formula feeding group never breastfed.

Nduati and colleagues postulated the combined metabolic burden of HIV infection and breastfeeding in a population that has inadequate nutrition intake as a cause of greater weight loss and higher mortality in the breastfeeding arm. Although this is plausible, the direct effects of breastfeeding on HIV disease course have not been clearly illustrated (Otieno et al., 2009).

There are also reports of breastfeeding women generally doing well, with no increased mortality during acute famine (Newell, 2001). Although breastfeeding may affect maternal nutrition status, it is not known to kill mothers (Gigante et al., 2001). These findings of Nduati et al. (2001) thus conflicted markedly with the findings of the subsequent studies that investigated mortality.

The second publication in 2001 described an observational study by Coutsoudis and colleagues of a cohort of HIV infected postnatal women in South Africa. This secondary analysis found no additional risks of mortality associated with breastfeeding. Mortality was very rare in this cohort, 2/410 (0.5%) among women who ever breastfed versus 3/156 (1.9%) among those who never breastfed. This study therefore lacked adequate power to demonstrate differences in the two feeding groups. Being an observational study, there could also be a possibility of selection bias. Interpreting data from observational studies can be difficult because there are many factors that influence a mother's infant feeding choice, including mother's health status. The "healthy breast-feeder effect" points out this misinterpretation of observational data. Sicker mums may opt either not to breastfeed or shorten the duration of breastfeeding while mothers who choose to breastfeed may do so because they are healthier, and thus may have overall better health outcomes. This selection bias according to Kuhn et al. (2005) may have confounded the outcome assessment. This selection bias was also evident in the Tanzanian cohort and BHITS compilation of African studies (Sedgh et al., 2004). In all of these studies, assessment of maternal outcomes was post hoc,

following cohorts designed primarily for assessment of mother- to-child HIV transmission.

Kuhn et al. (2005) study in 2006 based in Lusaka Zambia, avoids this bias in the afore discussed studies by assessing effect of duration of breastfeeding on mortality with a randomized study. Their finding of no association in a randomized, rather than non-experimental, study design carries particular salience. Additionally, analyses based on actual practice yielded the same conclusions, thus failure to adhere to random assignment was unlikely to have diluted associations. A limitation of this study is the sole evaluation of mortality as the outcome measure for HIV disease progression. Other markers of disease progression like viral load, CD4 counts, BMI, etc were not measured.

Acquired Immune Deficiency Syndrome (AIDS)

No literature on association between AIDS and feeding choice was found in this review. One study by Sedgh et al. (2004) investigated the effect of breastfeeding on markers of disease and progression of disease, and found no significant associations (Sedgh et al., 2004).

CD4 count, viral load

Three of the studies reviewed investigated the effect of breastfeeding on the CD4 counts. Sedgh et al. (2004) and the metanalysis by BHITS found no significant associations between breastfeeding and CD4 counts. The study by Otieno et al. (2009), prospectively compared immunological and viral markers of HIV progression, as well as the risk of mortality between breastfeeding and formula feeding HIV-positive women. Although breastfeeding was associated with significant decreases in CD4 cell counts and BMI. None of these associations reached clinical relevance. Breastfeeding was also not associated with clinically relevant adverse effects on viral levels or mortality. The women who breastfed had worse socioeconomic and educational characteristics than non-breastfeeding mothers. However, the conclusion was derived from a linear mixed-effects regression model that allowed women who had stopped breastfeeding to switch into a 'former' breastfeeding category to be compared to"current" and "never" groups (Kuhn et al., 2007).

To address some of the emerging concerns, Taha et al. (2006) also conducted a longitudinal study nested in a clinical trial, comparing mortality and morbidity in breastfeeding, mixed feeding and formula feeding groups of HIV-positive women in Malawi. The evidence indicated that breastfeeding by HIV-positive women was not associated with morbidity or mortality. Morbidity indicators investigated were maternal hospitalization/ use of medicines, symptomatic HIV disease or limitations of physical activity. These indicators were also good markers of disease progression. A limitation of this study

was the introduction of information/misclassification biases. Firstly, there is no certainty that reported exclusive breastfeeding was completely breastfeeding and no complementary foods were given. With even occasional provision of complementary foods, type of feeding will be predominant breastfeeding not exclusive. Secondly, the reported frequency of breastfeeding was crude and the cut- off point (5 times during day and night) was arbitrary, having no clinical relevance. Lastly, this study was not a randomized trial, thus changes in breastfeeding as HIV disease progressed could have introduced some bias.

In summary, breastfeeding in HIV-positive women has no significant association with disease progression markers like reduced CD4 counts and increased viral load.

Perceptions and social consequences

One study on perception and one on social consequences were reviewed. Although cross sectional studies are not the most rigorous study designs available, the study by Eide et al. (2006) provides us with pertinent information about the social consequences of women's infant feeding choices. HIV-positive women in resource-limited regions are already faced with the hard choice of exclusively breastfeeding (for the first 6 months) and risking vertical transmission if they cannot meet the AFASS guidelines for exclusive formula feeding. This study provides us with information about another hurdle these HIV-positive women have to deal with daily; interrogation, judgment and stigmatization by community members (depending on what feeding modality is acceptable in their society) (Eide et al., 2006).

Bentley et al's formative research on perceptions of the impact of breastfeeding on HIV gave in-depth qualitative information about the perceptions of some HIV-positive women in a resource limited setting in Malawi. Most of these women perceived that exclusive breastfeeding may increase the progression of HIV, unless they could supplement their diet with high quality foods. Most noted however that the high cost of infant formula would prohibit both options (Bentley et al., 2005). This may be a possible explanation of why most women do mix feeding in spite of the risk of vertical transmission.

In summary, although these are single studies on perceptions and social consequences for HIV-positive women, they raise important questions about self-efficacy of these women to breastfeed, knowledge of safe infant feeding practices, food insecurity and issues of stigmatization as genuine concerns that should be addressed in this population.

Maternal health: anemia, breast health, BMI (weight loss)

Three studies looked at maternal health indicators like weight loss, anemia and breast health. Sedgh et al.

(2006) concluded from evidence in their study that regardless of baseline health status, no significant associations was found between breast feeding and anemia or weight loss. However, Otieno et al. (2006) found significant association between breastfeeding and lower BMI.

Lastly, in 2007, Bland et al. prospectively followed a cohort of HIV infected and- uninfected women and conclude based on the evidence that although breast health problems (painful nipple, cracked nipple, bleeding nipple, engorgement, blocked milk duct, breast thrush, nipple oozing pus, breast oozing pus, and mastitis/ abscess) are generally rare, there was no difference in its occurrence among HIV-infected and uninfected women (Bland et al., 2007). Definition, diagnosis and management of these problems were based on the WHO/UNICEF Trainer's guide.

It is worthy of note that women with these breast health problems are more likely to pass on the virus to their breastfeeding infants. And thus, it is highly important that they receive prompt management of problems by breastfeeding counselors.

Overall, considering the different outcomes investigated in this review, breastfeeding in HIV-positive does not increase risk of mortality or decrease CD4 counts or increase viral loads (RNA level) in HIV-positive women. In addition, anemia and breast health problems have no significant association with breastfeeding in HIV-positive mothers. However, breastfeeding in these women may result in reduced BMI (weight loss) and dire social consequences like stigmatization and isolation in some communities. Finally, some HIV women may perceive breastfeeding to increase progression of HIV because of underlying food insecurity issues.

Implications for public health

In late 2009, the WHO's recommendation for ART therapy was revised to provide mothers known to be HIV-infected with lifelong antiretroviral prophylaxis or treatment, in order to reduce HIV transmission through breastfeeding. (WHO, 2010) This is a giant step towards slowing down disease progression in infected mothers and reducing significantly the likelihood of transmission to infant.

In light of current evidence, the above recommendations should be adhered to in these settings to promote health in both mother and child. However, there is still a need for more research to find solutions and advocate for policies to address nutritional inadequacies/ food insecurity in HIV-positive mothers. Social issues like stigmatization in the community, due to infant feeding choices of HIV-positive women need to be addressed. There is also the need to make up- to- date information on the progression of HIV disease and infant feeding choices available to these women.

CONCLUSIONS AND RECOMMENDATIONS

This review presents evidence that to a large extent, breastfeeding does not have an adverse effect on health of HIV-positive mothers. The WHO's revised recommendations (2009) on infant feeding and antiretroviral therapy in HIV-positive mothers should be used as guidelines in these settings to protect the health of both mother and child.

Although great milestones have been achieved in the area of expert and patient education, there is still a need to continually equip health professionals and educators with the most up to date information on the disease. At the same time, avenues should be created to bridge current gaps in knowledge. Mothers need information about the relative risks and benefits of breast-feeding, progression of HIV, early weaning, wet-nursing and formula feeding.

Additionally, all choices available to women with regards to infant feeding should be discussed and guidance provided to help infected women make an informed choice.

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