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Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study

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Summary

Background The observation that mother-to-child transmission of HIV-1 can occur through breastfeeding has resulted in policies that recommend avoidance of breastfeeding by HIV-1-infected women in the developed world and under specific circumstances in developing countries. We compared transmission rates in exclusively breastfed, mixed-fed, and formula-fed (never breastfed) infants to assess whether the pattern of breastfeeding is a critical determinant of early mother-to-child transmission of HIV-1.

Methods We prospectively assessed infant-feeding practices of 549 HIV-1-infected women who were part of a vitamin A intervention trial in Durban, South Africa. The proportions of HIV-1-infected infants at 3 months (estimated by use of Kaplan-Meier life tables) were compared in the three different feeding groups. HIV-1 infection was defined by a positive RNA-PCR test.

Findings At 3 months, 18.8% (95% CI 12.6–24.9) of 156 never-breastfed children were estimated to be HIV-1 infected compared with 21.3% (17.2–25.5) of 393 breastfed children ($p=0.5$). The estimated proportion (Kaplan-Meier) of infants HIV-1 infected by 3 months was significantly lower for those exclusively breastfed to 3 months than in those who received mixed feeding before 3 months (14.6% [7.7–21.4] vs 24.1% [19.0–29.2], $p=0.03$). After adjustment for potential confounders (maternal CD4-cell/CD8-cell ratio, syphilis screening test results, and preterm delivery), exclusive breastfeeding carried a significantly lower risk of HIV-1 transmission than mixed feeding (hazard ratio 0.52 [0.28–0.98]) and a similar risk to no breastfeeding (0.85 [0.51–1.42]).

Interpretations Our findings have important implications for prevention of HIV-1 infection and infant-feeding policies in developing countries and further research is essential. In the meantime, breastfeeding policies for HIV-1-infected women require urgent review. If our findings are confirmed, exclusive breastfeeding may offer HIV-1-infected women in developing countries an affordable, culturally acceptable, and effective means of reducing mother-to-child transmission of HIV-1 while maintaining the overwhelming benefits of breastfeeding.

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Introduction

Since the discovery that HIV-1 can be transmitted through breastfeeding, several policy recommendations have been developed,^{1,2} which are expected to have a global impact on maternal and infant health. Whether prevention of HIV-1 infection through avoidance of breastfeeding will in practice outweigh the adverse effects of not breastfeeding has yet to be discovered. Breastfeeding by HIV-1-infected women in more-developed countries has virtually ceased³ and in less-developed countries many thousands of seropositive women and women who believe they may be HIV-1 infected are expected to avoid breastfeeding. The cultural diffusion theory raises the possibility that a loss of confidence in breastfeeding will spread to all women.⁴

Advocates of child care consider breastfeeding to be one of the principal gains to current maternal and child health, regained through long-standing campaigns to protect mother and infant wellbeing. The reason why breastfeeding is believed to be pre-eminent in human nutrition derives from its well-recognised nutritional, immunological, social, psychological, and nurturing benefits, which are especially important in the first 3 months.⁵

Analyses of HIV-1 transmission via breastmilk are flawed because they have failed to account for the effects of different types of breastfeeding practices: exclusive or mixed breastfeeding (without or with water, other fluids, and foods that might contaminate and injure the immature gastrointestinal tract).⁶ Two studies have attempted to examine the effect of different breastfeeding patterns on mother-to-child transmission,^{7,8} but both have limitations. The most widely quoted meta-analysis on the risks of mother-to-child transmission by breastfeeding⁶ depended on studies with small sample sizes, short breastfeeding durations, and studies that do not distinguish exclusive from mixed breastfeeding.

We prospectively examined the impact of different patterns of breastfeeding on mother-to-child transmission of HIV-1 at 3 months of age.

Methods

Design

The mother-infant pairs enrolled in this study were participating in a vitamin A intervention trial to reduce the rate of mother-to-child transmission of HIV-1. The study took place at antenatal clinics of two hospitals in Durban, South Africa (King Edward VIII Hospital and McCord Hospital). Women were recruited between July, 1995, and April, 1998, and were randomly assigned vitamin A (daily supplement containing 5000 IU retinyl palmitate and 30 mg β -carotene) or placebo. Women started treatment at 28–32 weeks' gestation. At delivery, women in the vitamin A group received a single dose of 200 000 IU retinyl palmitate. Women in the placebo group received placebo on the same schedule. No woman received antiretroviral therapy.

During antenatal visits all women were counselled about the risks of HIV-1 transmission through breastmilk and about health benefits of breastfeeding. Women were asked to make an informed choice on whether to breastfeed or formula-feed in accordance with recent recommendations from UNAIDS, WHO, and UNICEF. Women who chose to breastfeed were counselled to consider exclusive breastfeeding because of the possible dangers of gut-wall damage, which was a difficult concept for most of the mothers because it is culturally acceptable to give water and herbal teas early during breastfeeding and to introduce solids, such as infant cereals, within the first month of life.⁹ Research staff were careful not to influence women's choices, and once a choice on feeding method was made, the woman was supported in her choice. However, women who chose to formula-feed were not supplied with free formula, but were given the option to purchase it from the hospital at a subsidised rate.

Mothers were asked to attend a follow-up clinic when their infants were 1 week, 6 weeks, and 3 months of age, and thereafter every 3 months. At each follow-up visit mothers were asked about infant-feeding and breastfeeding practices by staff who were not involved in the initial counselling. We asked specific questions about feeding of any fluid or solid and recorded responses on a data sheet that included the date at which each item was introduced to the infant.

Venous blood was drawn from mothers at entry to the study for baseline differential cell count and lymphocyte subset analysis. CD4-cell subset was counted by flow cytometry on a Coulter Epics Profile 2 flow cytometer (Coulter Electronics, Miami, FL, USA) with specific monoclonal antibodies. Baseline serum vitamin A concentrations were measured by reverse-phase high-performance liquid chromatography.¹⁰

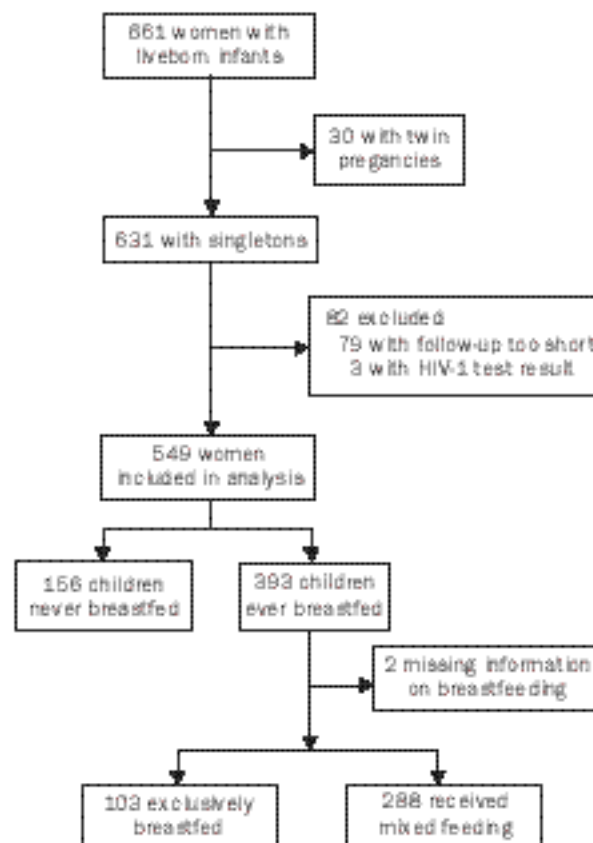
Venous blood was drawn from the infant on the first day after birth and again at 1 week, 6 weeks, and 3 months of age, and every 3 months thereafter until age 15 months. If the mother was still breastfeeding, venous blood was drawn from the infant at 3 months after the end of breastfeeding. Plasma was separated within 5 h and stored at -70°C for possible subsequent quantitative assay of HIV-1 RNA by PCR (Roche Molecular Systems, Branchburg, NJ, USA) at the South African National Institute of Virology.¹¹ RNA was extracted from 200 μL plasma in the presence of an internal RNA standard, and a sample was subjected to reverse-transcription PCR amplification with *Thermus thermophilus* HB8 DNA polymerase in the presence of dUTP and uracil-DNA-glycosylase. Internal standard and HIV-1-specific PCR products were quantified after PCR with a microtitre-format ELISA. The limit of detection of the assay was about 10 RNA copies (about 400 copies/mL) with a linear dynamic range of at least 4 log₁₀ units and a coefficient of variation of about 25%.

We did RNA tests in children who had two positive ELISA tests at 9 months and 15 months, starting with the earliest sample and testing sequentially until the first positive test. In children who had not yet reached 15 months of age but who had reached 9 months, an ELISA (Abbott Laboratories, Chicago, IL, USA) was done at 9 months and an RNA-PCR test at 6 months; if these results were positive, we did RNA tests on the stored plasma samples starting with the earliest sample until the first positive test. Children who had not yet reached 9 months had an RNA-PCR test on each of their last two samples, and if either of these were positive, samples were tested from the earliest, as described above.

The study was approved by the ethics committee of the University of Natal. Written informed consent was obtained from all women in the trial.

Statistical analysis

We restricted analysis to singleton infants because twins are more difficult to breastfeed and more vulnerable to early mortality. Breastfeeding duration was estimated by Kaplan-Meier life-table methods. For mothers known to have stopped breastfeeding, the reported age of the child when breastfeeding stopped was used as the endpoint. For mothers lost to follow-up or who had not



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stopped breastfeeding at the time of study, the child was censored at the age they were last seen.

The proportions of children in each feeding group HIV-1-infected by 3 months of age were estimated with Kaplan-Meier life-table methods, as used in the analysis of AIDS Clinical Trials Group protocol 076.¹² This method, which takes into account the prospective nature of the data, estimates the cumulative probability of a positive result at each timepoint. A single PCR-positive result was taken as evidence of infection. Children with no positive results were retained in the analysis as uninfected until the age of their last negative test, at which they were censored. Children with later negative results but who were missing earlier test results were assumed to be negative at earlier timepoints. We tested differences between the feeding groups using a z-statistic calculated as the difference in the probabilities of infection by 3 months in the two groups compared divided by the square root of the sum of their variances from the Kaplan-Meier life-table model. These probabilities estimate rates of transmission detectable by specific ages but may underestimate true rates of transmission occurring by the specific age, since there is a delay between actual and detectable infection and variable intervals between testing. This underestimation is greater for postnatal than for perinatal transmission because postnatal transmission occurs closer in time to the endpoint of the analysis. We used Cox's proportional-hazards models with follow-up data to 3 months for multivariate analysis to adjust for potential confounders.

Results

Study sample

661 women recruited into the vitamin A trial were known to have had a liveborn infant at one of the two study hospitals (631 women had singletons, 28 women had twins, and two women delivered a single infant after death of the co-twin in utero; figure). Among the 631 singletons, 79 (12.5%) were not followed up for long enough to establish their feeding practices, and three were followed

Characteristic	n*	Number breastfeeding	Breastfeeding women	
			Number still breastfeeding at 3 months	Number still exclusively breastfeeding at 3 months
Total	549	393 (71.6%)	226 (57.5%)	103 (26.3%)
Treatment				
Vitamin A	279	198 (71.0%)	119 (60.1%)	54 (27.4%)
Placebo	270	195 (72.2%)	107 (54.9%)	49 (25.3%)
Serum retinol ($\mu\text{g}/\text{dL}$)				
<30	320	236 (73.8%)	132 (55.9%)	65 (27.7%)
≥ 30	168	113 (67.3%)	69 (61.1%)	27 (23.9%)
Haemoglobin (mg/dL)				
<10	148	109 (73.7%)	61 (56.0%)	31 (28.4%)
≥ 10	354	249 (70.3%)	143 (57.4%)	61 (24.6%)
CD4-cell/CD8-cell ratio				
<0.5	207	154 (74.4%)	86 (55.8%)	41 (27.0%)
≥ 0.5	285	199 (69.8%)	115 (57.8%)	49 (24.6%)
Age (years)				
<30	416	305 (73.3%)	181 (59.3%)	85 (28.0%)
≥ 30	131	87 (66.4%)	44 (50.6%)	18 (20.9%)
Parity				
1	154	118 (76.6%)	63 (53.4%)	30 (25.4%)
2	189	132 (69.8%)	86 (65.2%)	40 (30.3%)
≥ 3	204	142 (69.6%)	77 (54.2%)	33 (23.4%)
Syphilis-screening test				
Positive	63	54 (85.7%)	29 (53.7%)	16 (29.6%)
Negative	379	262 (69.1%)†	157 (59.9%)	77 (29.5%)
Preterm delivery				
Yes	53	34 (64.2%)	24 (70.6%)	9 (26.5%)
No	461	332 (72.0%)	192 (58.7%)	91 (27.5%)
Infant sex				
Male	264	185 (70.1%)	105 (53.6%)	47 (25.4%)
Female	269	196 (72.9%)	117 (59.7%)	53 (27.0%)
Mode of delivery				
Vaginal	399	289 (72.4%)	166 (57.4%)	73 (25.3%)
Caesarean	144	101 (70.1%)	60 (59.4%)	30 (30.0%)
Maternal education				
Primary school or less	107	86 (80.4%)	47 (54.7%)	22 (25.9%)
Some high school	231	177 (76.6%)	117 (66.1%)	55 (31.3%)
High school or more	203	126 (62.1%)†	61 (48.4%)†	25 (19.8%)
Electricity in the home				
Yes	383	262 (68.4%)	139 (53.1%)	57 (21.9%)
No	160	128 (80.0%)†	86 (67.2%)†	46 (35.9%)†
Water source				
Indoors	246	169 (68.7%)	96 (56.8%)	39 (23.4%)
On property	166	113 (68.1%)	55 (48.7%)	29 (25.7%)
Communal/other	130	106 (81.5%)†	74 (69.8%)†	35 (33.0%)
Mother employed				
Yes	207	139 (67.2%)	69 (49.6%)	31 (22.6%)
No	339	253 (74.6%)	157 (62.1%)†	72 (28.5%)

*Numbers may not add up to 549 because of missing data. † $p < 0.05$, χ^2 test.

Table 1: Distribution of characteristics potentially associated with mother-to-child HIV-1 transmission

up but had no HIV-1 test results available. The remaining 549 singletons were included in the analysis. Those included did not differ significantly from those excluded in maternal factors—treatment group (vitamin A or placebo), CD4-cell counts, CD4-cell/CD8-cell ratio, haemoglobin, serum retinol, parity, syphilis-screening test results—or infant sex, birthweight, or preterm delivery, but those included were less likely to have been delivered by caesarean section.

Feeding practices

Of the 549 women, 393 (71.6%) initiated at least some breastfeeding. Among these women, 316 (80.4%) were still breastfeeding at 1 month and 226 (57.5%) at 3 months. The median duration of breastfeeding was 6 months (IQR 1–10). Among the 391 breastfeeders with information on exclusive breastfeeding, 191 (48.8%)

	Estimated proportion (%) HIV-1 infected (95% CI)		
	Never breastfed (n=156)	Exclusively breastfed ≥ 3 months (n=103)	Introduced other food <3 months (n=288)
Total sample			
By day 1	6.4 (2.5–10.3)	6.8 (1.9–11.7)	5.2 (2.6–7.8)
By 1 month	14.8 (9.2–20.4)	8.7 (3.3–14.2)	14.2 (10.1–18.3)
By 3 months	18.8 (12.6–24.9)	14.6 (7.7–21.4)	24.1 (19.0–29.2)
Infants HIV-1 negative on day 1			
By 1 month	8.3 (3.8–12.8)	2.1 (0–4.9)	9.5 (6.0–13.0)
By 3 months	13.2 (7.7–18.7)	8.3 (2.8–13.9)	19.9 (15.0–24.9)

Table 2: Estimated proportions of children who were HIV-1 infected by 3 months of age

breastfed exclusively to 1 month and 103 (26.3%) breastfed exclusively to 3 months. The median duration of exclusive breastfeeding was 1 month (0–3).

The proportions of women who initiated at least some breastfeeding and the duration of breastfeeding did not differ in terms of most maternal or child characteristics potentially associated with mother-to-child transmission of HIV-1 (table 1). The choice to initiate at least some breastfeeding was more common among women with less education, who lived in homes without electricity, and who had no water source in their home or on their property. Among breastfeeding women, duration of exclusive breastfeeding was not consistently related to these socioeconomic indicators (table 1).

HIV-1 transmission

There was no effect of vitamin A supplementation on the risk of HIV-1 infection by 3 months of age (data not shown) and the two groups were therefore examined together, but according to different feeding practices.

There was little difference in the estimated probabilities of HIV-1 infection by 3 months of age between infants of women who decided to breastfeed and those whose mothers avoided all breastfeeding (18.8% [95% CI 12.6–24.9] of 156 never-breastfed children and 21.3% [17.2–25.5] of 393 breastfed children, $p = 0.5$).

Women who breastfed were stratified into 103 who had exclusively breastfed to 3 months or more (ie, no other liquids, including water, or food had been given to the child before 3 months of age) and 288 who had introduced other liquids or foods during this period (two children were missing information on exclusive breastfeeding). The estimated proportions HIV-1 infected by 3 months were 14.6% for those exclusively breastfed and 24.1% with mixed feeding ($p = 0.03$; table 2).

At 1 day of age, the estimated proportion that were HIV-1 infected was 6.4% of 156 never-breastfed children compared with 6.8% of 103 exclusively breastfed children ($p = 0.91$) and 5.2% of 288 non-exclusively breastfed children ($p = 0.61$). In analyses that excluded 32 infants who were HIV-1 positive on their first day of life, the proportion infected by 3 months did not differ significantly in the never-breastfed group (13.2%) and in the exclusively breastfed group (8.3%, $p = 0.22$) but was higher in the non-exclusively breastfed group (19.9%, $p = 0.01$; table 2). We obtained similar results when we restricted the analysis to children alive and still in follow-up at 3 months of age (to investigate whether a survivor bias may have led to the lower transmission rates in the exclusively breastfed group).

None of the socioeconomic factors associated with the choice to breastfeed or with breastfeeding duration were

Characteristic	n*	Estimated proportion (%) HIV-1 infected	Hazard ratio (95% CI)	p
Maternal education				
Primary school or less	107	18.9		
Some high school	231	23.2	1.32 (0.78–2.23)	
High school or more	203	18.3	1.00 (0.57–1.74)	1.00
Electricity in the home				
Yes	383	20.9		
No	160	20.4	1.00 (0.66–1.50)	0.98
Water source				
Indoors	246	22.6		
On property	166	17.0	0.74 (0.46–1.17)	0.19
Communal/other	130	21.5	0.97 (0.61–1.54)	0.89
Mother employed				
Yes	207	22.0		
No	339	19.8	0.88 (0.60–1.29)	0.50

*Numbers may not add up to 547 because of missing data.

Table 3: **Unadjusted associations between socioeconomic indicators and risk of HIV-1 infection by 3 months of age in 547 children**

associated with the probability of HIV-1 infection by 3 months of age (table 3) and unadjusted estimates of the associations between infant-feeding practices and early transmission were unchanged after adjustment for these variables. After adjustment for maternal CD4-cell/CD8-cell ratio measured at enrolment, syphilis-screening test results, and preterm delivery, exclusive breastfeeding to 3 months or longer was associated with a significantly lower risk of infection (hazard ratio 0.52 [95% CI 0.28–0.98]). Never having breastfed carried a similar risk of infection to mixed feeding (0.85 [0.51–1.42]; table 4). Adjustment for treatment allocation (vitamin A or placebo) or maternal serum retinol concentration at enrolment (before supplementation) either alone or in combination with the other variables did not change the magnitude of the associations between the risk of HIV-1 infection by 3 months of age and feeding practices.

Discussion

Our results do not accord with conventional wisdom because they suggest that the vertical transmission of HIV-1 through breastmilk is dependent on the pattern of breastfeeding and not simply on all breastfeeding. Exclusive breastfeeding carries a significantly lower risk (almost half the risk) of mother-to-child transmission of HIV-1 than mixed feeding. Although the risks of HIV-1 transmission associated with non-exclusive breastfeeding seem to be substantial (risk of HIV-1 infection by 3 months was 24.1% in the mixed-feeding group and 18.8% in the never-breastfed group, giving a difference of 5.3% presumably due to postnatal infections), exclusive breastfeeding does not seem to convey any excess risk of HIV-1 transmission over formula feeding. Transmission rates by day 1 (about 6%), which reflect in-utero infections only, were similar in the three feeding groups. Therefore the groups did not differ initially in their risk of HIV-1 transmission. Our estimates of transmission rates by day 1 of life are within the upper limits of 95% CI for rates from other studies.¹³ After exclusion of those already shown to be HIV-1 infected at birth and therefore not at risk of postnatal infection, differences between exclusive (8.3%) and mixed breastfeeding (19.9%) groups were greater. These conclusions are based on the assumption that any misclassifications in infection status were similar between the groups. In addition, we assume that the proportions of intrapartum infections not detected at 1

Characteristic	n*	Estimated proportion (%) HIV-1 infected	Adjusted hazard ratio† (95% CI)	p
Breastfeeding				
Never breastfed	156	18.8	0.85 (0.51–1.42)	0.53
Exclusively breastfed	103	14.6	0.52 (0.28–0.98)	0.04
≥3 months				
Breastfed plus other food	288	24.1
<3 months				
Maternal CD4-cell/CD8-cell ratio at enrolment				
<0.5	207	29.3	2.08 (1.34–3.25)	0.001
≥0.5	285	14.8
Syphilis-screening test				
Positive	63	30.0	1.78 (1.03–3.07)	0.04
Negative	379	20.7
Delivery				
Preterm	53	23.4	1.96 (0.99–3.86)	0.05
Term	461	20.1

*Numbers may not add up to 547 because of missing data.

†Derived from a Cox proportional-hazards model with all characteristics shown as independent variables.

Table 4: **Associations between feeding practices and risk of HIV-1 infection by 3 months of age**

day of life were similar in the groups and, therefore, that differences reflect genuine differences in postnatal transmission due to feeding practices.

Among infants not already HIV-1 infected at birth, those who were exclusively breastfed had a lower probability of infection than those never breastfed. Although this difference was not significant, it raises a possibility that virus acquired during delivery could have been neutralised by immune factors present in breastmilk but not in formula feeds. Breastmilk contains non-specific immune factors that have antiviral and anti-HIV-1 effects in vitro. These factors include secretory leucocyte protease inhibitor,¹⁴ lactoferrin, complement, and glycosaminoglycan.¹⁵ The finding that mixed feeding carries the highest risk is not surprising because the beneficial immune factors of breastmilk are probably counteracted by damage to the infant's gut by contaminants or allergens in mixed feeds.

Breastmilk contains growth factors, such as epidermal growth factor and transforming growth factor α , which may enhance the maturation of the gut epithelial barrier, thus maintaining its integrity and hindering passage of virus.^{16,17} Preble and Piwoz¹⁸ postulated that exclusive breastfeeding may have lower risk of vertical transmission of HIV-1 than mixed feeding. Ingestion of contaminated water, fluids, and food may lead to gut mucosal injury and disruption of immune barriers. Since mixed feeding is unlikely to involve hygienic food preparation practices, bacteria and other contaminants may be introduced into the gut and result in inflammatory responses and subsequent damage to the mucosa. HIV-1 is less likely to penetrate intact and healthy gastrointestinal mucosa than damaged mucosa. Differing breastfeeding practices have been associated with varying risks of gastrointestinal infections, and different rates of absorption of nutrients and infant growth.¹⁸ La Gamma and colleagues¹⁹ showed that formula-fed infants had a six-fold to ten-fold higher rate of necrotising enterocolitis than infants who were exclusively breastfed; the disorder was three times more common in those fed a mixture of breastmilk and formula than in those exclusively breastfed. Once the integrity of mucosal surfaces has been compromised by infection, allergens, or trauma, the passage of HIV-1 across mucous membranes into body tissues is facilitated.

We used an early endpoint because early weaning is thought to retain the benefits of breastfeeding while lowering the risk of HIV-1 transmission. Models have

estimated that the best time for early weaning is 3 months.²⁰ A possible recommendation is for exclusive breastfeeding with early weaning. In addition, the benefits of breastfeeding are particularly important in the first 3 months of life. Finally, there is an urgent need to supplement existing inadequate data on HIV-1 transmission through breastfeeding. Our data can strengthen current UNAIDS policies on HIV-1 and breastfeeding without requiring any policy changes because exclusive breastfeeding is the existing recommendation for all women. All that is required is a change in emphasis.

No recommendations can be made on the advisability of exclusive breastfeeding by HIV-1-infected mothers beyond 3 months. The limited application of these data is important because of the problem of late postnatal mother-to-child transmission of HIV-1. Studies in Africa have shown that, in babies who have negative PCR results under the age of 6 months, the rate of mother-to-child transmission beyond this age is 4–12%.^{21–24} In a meta-analysis of infants who were HIV-1 infected after 3 months, Leroy and colleagues showed that breastfeeding transmission was 3% per year.²⁵

Two studies examined the effect of different breastfeeding patterns on mother-to-child transmission.^{7,8} The first study defined exclusive breastfeeding as breastfeeding with no formula but did not exclude other liquids or solids.⁷ The second study, in Brazil, distinguished between exclusive breastfeeding (using the WHO definition) and mixed feeding, and showed an increased risk of HIV-1 infection in infants who received mixed feeding; however, the association was not significant and the study was limited because data were collected retrospectively.⁸

Our study prospectively collected detailed information on feeding practices and we specifically advocated exclusive breastfeeding to women who chose to breastfeed. Thus, we had an opportunity to examine a large group of exclusively breastfed children. Our study was not a randomised controlled trial of feeding practices and mothers were self-selected to exclusive breastfeeding, mixed-feeding, and formula-fed groups. Most maternal or child characteristics potentially associated with mother-to-child transmission of HIV-1 did not differ between the three groups (table 1). However, positive syphilis tests and some indicators of socioeconomic status were more common among women who chose to breastfeed. There were no consistent differences in these characteristics between mothers who exclusively breastfed and those who gave mixed feeds. Nevertheless, our study is limited by possible differences between the groups in variables that we were unable to measure and which may have accounted for the feeding choices made. Women with healthier children may have been able to continue breastfeeding for longer; however, our own experience in interacting with the mothers suggests that those who introduced other food despite our advice tended to do so because of social pressure rather than because of their child's health. Another limitation of the study was that we were unable to validate mothers' reports of feeding practices. However, we did check that the information given at a visit was consistent with that given at previous visits. Mothers did not benefit by misrepresenting their feeding method, and individuals who counselled women on feeding choices were different from those collecting follow-up information. Specific care was taken not to pass judgment on choices made by the mother.

Exclusive breastfeeding is uncommon in Africa, and most women give mixed feeds to their babies.²⁶ Accordingly, if the results of this study were to be translated into practice, significant changes in infant-feeding practices would be required. These changes, however, would also have substantial benefits for overall child health, in contrast to the negative consequences associated with formula-feeding. These changes would require advocacy, mobilisation, information, education, and counselling on a huge scale. We should also consider ways of encouraging mothers to end breastfeeding abruptly, because this may be easier for a mother than some of the other methods that have been considered for protecting breastfeeding, such as heating of expressed milk. For those who choose to continue mixed feeding, other alternatives to reduce rates of transmission of HIV-1 through breastfeeding (such as antiretrovirals) should be tested. We believe that despite prevailing financial stringency, countries in Africa and elsewhere can afford a transformation in infant feeding, which is much cheaper than other proposals.

For developing countries we would reinforce the recommendations made by UNAIDS, WHO, and UNICEF, except to encourage exclusive breastfeeding by women who have no safe alternatives to breastfeeding.

Contributors

A Coutoudis wrote the protocol, supervised the study, and wrote the paper. K Pillay and E Spooner assisted with study design, were responsible for clinical management of the mothers and children, and edited the paper. L Kuhn was responsible for all the statistical analysis, and contributed to the writing of the paper. H M Coovadia assisted with study design and writing of the paper.

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