

# 18-month HIV-free survival by infant feeding practices in children of HIV-infected women in South Africa.

## The Vertical Transmission Study

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### BACKGROUND

- The dilemma of how best to feed infants and young children of HIV-infected mothers living in high HIV prevalent communities remains complex.
- Exclusive breastfeeding carries a lower risk of HIV transmission over the first 6 months of life (1) but is infrequently practiced by mothers, or effectively supported by health systems(2,3).
- Replacement feeding avoids all postnatal HIV transmission but has a significant risk of death (4,5) when given in household circumstances that are not ideal, especially in the first 6-9 months of the infant's life.
- Child survival without HIV infection, rather than avoidance of HIV infection alone, has emerged as the most important measure of PMTCT effectiveness (6). This reflects the availability and effectiveness of therapeutic interventions to prevent transmission but also the competing threats to child survival.
- The pattern of feeding beyond the first 6 months of an infant's life and the influence of maternal health are now recognised as important determinants of child survival.
- We report the 18 month HIV-free survival of HIV-exposed infants according to infant feeding practices a), implemented at birth; b), between 0-6 months; and c), beyond 6 months of age.

### METHODS

- HIV-infected pregnant women attending seven rural, one semi-urban and one urban antenatal clinics in KwaZulu Natal (KZN) were enrolled into a non-randomised intervention cohort study.
- All women were counselled antenatally regarding infant feeding options and supported in their choice. Mothers who chose to breastfeed were visited at home by infant feeding counsellors every two weeks until the infant was 6 months of age. HIV-infected mothers who chose to replacement feed were supported by study nurses when they visited the study clinics.

This counselling was highly effective at identifying mothers whose circumstances were suitable for safe replacement feeding (affordable, feasible, acceptable, sustainable and safe i.e. AFASS) and those mothers whose conditions precluded safe replacement feeding (7). Women with access to clean water and who had an independent source of income were more likely to replacement feed whereas women who relied on river and non-piped water and who were economically dependent on others were more likely to exclusive breastfeed. Furthermore, these women had access to medical and nursing care that exceeded the normal health services to women in the general population

- Mothers and infants attended study clinics at 6 weeks after delivery, then monthly to 9 months and 3 monthly to 18 months.
- At each visit a dried blood spot sample was collected for determination of HIV status by quantitative HIV RNA assay (sensitivity of 80 copies of HIV RNA per ml blood)
- Field monitors visited mothers at home every week from birth until the infant was 9 months of age and documented all feeds and morbidity episodes for each day of the preceding week.
- When infants were 5 months old, breastfeeding mothers were counselled to stop breastfeeding (at 6 months) and both breastfeeding and replacement feeding mothers were counselled regarding the introduction of complementary feeds.
- Single-dose nevirapine was provided for all HIV infected women and their infants for use during labour and delivery. At the time of the study, highly active antiretroviral treatment was not available through the Provincial health services.
- The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal.

### DISCUSSION

- HIV infection of infants remains the main driver of mortality in infants born to HIV-infected women [0.96 vs. 0.47];
- Low birth weight, maternal unemployment and low antenatal maternal CD4 counts significantly impact on early and late transmission, and survival;
- Maternal employment reduced child mortality and may reflect maternal health and increased household resource and possibly a proxy for maternal autonomy;
- Mortality rates between 6 months and 18 months of age of HIV exposed, but uninfected infants were similar amongst those that who continued to be breastfed beyond 6 months vs. those who received replacement milks i.e. no breastmilk;
- Continued transmission of HIV occurred in children who were breastfed during this period resulting in lower HIV-free survival rates at 18 months;
- These data, while demonstrating the continued transmission risk of breastfeeding, do not necessarily support a recommendation to stop breastfeeding at 6 months.
- In this cohort, the women who chose to replacement feed from birth were a highly selected group who could afford to do so and whose circumstances allowed them to do so - which reflect the minimal mortality risk differences with the BF group.
- Mothers who chose to continue breastfeeding possibly did so because no safe alternative was available.
- The potential survival advantages of breastfeeding might therefore be obscured

### CONCLUSIONS

- In communities where growth faltering and malnutrition are relatively common, a mothers decision to continue, or cease breastfeeding her infant beyond 6 months of age must consider the broader consequences of that choice.
- Counselling and advice to mothers at 5-6 months is equally important for child survival as counselling provided antenatally.
- Maintaining contact with mothers through the first 6 months is essential in order to assist with process of stopping BF and to advise on appropriate complementary feeds.
- Identifying women with low CD4 count and enabling them to start highly active antiretroviral drugs for life remains a high priority. For those mothers with a low CD4 count, there is a high priority to stop breastfeeding.
- Identifying interventions that prevent HIV transmission while still enabling a mother in resource poor settings to breastfeed until 18-24 months would improve child survival.

### FUNDING

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### RESULTS

#### 1,193 live-born infants born to HIV-infected mothers were included

#### Overall Survival of HIV infected and uninfected infants

- Overall probability of HIV-free survival was 0.76 (95%CI 0.73-0.78)
- 18-month probability of death (95%CI): HIV-uninfected children 0.04 (0.03-0.06) vs. HIV-infected children 0.53 (0.46-0.60)
- Infected children were 17-times more likely to die than uninfected children (unadjusted hazard ratio: 16.9 [11.5-24.8]).
- 18-month probability of survival among HIV-uninfected children was not significantly different for infants breastfed (n=800) or replacement fed (n=128) from birth.

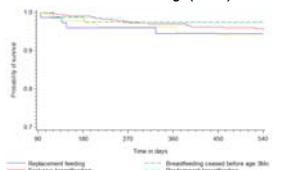
#### Determinants of HIV infection or death

- Adjusted hazard ratios (AHR) of HIV infection/death were:
  - 1.5 (1.1-2.2, p=0.03) for low birth-weight children,
  - 1.9 (1.3-2.9, p=0.004) for children of unemployed mothers and
  - 2.4 (1.7-3.2, p<0.001) for children of mothers with antenatal CD4 <200 cells/ml.

#### Infant feeding practices beyond 6 months

- Of 1,012 infants who received any breastmilk in the first week of life, 688 continued to receive breastmilk for > 6 months. Median duration of BF was 283 days (IQR: 206-491).
- Mothers who breastfed for less than 6 months (n=136) more often had access to piped water inside their home than mothers who continued to breastfeed beyond 6 months (n=688) (9.5% vs. 7.7%, p=0.25); but this was not significant
- Mothers in both groups had similar levels of education and access to toilets.
- The mean antenatal CD4 count was slightly lower in mothers who breastfed less than 6 months (487 vs. 514, p=0.24); the proportion of women with CD4 counts below 200 was also the same (BF<6 months 10.8% vs. BF>6 months 8.1%, p=0.31).

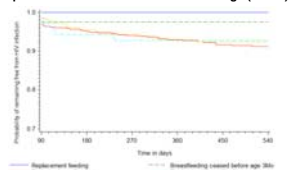
Probability of remaining free from death between 4 and 18 months of age, by infant feeding practices from birth until 3 months of age (n=952)



| Feeding Practice                    | Probability of remaining free from death between 4 and 18 months of age (95%CI) |
|-------------------------------------|---|
| Replacement feeding group           | 0.94 (0.86-0.98)  |
| Breastfeeding ceased before age 3Mo | 0.97 (0.93-0.99)  |
| Exclusive breastfeeding             | 0.95 (0.93-0.97)  |
| Predominant breastfeeding           | 0.97 (0.89-0.99)  |
| Mixed feeding                       | 0.94 (0.89-0.97)  |

Log-Rank test, p=0.74

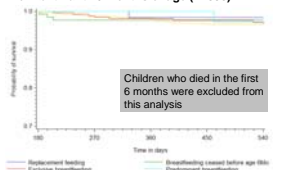
Probability of remaining free from HIV infection between 4 and 18 months of age, by infant feeding practices from birth until 3 months of age (n=952)



| Feeding Practice                    | Probability of remaining free from HIV infection between 4 and 18 months of age (95%CI) |
|-------------------------------------|---|
| Replacement feeding group           | 1.00 (1.00-1.00)  |
| Breastfeeding ceased before age 3Mo | 0.98 (0.91-0.99)  |
| Exclusive breastfeeding             | 0.91 (0.85-0.95)  |
| Predominant breastfeeding           | 0.93 (0.84-0.96)  |
| Mixed feeding                       | 0.92 (0.87-0.95)  |

Log-Rank test, p=0.05

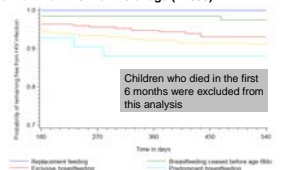
Probability of remaining free from death between 7 and 18 months of age, by infant feeding practices from birth until 6 months of age (n=893)



| Feeding Practice                    | Probability of remaining free from death between 7 and 18 months of age (95%CI) |
|-------------------------------------|---|
| Replacement feeding group           | 0.98 (0.89-1.00)  |
| Breastfeeding ceased before age 3Mo | 0.98 (0.93-0.99)  |
| Exclusive breastfeeding             | 0.97 (0.93-0.99)  |
| Predominant breastfeeding           | 0.97 (0.82-1.00)  |
| Mixed feeding                       | 0.97 (0.94-0.98)  |

Log-Rank test, p=0.94

Probability of remaining free from HIV infection between 7 and 18 months of age, by infant feeding practices from birth until 6 months of age (n=893)



| Feeding Practice                    | Probability of remaining free from HIV infection between 7 and 18 months of age (95%CI) |
|-------------------------------------|---|
| Replacement feeding group           | 1.00 (1.00-1.00)  |
| Breastfeeding ceased before age 3Mo | 0.98 (0.93-0.99)  |
| Exclusive breastfeeding             | 0.93 (0.89-0.96)  |
| Predominant breastfeeding           | 0.88 (0.74-0.95)  |
| Mixed feeding                       | 0.91 (0.88-0.94)  |

Log-Rank test, p=0.01

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