

## Comparison of Feeding Options for HIV-Exposed Infants: A Retrospective Cohort Study

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**Objectives:** To compare growth, anemia prevalence, and sickness frequency in HIV-exposed uninfected infants on different feeding modes. **Methods:** In this retrospective cohort study, 109 HIV-exposed uninfected infants registered at our center were categorized into three groups as per their feeding mode during first 6 months viz. exclusively breast fed ( $n=50$ ), animal milk fed ( $n=40$ ) and commercial infant formula fed ( $n=19$ ). Their anthropometric parameters, hemoglobin and frequency of sickness at the age of 6 months were compared. **Results:** There were no significant inter-group differences in the weight for age, weight for length, length for age z-scores ( $P=0.16$ ,  $0.37$  and  $0.12$ , respectively); proportion of infants with underweight ( $P=0.63$ ), wasting ( $P=0.82$ ), or stunting ( $P=0.82$ ), and mean hemoglobin levels among the 3 groups at 6 month of age. Animal milk fed and formula fed infant had increased risk of sickness compared to exclusively breastfed infants (OR 2.5 and 2.49, respectively;  $P<0.01$ ). **Conclusions:** In circumstances where breastfeeding is not feasible or preferred, animal milk feeding offers a viable alternative to commercial infant feeding formula in HIV exposed infants.

**Keywords:** Animal milk, Breastfeeding, Infant feeding, Formula-milk, Growth.

World Health Organization (WHO) and National AIDS Control Organisation (NACO) recommend exclusive breastfeeding (EBF) with provision of lifelong antiretroviral treatment as the strategy of choice to optimize HIV-free survival among HIV-exposed infants. In situations where mothers cannot/choose not to breastfeed, the only option recommended by WHO for infants <6 months is commercial infant formula (CIF). Animal milk (AMF) is not recommended as a replacement feeding option in the first six months of life [1]. However, the cost of CIF is prohibitive in low- and middle-income countries and it may not be economically feasible for mothers to use CIF exclusively for the first 6 months. In its recommendations, NACO has included locally available unmodified animal milk apart from CIF as an option for replacement feeding [2]. The former includes fresh boiled animal milk or pre-packed processed toned dairy milk along with multi-vitamin and iron supplementation. The Infant and Young Child Feeding (IYCF) Guidelines (2010) of Indian Academy of Pediatrics also included unmodified animal milk as an alternative option where EBF is not possible [3].

It is highly pertinent that AMF be formally evaluated for its suitability as an alternative feeding option for HIV-

exposed infants. Otherwise, cost-cutting can compromise the infants' growth and development in the long run, an unacceptable consequence. This study aimed to assess the impact of AMF on growth parameters, prevalence of anemia and episodes of sickness in HIV-exposed infants as compared to infants who received EBF or CIF during the first 6 months of life.

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### METHODS

The present study is a retrospective analysis of records of HIV-exposed infants registered at anti-retroviral therapy center of Lady Hardinge Medical College and associated Kalawati Saran Children's Hospital at New Delhi during October 2007 to December 2015.

In accordance with the national policy, all pregnant/lactating women with HIV infection and their infants registered at our centre are given antiretroviral drugs (ARVs) for prevention of HIV transmission to their infants [4]. They are counseled regarding infant feeding options during pregnancy and again soon after birth by trained counselors. In women opting for it, EBF is initiated within first hour of birth. In situations where the woman opts for replacement feeding or where EBF is not

possible (maternal death or sickness), feeding with locally available AMF (fresh boiled animal milk or pre-packed processed toned dairy milk containing 3% fat, 3.1% protein providing 58 kcal/100 mL) or CIF is decided upon after discussion with the family depending upon their socio-economic condition and socio-cultural factors [2]. Depending upon the opted feeding method, the family is counseled regarding correct breastfeeding practices, avoidance of mixed feeding and proper method of preparing and administering RF using *katori*-spoon. Multi-vitamins to meet the RDA are started at birth/time of registration at our centre and iron supplementation at the rate of 2 mg/kg/day is prescribed at 6 weeks of age to all infants on AMF. The compliance to feeding practices and supplements is ensured at time of each contact by taking regular feedbacks and targeted counseling.

For this study, we reviewed records of all HIV-exposed infants registered at our ART centre within 15 days of birth and followed up till at least 6 months of age. We excluded infants who were lost to follow-up, who had less than two growth parameter reading during the 6-month period, those who were given mixed feeding, and those whose final HIV status was not determined at six months of age.

There was a change in National policy for prevention of parent to child transmission of HIV (PPTCT) during this time. Prior to January 2014, all women with HIV and their newborns were given a single dose of nevirapine (NVP) during labour and immediately after birth, respectively. After January 2014, all HIV-infected pregnant women were initiated on ART soon after detection of their HIV status [4]. Infants born to these women were started on daily NVP prophylaxis at birth and continued for a minimum of 6 weeks. Mothers who were detected to be HIV-infected during labour/after delivery were started on ART upon detection and their infants were given NVP prophylaxis. The study therefore included data from participants registered before and after change in recommendations. Determination of HIV status was done through virological tests [4] i.e. HIV-1 DNA PCR by dried blood spot followed by confirmation on whole blood if positive, at ages 6 weeks, 6 months and 6 weeks after stopping breastfeeding. The enrolled infants were classified into three groups on basis of feeding strategy adopted during first 6 months following birth: (i) EBF: Infants exclusively breastfed; (ii) AMF: infants receiving fresh animal milk (cow, buffalo or goat milk) or commercially available pre-packed toned milk fed after boiling without any modification; and (iii) CIF: infants receiving age-appropriate commercially available infant feeding formula.

The nutritional status of infants was determined by

calculating z-scores for weight for age (WFA), weight for length (WFL) and length for age (LFA) at birth and 6 months using WHO growth reference standards [5], and prevalence of underweight (WFA  $<-2$  z-score), wasting (WFL  $<-2$  z-score) and stunting (LFA  $<-2$  z-score) was estimated. Episodes of sickness and serious sickness (requiring hospitalization) till 6 months age, mean serum hemoglobin at 6 ( $\pm 1$ ) months and grading of anemia severity as per WHO guidelines was also assessed among the study infants [6]. The study protocol was approved by the Institutional Ethics Committee.

*Statistical analysis:* Paired t-test was used to compare the WFA, WFL and LFA z-scores of infants at birth and six months in each feeding group. Analysis of co-variance (ANCOVA) was used to compare the z-scores at six months among the three feeding groups taking baseline z-score at birth as co-variant. McNemar test was applied to compare the proportion of babies with underweight, wasting and stunting at birth with that at six months. Fisher Exact test was used to compare the proportion of babies with underweight, wasting and stunting at six months among the three feeding groups and for comparison of disease specific morbidities among the three groups. For comparing the episodes of illness in infants among different feeding groups, Poisson regression method was adopted. SPSS version 23.0 (IBM, New York, USA) was used for statistical analyses.

## RESULTS

We evaluated case records of 189 infants (105 males) for this study. At 6 months of age, 109 (57.7%) among these were confirmed to be HIV-negative and 4 HIV-positive, while status of remaining 76 infants was not determined. All the infants were intra-mural referrals except 2 (4%) in EBF group. Baseline characteristics of the 109 HIV-exposed uninfected infants included for analysis are described in **Table I**. There was no mortality among these infants during the first 6 months of age.

The anthropometric parameters in the three feeding groups at 6 months, and mean change in z-scores at 6 months compared to birth are shown in **Table II**. There was no difference in LFA, WFA or WFL z-scores or in proportion of infants with underweight, wasting or stunting at the age of six months among the three groups (**Table II**).

**Tables III** shows frequency and nature of illness among infants in the study groups. Two infants required hospitalization during the study period, 1 each for sepsis (EBF group) and diarrhea (AMF group). The AMF infants had higher odds (OR 2.5; 95% CI: 1.4-4.4) of having an episode of illness compared to EBF group.

**TABLE I** BASELINE CHARACTERISTICS OF HIV-EXPOSED UNINFECTED INFANTS (N=109)

Parameters, n (%)	AMF (n=40)	CIF (n=19)	EBF(n=50)	P value
Vaginal delivery	9 (22.5)	7 (36.8)	27 (54)	
Caesarean section	31 (77.5)	12 (63.2)	23 (46)	
<i>ART therapy in mothers*</i>				
Started antenatally	26 (65)	13 (68.4)	41 (82)	
Started perinatally	12 (30)	6 (31.6)	6 (12)	
Not on ART at registration	2 (5)	0	3 (6)	
<i>ARV prophylaxis status in infants</i>				
Single dose nevirapine at birth	19 (47.5)	5 (26.3)	14 (28)	
Nevirapine for 6-12 weeks after birth (with maternal ART)	18 (45)	12 (63.2)	33 (66)	
Zidovudine till 12 wks age	3 (7.5)	2 (10.5)	3 (6)	
Male infants	25 (62.5)	12 (63.1)	29 (58)	
<i>Gestational maturity, (n=30)</i>				
Full-term	11 (68.7)	5 (83.3)	6 (75)	0.92
Preterm	5 (31.3)	1 (16.7)	2 (25)	0.47
<i>Birthweight</i>				
<2.5 kg (Low birth weight)	11 (27.5)	5 (20.3)	15 (30)	0.18
≥2.5 kg	29 (72.5)	14 (73.6)	35 (70)	0.95
Age at registration at ART center (d), mean (SD)	3.1 (1.9)	2.7 (1.7)	2.3 (2.2)	0.18
<i>Anthropometric parameters at birth, mean (SD)</i>				
Birthweight (kg)	2.6 (0.5)	2.7 (0.6)	2.7 (0.4)	0.68
WFA z-score	-1.3 (1.4)	-1.3 (1.6)	-1.3 (1.1)	0.98
WFL z-score	-1.5 (1.3)	-1.0 (1.6)	-1.0 (1.3)	0.21
LFA z-score	-0.7 (1.1)	-0.4 (1.0)	-1.0 (1.4)	0.18
Underweight, n (%)	8 (20)	4 (21)	13 (26)	0.41
Washed, n (%)	11 (31.4)	5 (29.4)	9 (21.9)	0.40
Stunted, n (%)	4 (10.8)	0	8 (17.7)	0.53

\*ART consisting of: T (Tenofovir), L (Lamivudine), E (Efavirenz); AMF: Animal milk; CIF: Commercial infant formula; EBF: Exclusive breastfeeding.

Likewise, CIF infants had higher odds (OR 2.49; 95% CI: 1.3-4.8) of having an episode of illness compared to EBF group. There was no significant difference between frequency of sickness among the AMF and CIF groups.

Hemoglobin levels at 6 months were available for 53 infants (AMF 16, CIF 9, EBF 28). Mean (SD) hemoglobin levels in infants of AMF, CIF and EBF groups were 10.8 (1.41) g/dL, 11.0 (1.06) g/dL and 10.2 (1.1) g/dL, respectively. There was no significant difference in the mean hemoglobin level as well as proportion of infants with different grades of anemia among the three groups (**Fig. 1**).

## DISCUSSION

This study documented no significant difference in

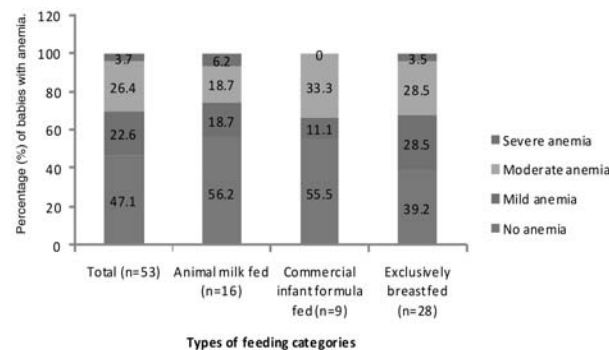
growth parameters or prevalence of anemia in HIV-exposed infants on AMF as compared to CIF or EBF during first 6 months of life. Despite ongoing feeding counseling, incidence of sickness, especially diarrhea, was significantly higher in infants on AMF and CIF as compared to those on EBF. There was no evidence of any significant difference between AMF and CIF with respect to frequency of sickness.

The search for an option for replacement feeding that would be culturally acceptable, economically viable while being nutritionally adequate, is a felt need for HIV exposed infants [7]. AMF has been widely used for infant feeding by women with HIV infection [8,9]. Papatthakis, *et al.* [10] have shown home prepared modifications of evaporated milk, powdered full cream milk and fresh full

**TABLE II** COMPARISON OF ANTHROPOMETRIC PARAMETERS AT 6 MONTHS OF AGE AMONG THE STUDY INFANTS

Parameters	AMF (n=40)	CIF (n=19)	EBF (n=50)	P value
WFA z-score	-1.5 (1.4)	-0.7 (1.7)	-1.4 (1.4)	0.16
Change in z-score*	-0.2 (1.8)	0.5 (1.1)	-0.1 (1.1)	
WFL z-score	-0.7 (1.4)	-0.2 (1.4)	-0.7 (1.4)	0.37
Change in z-score*	0.8 (2.5)	1 (1.4)	0.5 (1.5)	
LFA z-score	-1.4 (1.4)	-0.8 (1.7)	-1.4 (1.0)	0.12
Change in z-score*	-0.6 (1.3)	-0.2 (1.4)	-0.6 (0.9)	
Underweight (%)	29.4	26.7	37.8	0.63
Wasting (%)	16.7	7.1	18.9	0.82
Stunting (%)	31.2	28.6	30	0.82

\*as compared to birth z-score WFA; weight for age, WFL: weight for length, LFA: length for age; AMF: fresh animal milk fed, CIF: commercial infant formula fed, EBF: exclusively breast fed.



**FIG. 1** Proportion of infants with different grades of anemia in different feeding categories.

cream milk to be deficient in vitamins and essential minerals. We could not find any published work which has reported on growth parameters or anemia prevalence among infants (HIV-exposed or otherwise) fed on animal milk. While no difference has been reported in anthropometric parameters of HIV-exposed infants on EBF or CIF from South Africa [11], higher weight for height z-scores over a two year follow-up have been reported in breast fed as compared to formula fed infants from Kenya [12]. No difference in anemia prevalence has been reported in infants fed on EBF and CIF [11,13]. An increased risk of morbidity and hospitalization in HIV-exposed infants on replacement feeding, compared to those on EBF, has been shown in a previous Indian study [9]. Studies from other parts of the world have also shown higher frequency of respiratory tract infections [14] and diarrhea [11,12,14] in non-breastfed infants. WHO has published a meta-analysis showing breastfeeding to be

**TABLE III** COMPARISON OF MORBIDITY PROFILE AMONG THE STUDY INFANTS DURING FIRST 6 MONTHS OF LIFE

Illness type	AMF (n=40)	CIF (n=19)	EBF (n=50)
Total morbidities	36	17	18
Number of episodes/child / 6 mo	0.9	0.9	0.4
Diarrhea*	28	6	7
LRTI	1	3	1
URTI	6	3	5
Meningitis	0	1	0
Skin (pyoderma/scabies)	0	1	2
Sepsis	0	2	1
Otitis media	0	1	0

LRTI: lower respiratory tract infections; URTI: upper respiratory tract infections; \*significantly different among the 3 study groups (P<0.001).

protective against deaths due to infectious diseases, the odds being significantly more in first six months of life than in later ages [15].

Despite widespread use of animal milk in infant feeding, especially in context of maternal HIV infection, the evidence for suitability of animal milk as an option for replacement feeding in HIV-exposed infants is lacking. Retrospective nature of data is a major limitation of this study. While we have demonstrated that use of AMF along with multi-vitamin and iron supplementation in HIV-exposed infants leads to an equivalent growth, anemia prevalence and similar morbidity outcomes as compared to CIF, we have not been able to assess the status of other micro-nutrients in these infants. We have also not measured serum ferritin levels, a better marker for iron deficiency.

This work provides data that AMF along with iron and multivitamin supplementation is a possible alternative to CIF in HIV-exposed infants where breastfeeding is not feasible/opted for. However, there is a need to standardize the nutrient value of these milk preparations as well as study the micronutrient status of the infants fed exclusively on AMF, so that holistic growth and development of an infant does not suffer.

*Contributors:* SR: extracted the data, analyzed it and drafted the paper; AS: conceptualized the paper, was overall responsible for quality of data collection and maintenance, modified & finalized the draft; NB, SS, GS: clinical care, and data recording and analysis; JC, PK: patient care, quality maintenance and modification of draft of the paper. All authors provided inputs to manuscript writing, and its final approval.

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#### WHAT THIS STUDY ADDS?

- Animal milk feeding, along with iron and multivitamin supplementation, offers a viable alternative to commercial infant feeding formula in terms of anthropometric and morbidity-related outcomes in HIV-exposed infants.

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