

## GROWTH PATTERNS OF HIV-EXPOSED (UNINFECTED), HIV-INFECTED, AND NORMAL INFANTS – DO FEEDING PRACTICES HAVE A ROLE?

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Received : 20/03/2023  
Received in revised form : 28/04/2023  
Accepted : 10/05/2023

### Keywords:

*HIV-exposed infants, HIV-infected infants, HIV-uninfected infants, HIV-unexposed infants, breastfeeding, formula feeding, growth patterns, wasting, stunting, underweight, standard deviation.*

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DOI: 10.47009/jamp.2023.5.3.324

Source of Support: Nil,  
Conflict of Interest: None declared

*Int J Acad Med Pharm*  
2023; 5 (3); 1612-1619

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### Abstract

**Background:** The goal of the study was to compare the growth patterns of HIV-infected infants, HIV-exposed uninfected infants, and normal (HIV-unexposed) infants and the impact of feeding practices on their growth. **Materials and Methods:** This is a prospective, longitudinal, comparative study. Fifty Term ( $\geq 37$  and  $\leq 42$  weeks of gestation) inborn neonates born to HIV-positive mothers and fifty Term inborn neonates born to HIV-negative mothers were enrolled and were followed up till the age of 2yrs and their growth patterns were compared. All the mothers of fifty enrolled HIV-exposed infants were counseled about AFASS criteria and the option of breastfeeds/formula feeds was chosen for them. All the enrolled infants were followed up at 6 weeks, 6, 12, 18 months, and 2 years of age, and their anthropometric data were recorded and compared. **Result:** Among 50 HIV-exposed infants, 3 (6%) were diagnosed to be HIV-infected. Among HIV-infected and uninfected babies at 6 weeks follow-up, the prevalence of underweight (100% vs. 21.3%), stunting (100% vs. 19.14%), wasting (100% vs. 21.3%) were significantly higher in HIV-infected babies ( $p = 0.003$ ). At 6 months of follow-up, the prevalence of underweight, stunting, and wasting was the same as that at 6 weeks in both groups. At the 12-month follow-up, the prevalence of underweight, stunting, and wasting were similar (33.3% vs. 17%) and statistically not significant. At 18 months follow-up of both the groups, the prevalence of underweight (66.6% vs. 12.7%), stunting (66.6% vs. 10.6%), and wasting (100% vs. 12.7%) were found to be significantly higher in HIV-infected babies. At 2 years follow-up, the prevalence of underweight (100% vs. 8.5%), stunting (100% vs. 6.4%), and wasting (100% vs. 8.5%) were found to be significantly higher in the HIV-infected group. The growth patterns of HIV-exposed uninfected breastfed babies ( $n = 14$ ) and non-breastfed babies ( $n = 33$ ) showed the prevalence of underweight, stunting, and wasting were significantly higher in non-breastfed babies. And the growth patterns of HIV-exposed uninfected breastfed babies ( $n = 14$ ) and normal breastfed babies ( $n = 40$ ) were similar and no poor growth was recorded in both groups. **Conclusion:** The prevalence of stunting, wasting, and being underweight was high in HIV-infected infants compared to HIV-uninfected infants. Hence in developing countries like India, breastfeeding should be strongly recommended in all HIV-exposed babies in order to prevent the complications of bottle feeding and other faulty feeding practices. Hence ensuring ARV prophylaxis according to WHO guidelines and advising proper feeding practices with effective disease control and nutritional rehabilitation of all HIV-exposed infants is an important low-cost strategy for improving the health and survival outcomes of these infants.



## INTRODUCTION

Data from developing countries found that the percentage of child deaths attributable to the potentiating effects of malnutrition ranged from 13% to 67%, highlighting the significant impact of nutritional status on child survival. HIV infection further negatively impacts growth. Among infants exposed to HIV- infection in utero, during birth, or postnatally through breastfeeding, growth faltering or failure is now recognized as an early marker of HIV infection and disease progression, and as a prognostic tool for survival. For children who are already suffering from poor nutritional status, concurrent HIV infection poses substantial additional risks for morbidity and mortality. India has the world's third-largest number of HIV-infected individuals.

To date, there have been very few studies in India comparing growth patterns of HIV-infected infants, HIV-exposed but uninfected infants with normal (HIV-unexposed) infants.

The objectives of our study were to: a) compare the growth patterns of HIV-infected and HIV-exposed but uninfected infants with normal infants and b) compare the growth patterns of HIV-exposed uninfected breastfed infants with artificially fed infants. We also noted the incidence of various infections in both groups which further impacted their growth.

## MATERIALS AND METHODS

Enrolled HIV-exposed neonates and normal term inborn neonates in Government general hospital; Siddhartha Medical College Vijayawada; Andhra Pradesh.

### Method of Collection of Data

#### Sample Size

The sample size was 100 neonates out of which 50 were HIV-exposed and 50 normal inborn neonates.

**Duration of Study:** November 2020 – October 2022 (2 years).

**Type of Study:** Prospective, longitudinal comparative study

#### Inclusion Criteria

Infants eligible for the study fulfilled the following criteria

1. All the infants are full-term, appropriate for gestational-age neonates with no NICU admissions.
2. Infants of all HIV-positive mothers who received ART regardless of their CD4 count and clinical staging, at least from 28wks of gestation or earlier or who are already receiving ART for their own health
3. All the reactive mothers had no other illness during the antenatal period except for the HIV

#### Exclusion Criteria

1. Preterm, low birth weight babies and small for gestational age babies were excluded.

2. Babies with congenital abnormalities.
3. Babies born to mothers with Hypertension, hypothyroidism, gestational diabetes, severe or very severe anemia (WHO grading), or other illness during the antenatal period.

#### Method of Study

50 HIV-exposed neonates and 50 healthy full-term normal neonates were enrolled in the study after parental consent. The study was approved by the hospital ethics committee.

All the HIV-positive mothers have explained the AFASS criteria proposed by WHO so that some of them opted to breastfeed their babies and others opted for formula feeds.

#### AFASS Criteria

##### Acceptable

The mother perceives no problem in replacement feeding. Potential problems may be cultural, social, or due to fear of stigma and discrimination.

##### Feasible

The mother (or family) has adequate time, knowledge, skills, resources, and support to correctly mix formula or milk and feed the infant up to 12 times in 24 hours.

##### Affordable

The mother and family, with community or health system support if necessary, can pay the cost of replacement feeding without harming the health or nutrition status of the family.

##### Sustainable

Availability of a continuous supply of all ingredients needed for safe replacement feeding for up to one year of age or longer.

##### Safe

Replacement foods are correctly and hygienically prepared and stored, and fed preferably by cup.

##### Source

IMCI Complementary Course on HIV/AIDS; Module 3; Counseling the HIV Positive Mother. WHO 2007.

All the HIV-positive mothers who opted to formula feed their babies were clearly explained regarding appropriate dilutions of the formula and the method of giving feeds by cup and spoon or paladay. And HIV-positive time mothers who opted to breastfeed and all the HIV-negative mothers were recommended to exclusively breastfeed their babies till 66 months of age.

All the babies were supplemented with vitamin D3 and multivitamin drops till 2yrs of age. Both HIV-exposed and HIV-unexposed babies received all the vaccinations according to the IAP schedule.

For all the HIV-exposed babies, nevirapine was started at birth and given till 6 weeks of age at a dose of 15mg/day as a single dose, and for those who are on breastfeeds, it is given till 1 week of cessation of breastfeeding.

Co-trimoxazole prophylaxis was started at 6 weeks of age and continued till 18 months of age in all HIV-exposed babies.

Early Infant Diagnosis (EID) using Dried Blood Spot (DBS) and HIV DNA PCR at 6 weeks of age

was done, as per the EID guidelines. Repeated testing was done at 6 months (DBS-DNA PCR) and 18 months of age (antibody testing - ELISA).

At 6 months of age, all the HIV-exposed infants were gradually weaned off breast milk over a period of one month, and nutritionally adequate complementary feeding was started and breastfeeding continued till 2 years of age in all EID-negative infants.

All the HIV-exposed breastfeeding infants who were diagnosed as HIV positive through EID at 6 weeks of age were continued to breastfeed till 2 years of age. HIV care and Pediatric ART were started for them, irrespective of the CD4 count.

All 100 infants (both HIV-exposed and HIV-unexposed) were followed up at the age of 6 weeks, 6 months, 12 months, 18 months, and 2 years, and their anthropometric data were documented and their growth patterns were compared.

### Statistics

Standardized Z-scores for Weight-for-Age (WAZ, referring to underweight), Length-for-Age (LAZ, referring to stunting), and Weight-for-Length (WLZ, referring to wasting) were calculated using the WHO Anthro version 3.2.2 software

The chi-square test is used to calculate the probability value (p-value). This is done using a chi-square online calculator.

The Z-score measures the number of standard deviations above/below the median for age and gender of a reference population, drawn from the WHO Multi-centre Growth Reference Study.

We defined poor growth as categorical variables using the following three anthropometric indices: Underweight, if WAZ score was  $<-2.0$  SD units; Stunted, if LAZ was  $<-2.0$  SD units; and Wasted if WLZ was  $<-2.0$  SD units.

## RESULTS

A total of 100 neonates were included in the study out of which 50 were HIV-exposed (born to HIV-positive mothers) and 50 were normal (HIV-unexposed) babies. There were 58 male babies and 42 female babies. There were no significant differences in gestational age, birth weight, length, or gender, between the two groups. Cesarean delivery was significantly higher in HIV-exposed babies.

**Table 1: Clinical characteristics of HIV-exposed and HIV-unexposed babies at birth**

	HIV-exposed babies N=50	HIV-unexposed babies N=50	p-value	Statistical significance
Male (n%)	28 (56%)	30 (60%)	0.68	Not significant
Gestational age (Mean± SD) weeks	38.4 ± 1.3	39.6 ± 1.4	0.38	Not Significant
Cesarean delivery (n%)	32 (64%)	18 (36%)	0.005	Significant
Birth Weight (mean± SD) grams	2950 ± 304	3100 ± 280	0.31	Not significant
Birth Length (mean± SD) cms	48.5 ± 1.1	49.1 ± 1.2	0.42	Not significant

**Table 2: Prevalence of underweight (weight-for-age < -2SD) in HIV-infected and HIV-exposed, uninfected babies during 2 year follow up**

	HIV-Infected N = 3	HIV-Exposed, Uninfected N = 47	P value	Statistical Significance
6weeks	3 (100%)	10 (21.3%)	0.003	Significant
6months	3 (100%)	10 (21.3%)	0.003	Significant
12months	1 (33.3%)	8 (17%)	0.47	Not significant
18months	2 (66.6%)	6 (12.7%)	0.014	Significant
2years	3 (100%)	4 (8.5%)	0.0001	Significant

**Table 3: Prevalence of stunting (length/height-for-age < -2SD) in HIV-infected and HIV-exposed, uninfected babies during 2 year follow-up**

	HIV-Infected N = 3	HIV-Exposed, Uninfected N = 47	P-value	Statistical significance
6weeks	3 (100%)	9 (19.14%)	0.001	Significant
6months	3 (100%)	9 (19.14%)	0.001	Significant
12months	1 (33.3%)	8 (17%)	0.47	Not significant
18months	2 (66.6%)	5 (10.6%)	0.007	Significant
2years	3 (100%)	3 (6.4%)	0.0001	Significant

**Table 4: Prevalence of wasting (weight-for-length/height < -2SD) in HIV-infected and HIV-exposed, uninfected babies during 2-year follow-up.**

	HIV-Infected N = 3	HIV-Exposed, Uninfected N = 47	P value	Statistical Significance
6weeks	3 (100%)	10 (21.3%)	0.003	Significant
6months	3 (100%)	10 (21.3%)	0.003	Significant
12months	1 (33.3%)	8 (17%)	0.47	Not significant
18months	2 (66.6%)	6 (12.7%)	0.014	Significant
2years	3 (100%)	4 (8.5%)	0.0001	Significant

**Table 5: Prevalence underweight in HIV-exposed, uninfected breastfed and non- breastfed babies during 2year follow-up**

	HIV-exposed, uninfected, breastfed N = 14	HIV-exposed, uninfected, non-breastfed N = 33	p-value	Statistical significance
6weeks	None	10 (30.3%)	0.02	Significant
6months	None	10 (30.3%)	0.02	Significant
12months	None	8 (24.2%)	0.043	Significant
18months	None	6 (18.1%)	0.08	Not significant
2years	None	4 (12.1%)	0.173	Not- Significant

**Table 6: Prevalence of stunting (length/height-for-age < -2SD) in HIV-exposed, uninfected breastfed and non-breastfed babies during 2year follow up**

	HIV-exposed, uninfected, breastfed N = 14	HIV-exposed, uninfected, non-breastfed N = 33	p-value	Statistical significance
6weeks	NONE	9 (27.2%)	0.03	Significant
6months	NONE	9 (27.2%)	0.03	Significant
12months	NONE	8 (24.2%)	0.043	Significant
18months	NONE	5 (15.1%)	0.123	Not-Significant
2years	NONE	3 (9.09%)	0.244	Not-Significant

**Table 7: Prevalence of wasting (weight-for-length/height < -2SD) in HIV-exposed, uninfected breastfed and non-breastfed babies during 2-year follow-up.**

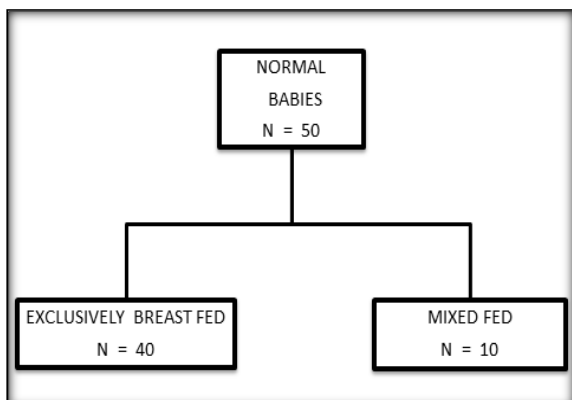
	HIV-exposed, uninfected, breastfed N = 14	HIV-exposed, uninfected, non-breastfed N = 33	p-value	STATISTICAL SIGNIFICANCE
6weeks	NONE	10 (30.3%)	0.02	Significant
6months	NONE	10 (30.3%)	0.02	Significant
12months	NONE	8 (24.2%)	0.043	Significant
18months	NONE	6 (18.1%)	0.08	Not-Significant
2years	NONE	4 (12.1%)	0.173	Not-Significant

**Table 8: Incidence of infections in HIV-infected and HIV-exposed, uninfected babies during 2-year follow-up.**

Illness	HIV-infected (n=3)	HIV-exposed uninfected (n=47)	p-value	Statistical Significance
Lower respiratory tract infections	3 (100%)	14 (29.7%)	0.013	Significant
Diarrhea	3 (100%)	13 (27.6%)	0.009	Significant

**Table 9: Incidence of infections in HIV-exposed, uninfected breastfed and non-breastfed babies during 2-year follow-up.**

Illness	HIV-exposed, uninfected Breastfed (n=14)	HIV-exposed, uninfected Non breastfed (n=33)	P value	Statistical Significance
Lower respiratory tract infections	1 (7.1%)	13 (39.3%)	0.027	Significant
Diarrhea	1 (7.1%)	12 (36.3%)	0.041	Significant



**Chart 1:**

Out of 50 normal infants, 40(80%) were on exclusive breast feeds and 10(20%) were on mixed feeds [Chart 1].

Mothers/caretakers of 50 HIV-exposed infants, were explained regarding the AFASS criteria at

birth and 20 (40%) of them opted to breastfeed and 30 (60%) opted to formula feed. [Chart 2]

At 6 weeks of follow-up, out of 20 infants who were started on breastfeeds, only 15(75%) remained on breast feeds and 5(25%) were on mixed feeds. And in 30 infants who were started on formula feeds only 25(83.3%) remained on formula feeds and 5(16.7%) infants were on mixed feeds.

Out of the 50 HIV-exposed infants, 3(6%) were found to be HIV positive at 6 weeks DBS- DNA PCR testing. 1 out of 15 exclusively breastfed infants and 2 out of 10 mixed-fed infants were found to be HIV positive.

Growth pattern of HIV-infected, HIV-exposed but uninfected, and normal infants during 2year follow-up:

The growth patterns of HIV-infected and HIV-uninfected babies were compared.

Mean weight for age Z scores in both groups were plotted.

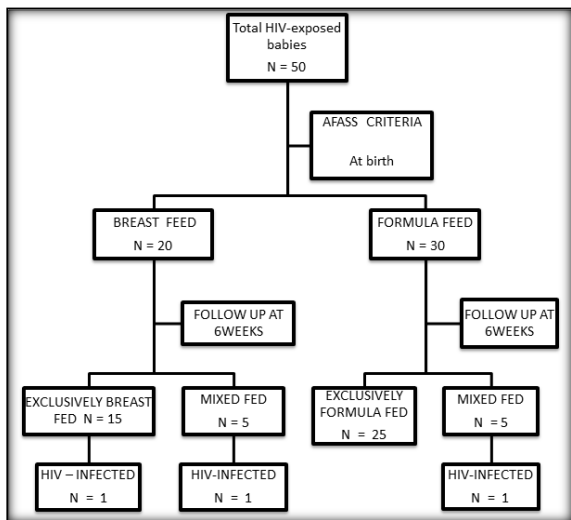


Chart 2: ?

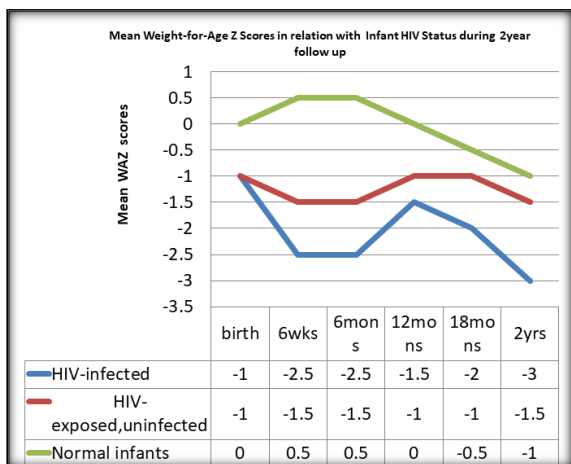


Figure 1: Mean weight – for – Age Z Scores in relation with Infant HIV Status during 2year follow-up

The mean weight for age Z scores remained lowest throughout the study period in HIV-infected infants. And underweight was found to be significantly higher in HIV-infected infants by the end of 2 years. Mean length/height-for-age Z scores in HIV-infected and uninfected babies were plotted.

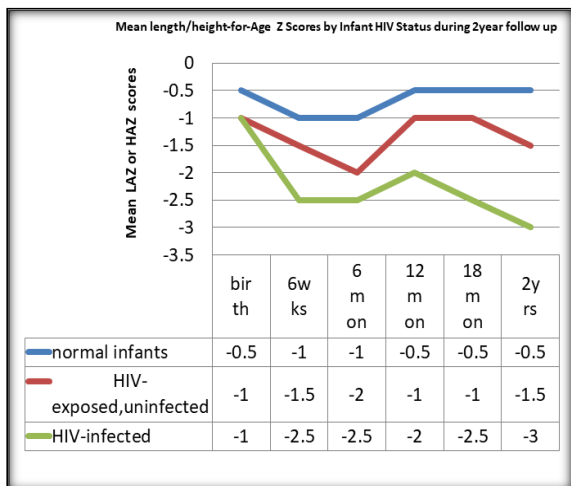


Figure 2: Mean length/height-for-Age Z Scores by Infant HIV Status during 2year follow up

The mean length/height for age Z scores remained lowest throughout the study period in HIV-infected infants. And stunting was found to be significantly higher in HIV-infected babies by the end of 2 years. Mean weight for length/height Z scores in HIV-infected and uninfected infants were plotted.

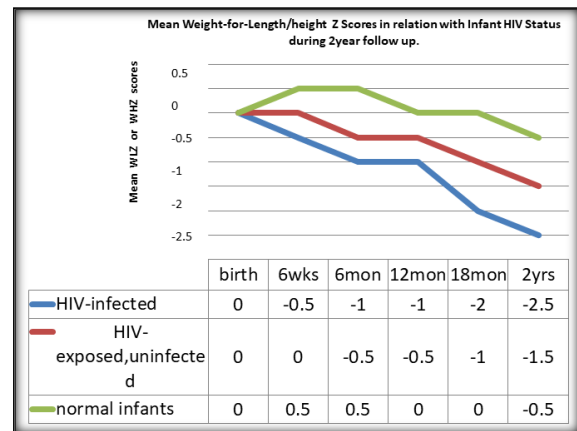


Figure 3: Mean Weight-for-Length/height Z Scores in relation to Infant HIV Status during 2-year follow-up.

The mean weight for length/height Z scores remained lowest throughout the study period in HIV-infected infants. And wasting was significantly higher in HIV-infected children by the end of 2 years.

Mean weight for age Z scores of HIV-exposed, uninfected breastfed babies, non-breastfed babies (formula-fed and mixed-fed), and normal breastfed infants were plotted.

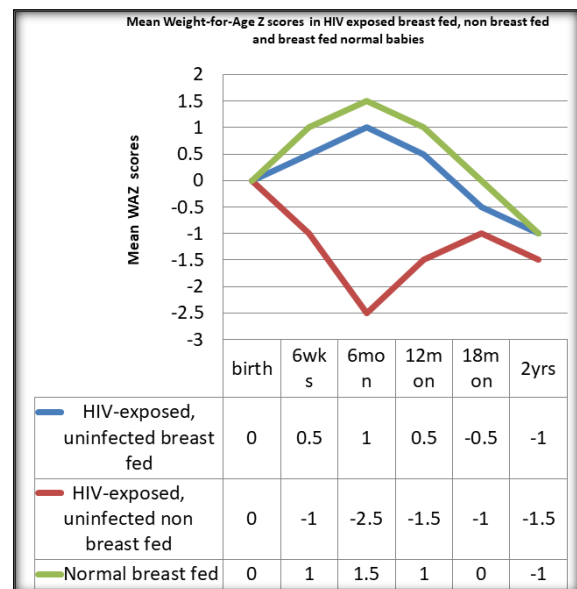
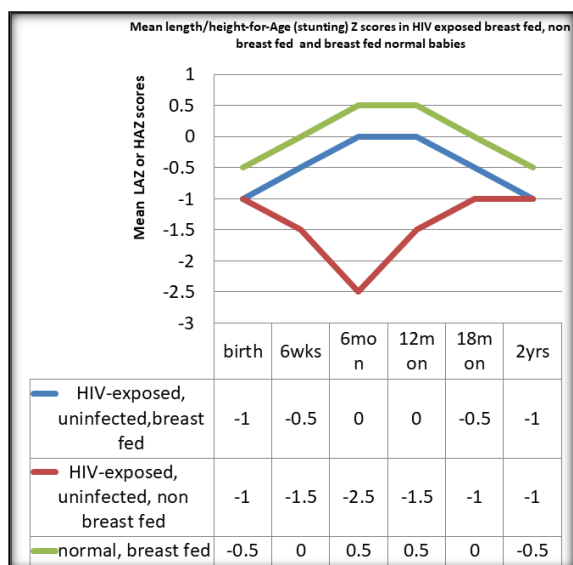


Figure 4: Mean Weight-for-Age Z scores in HIV-exposed breastfed, non-breastfed, and breastfed normal babies

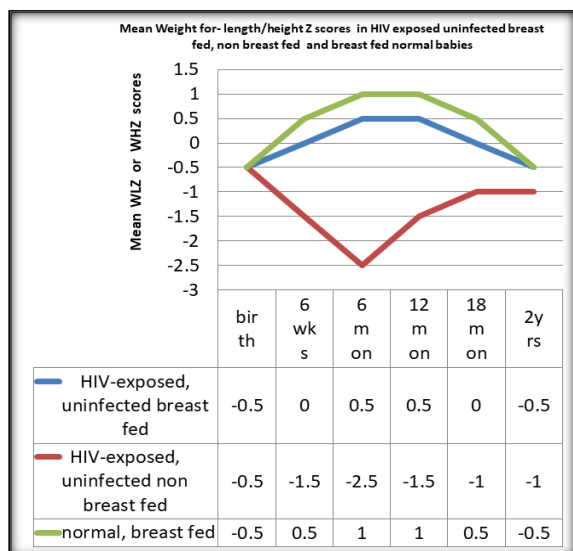
It was found that underweight was significantly higher in HIV-exposed, uninfected non-breastfed infants. and the growth pattern of HIV-exposed uninfected breastfed babies was similar to that of normal breastfed babies.

Mean length/height for age Z scores of HIV-exposed, uninfected breastfed, non-breastfed babies, and normal breastfed babies were plotted.



**Figure 5: Mean length/height-for-Age (stunting) Z scores in HIV exposed breast fed, non breast fed and breast fed normal babies**

It was found that stunting was significantly higher in HIV-exposed, uninfected non-breastfed infants. The mean length/height for age in HIV-uninfected breastfed babies were similar to that of normal breastfed babies ring the follow-up till 2 years. The mean weight for length/height Z scores in HIV-exposed uninfected breastfed, non-breastfed and normal breastfed babies were plotted.



**Figure 6: Mean Weight for length/height Z scores in HIV-exposed uninfected breastfed, non-breastfed, and breastfed normal babies**

It was found that wasting was significantly higher in HIV-exposed uninfected non-breastfed infants. The mean weight for length/height in HIV-uninfected breastfed babies was similar to that of normal breastfed babies during the follow-up till 2 years.

Among HIV-infected and uninfected babies at 6 weeks follow-up, the prevalence of underweight (100% vs. 21.3%), was significantly higher in HIV-infected babies ( $p = 0.003$ ). At 6 months of follow up the prevalence of underweight, was the same as that at 6 weeks in both groups. At the 12-month follow-up, the prevalence of underweight was (33.3% vs. 17%) and statistically not significant. At 18 months follow-up of both the groups, the prevalence of underweight (66.6% vs. 12.7%), was found to be significantly higher in HIV-infected babies. At 2 years follow-up, the prevalence of underweight (100% vs. 8.5%), was found to be significantly higher in the HIV-infected group. [Table 2]

Among HIV-infected and uninfected babies at 6 weeks follow-up, the prevalence of stunting (100% vs. 19.14%), was significantly higher in HIV-infected babies ( $p = 0.001$ ). At 6 months of follow up the prevalence of stunting, was the same as that at 6 weeks in both groups. At 12 months follow-up, the prevalence of stunting was (33.3% vs. 17%) and statistically not significant ( $p = 0.47$ ). At 18 months follow-up of both the groups, the prevalence of stunting (66.6% vs. 10.6%), was found to be significantly higher in HIV-infected babies ( $p = 0.007$ ). At 2 years follow-up, the prevalence of stunting (100% vs. 6.4%) was found to be significantly higher ( $p = 0.0001$ ) in the HIV-infected group. [Table 3]

Among HIV-infected and uninfected babies at 6 weeks follow-up, the prevalence of wasting (100% vs. 21.3%) was significantly higher in HIV-infected babies ( $p = 0.003$ ). At 6 months of follow up the prevalence of wasting was the same as that at 6 weeks in both groups. At the 12-month follow-up, the prevalence of wasting was (33.3% vs. 17%) and statistically not significant ( $p = 0.47$ ). At 18 months of follow-up of both groups, the prevalence of wasting (100% vs. 12.7%) was found to be significantly higher ( $p = 0.014$ ) in HIV-infected babies. At 2 years follow-up, the prevalence of wasting (100% vs. 8.5%) was found to be significantly higher ( $p = 0.0001$ ) in the HIV-infected group. [Table 4]

Among HIV-exposed uninfected breastfed babies and non-breastfed babies, at 6 weeks of follow-up, the prevalence of underweight (0 vs. 30.3%) was significantly higher in non-breastfed babies ( $p = 0.02$ ). At 6 months of follow up the prevalence of underweight was the same as that at 6 weeks in both the groups. At 12 months follow-up, the prevalence of underweight was (0% vs. 24.2%) and statistically significant ( $p = 0.043$ ). At 18 months follow-up of both groups, the prevalence of underweight (0% vs. 18.1%) was not significant ( $p = 0.08$ ). At 2 years follow-up, the prevalence of underweight (0% vs. 12.1%) was not significant ( $p = 0.173$ ). Thus underweight was significantly higher in non-breastfed HIV-uninfected infants during the first 6 months which was attributed to improper feeding practices. [Table 5]

Among HIV-exposed uninfected breastfed babies and non-breastfed babies, at 6 weeks follow-up, the prevalence of stunting (0 vs. 27.2%) was significantly higher in non-breastfed babies ( $p=0.03$ ). At 6 months of follow up the prevalence of stunting was the same as that at 6 weeks in both the groups. At 12 months follow-up, the prevalence of stunting was (0% vs. 24.2%) and statistically significant ( $p = 0.043$ ). At the 18-month follow-up of both groups, the prevalence of stunting (0% vs. 15.1%) was not significant ( $p = 0.123$ ). At 2 years follow-up, the prevalence of stunting (0% vs. 9.09%) was not significant ( $p = 0.244$ ). Thus stunting was significantly higher in non-breastfed HIV-uninfected infants during the first 6 months which was attributed to improper feeding practices. [Table 6]

Among HIV-exposed uninfected breastfed babies and non-breastfed babies, at 6 weeks follow-up, the prevalence of wasting (0 vs. 30.3%) was significantly higher in non-breastfed babies ( $p = 0.02$ ). At 6 months of follow-up, the prevalence of wasting was the same as that at 6 weeks in both groups. At 12 months follow-up, the prevalence of wasting was (0% vs. 24.2%) and statistically significant ( $p = 0.043$ ). At 18 months of follow-up of both groups, the prevalence of wasting (0% vs. 18.1%) was not significant ( $p = 0.08$ ). At 2 years follow-up, the prevalence of wasting (0% vs. 12.1%) was not significant ( $p = 0.173$ ). Thus stunting was significantly higher in non-breastfed HIV-uninfected infants during the first 6 months which was attributed to improper feeding practices. [Table 7]

During the 2year follow-up, the incidence of common illnesses like diarrhea and lower respiratory tract infections was recorded in HIV-infected and HIV-exposed, and uninfected babies [Table 8]

The incidence of lower respiratory tract infections and diarrhea was found to be significantly higher in HIV-infected babies.

The incidence of these illnesses was also recorded in HIV-exposed, uninfected breastfed, and non-breastfed babies [Table 9]

The incidence of lower respiratory tract infections and diarrhea was found to be significantly higher in non-breastfed babies (bottle or formula fed or mixed fed).

## CONCLUSION

1. Anthropometric indices showed poor growth as early as 6 weeks in HIV-infected infants.
2. Baseline stunting, wasting, and underweight were high in HIV-infected infants during the 2-year follow-up.
3. The growth patterns of HIV-exposed uninfected infants who were breastfed were similar to the growth patterns of normal (HIV-unexposed) breastfed infants.

4. In HIV-exposed uninfected babies who were on artificial feeds, being underweight, stunting, and wasting were significantly higher when compared to breastfed babies.
5. Faulty feeding techniques, which are being practiced by mothers or caregivers who bottle feed their babies with improper cleaning and hygiene or provide over-diluted artificial feeds/animal milk even after effective counseling, is a major risk factor for malnutrition and poor growth in HIV-exposed, uninfected infants.
6. Hence in developing countries like India, breastfeeding should be strongly recommended in all HIV-exposed babies in order to prevent the complications of bottle feeding, other faulty feeding practices, and the consequences of malnutrition.
7. In HIV-infected infants the growth is also impaired because of recurrent infections like diarrhea, pneumonia etc.
8. Hence growth monitoring with early intervention and nutritional rehabilitation and effective management of illnesses in all HIV-exposed infants is a must.
9. Even in normal (HIV-unexposed) infants, the exclusive breastfeeding for 6 months is not followed to 100%, some of them shifted to bottle feeding, because of various reasons. Hence effective counseling and maternal education by medical personnel regarding the importance of exclusive breastfeeding is necessary.
10. In view of high maternal and infant malnutrition rates in India, and the low availability of early infant HIV testing, early growth monitoring of all HIV-exposed infants coupled with nutritional advice to the parents stand to be effective low-cost strategies for improving the health and survival outcomes of these infants.

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