

Growth of HIV-exposed infants from birth to 6 months in the prevention of mother-to-child transmission program

Maria Priskila, Ketut Dewi Kumara Wati, Ni Putu Siadi Purniti

Abstract

Background Human immunodeficiency virus (HIV) infection is a global health issue. Most cases of HIV infection in children are acquired through transmission from HIV-infected mothers. Maternal HIV infection affects infant growth.

Objective To evaluate the first six months of growth in HIV-exposed infants born to mothers in the prevention of mother-to-child transmission (PMTCT) program.

Methods This prospective cohort study was done in 40 HIV-exposed infants born in Sanglah General Hospital, Bali. Subjects' underwent weight and length measurements at birth and monthly for 6 months. Data analyses used were repeated ANOVA test with Bonferonni post-hoc analysis for normally distributed data and Friedman test with Wilcoxon post-hoc analysis for abnormally distributed data. Correlations between birth weight and length to weight and length at 6 months of age were analyzed with Spearman's test.

Results Subjects' mean birth weight was 2,900 (SD 546) grams and median birth length was 48 (range 36-52) cm. Subjects' body weight and length increased monthly throughout the measurement period ($P < 0.001$). There was a strong negative correlation between birth weight and infant weight gain at 6 months of age ($r = -0.678$), and a moderate negative correlation between birth length and infant length gain at 6 months of age ($r = -0.564$).

Conclusion HIV-exposed infants born to mothers in the PMTCT program have a significant body weight and body length growth in the first 6 months of life, and followed general WHO weight and length curves for age. [Paediatr Indones. 2019;59:183-7; doi: <http://dx.doi.org/10.14238/pi59.4.2019.183-7>].

Keywords: HIV-exposed infant; body weight; body length

Human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) are worldwide health problems, due to high transmission of infection, morbidity, and mortality. *The World Health Organization* (WHO) reported that 3.3 million children have HIV infection,¹ with most infections occurring perinatally.² HIV transmission from mother to child in Indonesia was reported to be 3.76%, and continues to increase every year.³ The main pathways of HIV infection transmission to children are intrauterine, intrapartum, and post-natal (breastfeeding).⁴ Maternal HIV infection affects infant growth. Several studies have shown that HIV-exposed infants had higher risk of morbidity and mortality than HIV-unexposed infants, but another US study showed similar growth in HIV-exposed uninfected infants and HIV-unexposed infants. The PMTCT program has been effective in decreasing HIV transmission risk 1-2%.⁵

From the Department of Child Health, Universitas Udayana Medical School/Sanglah Hospital, Denpasar, Bali, Indonesia.

Corresponding author: Maria Priskila, Pulau Nias street, Denpasar 80114, Indonesia. Tel. +62 361 244038; Email: dr.priskila@gmail.com.

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Methods

A prospective cohort study on HIV-exposed infants was conducted to evaluate growth within the first 6 months of life. This study was conducted at Sanglah Hospital, Denpasar, Bali, from April 2017 to August 2018. The inclusion criteria were HIV-exposed infants, born to HIV-infected mothers in the PMTCT program. Exclusion criteria were infants with major congenital abnormalities or whose parents did not agree to participate. Drop out criteria were skipping the measurement schedule two or more times, or being diagnosed with presumptive HIV during the study period. Data analyses in this study consisted of descriptive statistical and bivariate analyses. Comparative analyses were done using repeated measurement ANOVA test with Bonferonni post-hoc analysis for normal data distribution, and Friedman test with Wilcoxon post-hoc analysis for abnormal data distribution. Correlative analysis was done by Spearman's test. Infant growth rates were expressed using the infant weight gain percentage (IWG%), and defined as $[(\text{infant weight} - \text{birth weight}) / \text{birth weight} \times 100]$, as well as the infant length gain percentage (ILG%) defined as $[(\text{infant length} - \text{birth length}) / \text{birth length} \times 100]$. All data were analyzed using SPSS version 23 software. Results with P values <0.05 were considered to be statistically significant. This study was approved by the Research Ethics Committee of the Universitas Udayana Medical School/Sanglah Hospital.

Results

From 50 patients, 40 were included in the analysis, in accordance with the required minimum sample size calculation. The basic characteristics of subjects and their mothers are shown in **Table 1**. Subjects were mostly boys (60%), born full-term (95%), without asphyxia (92.5%), and with birth weight $\geq 2,500$ grams (80%).

Comparative analysis for infant weight from birth to 6 months with repeated measurement was done with ANOVA test, followed by Bonferoni post-hoc analysis (**Table 2**). Mean weight significantly increased in at least 2 periods of time throughout the measurement period ($P < 0.001$). Body weight growth

in HIV-exposed infants in the PMTCT program followed the growth curve for weight-to-age on the WHO growth chart.

Table 1. Characteristics of subjects and mothers

Characteristics	(N=40)
Subjects	
Males, n (%)	24 (60)
Full-term, n (%)	38 (95)
Vigorous baby, n (%)	37 (92.5)
Mean birth weight (SD), grams	2900 (80)
Median birth length (range), cm	48 (36-52)
Mothers	
Mean age (SD), years	28 (4)
Multiparous, n (%)	32 (80)
Mean CD4 level (SD), cells/ μ L	423 (192)

Table 2. Mean infant body weight by age

Age, months	Mean body weight (SD), g	P value*
0	2,900 (546)	<0.001
1	3,832 (826)	
2	4,717 (908)	
3	5,660 (908)	
4	6,375 (855)	
5	7,082 (945)	
6	7,655 (975)	

*repeated measurement (ANOVA) test

Comparative analysis for length from birth to 6 months was done with Friedman test, followed by Wilcoxon post-hoc analysis (**Table 3**). Median body length significantly increased in at least 2 periods of time throughout the measurement period ($P < 0.001$). Body length growth in HIV-exposed infants in the PMTCT program followed the length-to-age growth curve of the WHO growth chart. Correlative analysis between subjects' birth weight and weight gain at 6 months of age was done with Spearman's test for

Table 3. Infant body length based on age

Age, months	Median body length (range), cm	P value*
0	48 (36-52)	<0.001
1	53 (40-59)	
2	56 (45-65)	
3	60 (51-66)	
4	63 (56-69)	
5	64.5 (60-71)	
6	67 (64-74)	

*Friedman test with Wilcoxon post-hoc analysis

Discussion

Subjects were forty HIV-exposed infants in the PMTCT program, comprising 60% boys, 95% full-term, 92.5% without asphyxia, and 80% with birth weight $\geq 2,500$ grams. Subjects' mean birth weight was 2,900 grams and mean weight-for-age z-score (WAZ) was -0.86. Subjects' mean birth length was 48 cm and mean length-for-age z-score (LAZ) was -0.78. A previous study in 2016 show similar results, with median WAZ in HIV-exposed infant of -0.65 (-1.46) at birth.⁹

Long-term nutritional and neurodevelopmental outcomes are influenced by environmental factors during the first 1,000 days after conception - the period from conception to 2 years of age. HIV exposure during this period could, therefore, crucially affect birth, growth, and development. In developing countries, HIV-exposed, uninfected newborns are likely to be small-for-gestational age or have low birth weight compared to HIV-unexposed newborns.⁵ Anti-retroviral exposure in HIV-infected mothers was associated with significantly lower mean LAZ and lower head circumference for age z score (HCAZ) at the age of one year, but not at birth. Siberry *et al.*⁶ also found no association between antiretroviral exposure during pregnancy and lower weight, shorter length, or smaller head circumference in the newborn period.

In our study, subjects significantly increased in weight and length throughout the measurement period during the first six months of life ($P < 0.001$). The median weight and length based on monthly age for the first six months followed the WHO growth chart curve, but was still below the curve. A previous study showed no difference in growth between HIV-exposed, uninfected infants and HIV-unexposed infants.⁷ However, Evans *et al.*⁵ showed that HIV-exposed infants tended to be small-for-gestational age, or have lower birth weight than HIV-unexposed infants. The PMTCT program is a strategy to reduce HIV infection transmission from mother to baby. The program includes antiretroviral (ARV) therapy for the mother, Caesarean section delivery, anti-retroviral and cotrimoxazole prophylaxis for the infant, and formula milk for infant nutrition.

Current national and international reference growth charts are based on cross-sectional data. Their primary limitation is that they do not monitor

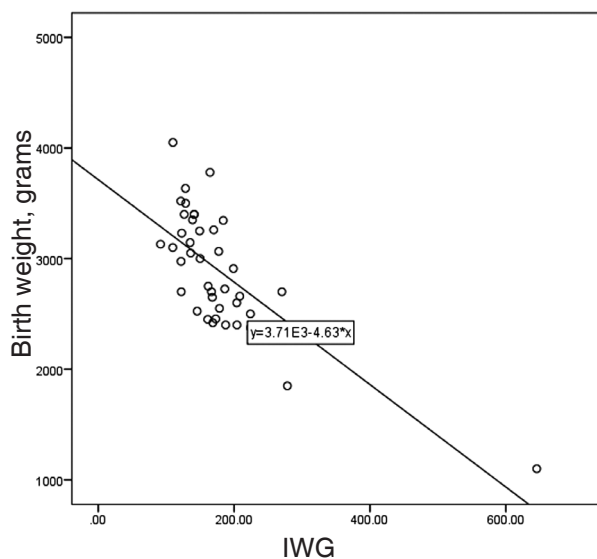


Figure 1. Correlation between birth weight and weight gain at 6 months

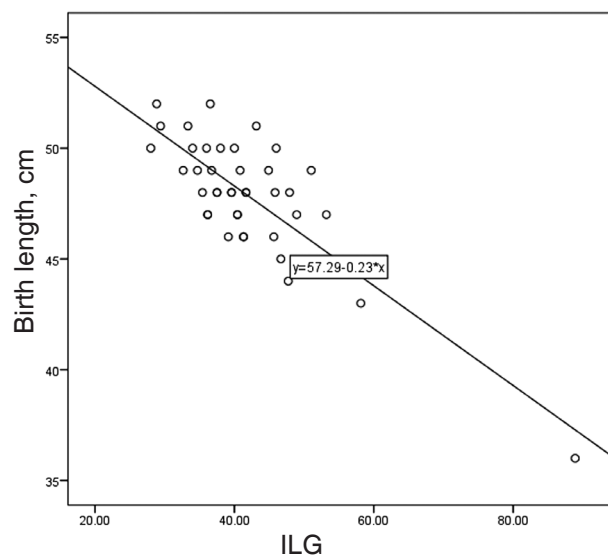


Figure 2. Correlation between birth length and length gain at 6 months

abnormal data distribution. The median IWG% was 163 (range 92-645%) with $r = -0.678$, which indicates a negative and strong correlation; lower birth weight was correlated to higher weight growth at 6 months. Spearman's test revealed a median ILG% of 40% (28-89%), with $r = -0.564$, which indicates a negative and moderate correlation; lower birth length was correlated to the higher length growth at 6 months.

growth as such, but identify infants whose weight and length centiles are considered low and/or falling. A better approach for monitoring infant growth would be based on longitudinal data - that is, comparisons of current growth measures with previous growth measures to assess whether or not infants are growing at a faster or slower rate.⁸ Infant weight gain percentage (IWG%) could be used as an alternative to assess infant weight gain, as can infant length gain percentage (ILG%) be used to assess length gain. Birth weight and length are an important determinants for infant growth. By expressing the weight gain as a percentage of birth weight, IWG% has an advantage over a simple measure of weight gain, as it represents the extent of an infant's weight gain relative to birth weight.⁸

Birth weight and length appear to affect later growth. Hence, we assessed growth by measuring infant weight gain relative to birth weight, and infant length gain relative to birth length. We found negative correlations between birth weight and weight growth at 6 months as well as between birth length and length growth at six months. The negative correlation means that lower birth weight and birth length was related to higher weight and length gain at 6 months old. Similarly, Borah et al. reported that lower birth weight and birth length babies had higher weight and length gain at 6 months old.⁹ Another study said that very low birth weight infants showed catch-up growth during the first year, but their weight and length remained less than full-term peers. Significant catch-up growth for weight and length was observed during the first year with mean z-score change of 0.40 (SD 1.05) and 1.01 (SD 1.25), respectively.¹⁰ The strong correlation in weight gain at 6 months and moderate correlation in length gain at 6 months could have been caused by slower length growth than weight growth.

Body weight is one of clinical indicators used to decide when to stop prophylaxis co-trimoxazole in HIV-exposed infants. The WHO guidelines recommend co-trimoxazole prophylaxis for HIV-exposed infants aged 4-6 weeks, to be continued until HIV infection has been excluded by an age-appropriate HIV test to establish a final diagnosis or until 6 months - 1 year of age if children's growth, development, and health status are good. In other words, good weight gain in HIV-exposed infants could be a determining factor to stop prophylaxis cotrimoxazole earlier.

The limitations of this study were not comparing growth to HIV-unexposed infants, and not analyzing the HIV infection status of the infant. Because the virology examination that can be done at 6 weeks on HIV-exposed infants is not a routine procedure, so it was not possible to test them before the study. The routine procedure to diagnose HIV in HIV-exposed infant is usually done at 18 months of age by HIV antibody test. We also did not evaluate the head circumference of subjects as a growth parameter in infants.

In conclusion, HIV-exposed infants born to mothers in the PMTCT program have a significant body weight and body length growth in the first 6 months of life.

Conflict of Interest

None declared.

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