The Outcomes of Infants with HIV Infected Mother in a Tertiary Hospital in Indonesia

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ABSTRACT

Background: Infant from HIV mother face the risk of HIV infection. Effective prevention on mother-to-child transmission (PMTCT) program increasing the number of uninfected infants in East Java Indonesia. This study describes the outcomes of infants with HIV mother in Dr. Soetomo Hospital, a tertiary referral hospital in East Java, related to outcome (infectious morbidity, nutritional status, immunodeficiency status, growth/development, and incidence of anemia).

Method: This cross-sectional study analyzed 0-18 months infant and HIV mother pairs at HIV outpatient clinic Dr. Soetomo General Hospital from January to April 2017. The data were collected and analyzed using Fisher's exact test and chi-square test with $P<0.05$.

Results: Fourty HIV-infected mothers and infants pairs were analyzed, separated into two groups positive (3 infants) and negative (37 infants) Anti HIV PCR. There were 19 male. Age distribution (6 weeks-5 months 40%; 6-11 months 47.5%; 12-18 months 12.5%). Five percent were born prematurely, 77.5% infant has normal birth-weight. Only 2.5% were fed breast milk, AZT-cotrimoxazole were given to 87.5% infant while the rest received AZT/3TC/NVP. Immunizations of the infants were mostly (60%) up to date. Infectious morbidity (P=0.433), WAZ-score (P=0.666), LAZ-score (P=0,973), WLZ-score (P=0.219) and incidence of anemia (P=0.548) were not significant differences between groups. The development test using DDST II (P=0,001), as well as immunodeficiency status [presence of immunodeficiency (P<0.001)] was significantly different between groups.

Conclusion: There were significant effects of HIV exposed on the development and immunodeficiency status in 0-18 months infant.

Keywords: *HIV-exposed infants, outcomes, Prevention on mother-to-child transmission/PMTCT.*

Introduction

HIV infection in children has become a major problem in family, community, and health care throughout the world. Most of the causes of HIV-exposed-infected (HEI) children are a vertical transmission from mother to infant. HIV infection progression occurs very quickly in the first few months after birth. It often leads to death.[1] HIV-exposed-infected infants are infants born to mother possessing HIV positive and/or positive antibody results. HIV-exposed-uninfected (HEU) infants are infants with negative PCR DNA results.[2]

Vertical HIV transmission was first reported in 1983.[3] It was estimated that 1.8 million children under 15 were HIV infected in 2017. About 180.000 children were newly infected with HIV, mainly through transmission of the virus from their mother during pregnancy, delivery, or breastfeeding.[4] An estimated 110.000 children died of AIDS-related causes globally. HIV-infected infants through mother-infant transmission

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significantly increase the risk of death, in which 20% of them who do not receive therapy during the perinatal period will die within 1 year.[3]

HIV related to infant mortality increases in 2-3 months of age and can only be addressed with Prevention of Mother to Child Transmission (PMTCT) by limiting the vertical transmission and providing initial therapy for HEI infants. A study in health outcomes of HEU infants has increased in the past decade. Several studies suggested that these infants have increased mortality rates, infectious morbidity, and impaired growth compared with HEU infants. However heterogeneous results might reflect the inherent challenges in the study of HEU infants.[3] This research evaluates the outcome of HIV-exposed infants from infected mother in Dr. Soetomo Hospital related to infectious morbidity, nutritional status, immunological status, growth and development, as well as incidence of anemia.

Method

This research was a prospective cohort, conducted at Child Health Department, Dr. Soetomo General Hospital Surabaya within January 1st-April 30th, 2017. Data were taken through history-taking, physical, and supporting examination. The research subjects were all 0-18 months infant with HIV-infected mother in Dr. Soetomo General Hospital since January 1st-April 30th, 2017. The status of HIV infection determined by the Anti HIV PCR DNA or RNA test. The inclusion criteria are 0-18 months infant with HIV-infected mother diagnosed either before or during pregnancy, during or after the delivery and infants whose parents have agreed to participate as research sample and have signed informed consent. Parents who withdraw participation were excluded. Data collected were age, gender, nutritional status, gestational age, birth-weight, birth history, breastfeeding history, immunization status, mother's and infant's ARV, and infant condition (infectious morbidity, incidence of anemia, immunodeficiency status, growth and development). Infectious morbidity recorded as present if there were diarrhea, fever or cough more than three times all their life. Definition of anemia was according to WHO (Hb<13.5g/dL). Descriptive analysis were performed using Fisher's exact test, chi-square test with significant value when P<0.05.

Results

A total of 40 infants with HIV-infected-mother were analyzed and divided into 2 groups positive (3 infants) and negative (37 infant) Anti HIV PCR DNA or RNA. No patients were excluded. Characteristics of research subjects are listed in table 1. In this study there were 3 infants infected of HIV infection, 2 infants with no PMTCT (spontaneous delivery, mother with no ARV, breastfeed) and 1 infant with PMTCT after-delivery (no ARV before and during pregnancy). Infection morbidity occurred in 18 infants were 4(10%) diarrhea infection, 14(35%) cough, 7(17.5%) fever.

Table 1: Outcomes of HIV-infected mother born infants

Outcome	PCR (-)	PCR (+)	p-value
Anthropometry			
Weight for age (Z-score)			
Median	31	1	0,666
Underweight	5	2	
Severely underweight	1	0	
Length for Age (Z-score)			
Median	32	3	0,973
Stunted	2	0	
Severely stunted	3	0	
Weight for Length (Z-score)			
Overweight	2	0	0,219
Median	27	1	
Wasted	8	2	
Infection morbidity			
Present	16	2	0,433
Not present	21	1	
Anemic incidence	18	2	0,548
Immunodeficiency (CD4 %)			
No deficiency	29	0	<0,001
Mild	5	0	
Moderate	3	1	
Severe	0	2	
Developmental (DDST II)			
Suspect	5	3	<0,001
Normal	32	0	

***DDST II** = Denver Development Screening Test II; **CD4% immunodeficiency** [(< 11 months : no deficiency (>35); mild (30-35); moderate (25-30); severe(<25)]; [(12-35 months : no deficiency (>30); mild (25-30); moderate (20-25); severe(<20)].

Table 2: Infectious morbidity in HIV exposed Infants

Infectious Morbidity	Number of Cases n (%)		p-value
	HIV exposed-uninfected	HIV exposed-infected	
Fever	6 (15)	1 (2,5)	0,453
Diarrhea	3 (7,5)	1 (2,5)	0,161
Cough	2 (5)	12 (30)	0,232

Discussion

This research described the outcomes of 40 infants born from HIV-infected mothers, 3 infants-infected with HIV and 37 infants were not infected. Two of HEI infants with no PTMCT program and 1 infant with PMTCT program after birth. One of HIV infected infant use only 1 type of ARV, while recommendations from ARV treatment in developing country recommend giving 3 types of antiretroviral drugs, for infants who have never received ARV during pregnancy. This is in accordance with the previous research in which HEU infants population will increase.[5] It is said that an effective intervention PMTCT has decreased the HIV antenatal prevalence.[6]

Infectious Morbidity: In the recent study found the prevalence of infectious morbidity possesses no significant difference in both groups. This result differs from Venkatesh study of HEI infant had over twice at risk of morbidity and over four-times at risk of death compared to HEU infants.[9] Mofenson in 1999 founded that maternal PVL was not only a major predictor of the risk of perinatal HIV transmission,[10] but may also closely predict viral levels in maternal breast milk and the health of both HIV-infected and HIV-uninfected infants.[11,12,13] The risk of hospitalization due to diarrhea and pneumonia was close to four times greater among HEI than HEU infants. The most common cause of infant pneumonia requiring hospitalization in Rufini study population exhibited PCP.[14] The source of data in this study comes from recalling interviews with parents so that there is a high probability of bias recalling.

Incidence of Anemia: Anemia has been recognized as an important clinical problem in HIV-infected patients[15,16] with an estimated prevalence ranging from 10% in asymptomatic HIV-infected patients to 92% in patients with AIDS.[17] This study exhibited no significant difference between HEI infants compared to HEU infants. History of administration of antiretroviral drugs and cotrimoxazole in HIV exposed infants did not result in an increased incidence of anemia. The high number of anemia in this study caused by high incidence of anemia in Indonesia. The 2001 Household Health Survey showed the prevalence of ADB in infants 0-6 months, infants 6-12 months, and children under five respectively at 61.3%, 64.8% and 48.1%.[18] About 66.7% anemia occurred in HEI infants in this study. Anemia could be correlated with several factors as described in several previous studies such as advanced clinical and immunological HIV disease stage[19,20], breastfeeding period[21], highly active antiretroviral therapy (HAART), and cotrimoxazole.[7] Further research is needed to determine the cause of anemia in this group.

Growth and Development: Research results exhibited that the effects of ARV regimens may cause deficits of height and abnormality of body composition. Treatment with ARV containing protease inhibitors had a significant impact on body weight and weight to height ratio and the limit of height. This is in line with research conducted by Kerr in 2014. It stated that growth failure is a sensitive indicator of HIV disease.[22] In addition, the research of potential effects of the ARV regimen category leads to a deficit in body height and abnormality of the body composition. Treatment with an ARV regimen containing protease inhibitors has a significant impact on body weight and weight-to-height ratios as well as borderline effects on height.[8] However, no significant differences in growth between HIV-exposed-infected infants compared with HIV-exposed-uninfected infants in this study.

The growth failure occurs in mother with antiretrovirals. As a result of the use of nevirapine in mothers, in this study the results were not statistically significant. According to Ram (2012) studies Infants who were HIV-infected and breastfed notes were higher risk of being stunted and underweight, but not wasted, and two variables were not statistically significant. Maternal anemia has significantly increased the risk of stunting but not underweight. Infant morbidity, increased risk of underweight and wasting, but not stunting. In this study maternal education data is absent so that it cannot be assessed, while breastfeeding history, birth weight, gestational age and delivery method have no significant relationship to the incidence of stunted, underweight and wasted.

Delayed development was assessed by the Denver Developmental Screening Test and the result was a significant difference between HEI and HEU infants in this study. These results are consistent with recent findings from a trial in South Africa, in which HIV infected infants randomized to deferred ART had lower locomotors scores at 11 months of age compared with HIV-uninfected infants.[23] Another study in South Africa found differences in language and motor scores among HIV-infected-infants who had initiated ART at a mean age of approximately 5 months. They were observed for six-months and compared with HEU infants.[24] The study showed significant differences between the two groups. About 5 infants in HEU and 2 infants in HEI. In HEU there is a high possibility that a developmental disorder will occur so that it needs longer observation.

Immunodeficiency: Recent studies revealed significant differences in immunological status between two groups according to CD4%. Two-infants with HEI suffers from severe immunodeficiency and 1 infant suffers from moderate-immunodeficiency. Infants with uninfected HIV infection, 3 suffers moderate-immunodeficiency, and 5 suffers from mild-immunodeficiency.

CD4 is the parameter to measure immunodeficiency in HIV infection. It was used in conjunction with clinical criteria, therefore CD4 can be used as an early indication of disease progression because it will decrease compared to clinical condition.[25] Infants under 18 months require assessment on two important parameters (HIV-infection and %CD4) prior to initiating HAART. Infants who are positively identified as HIV-infected and meet clinical criteria are likely to benefit from HAART.[26] In this study accordance with the course of the HIV, in HIV-infected patients the value of CD4 is much lower than that of those infected.

Conclusion

In conclusion, outcome evaluation of the presence of 0-18 months HIV exposed infants have determined significant value on immunological status and growth.

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Ethical Clearance: This study was approved by the Research Ethics Committee of Dr. Soetomo General Hospital.

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