Differences in the Expression of HIV-1 RNA of Infants aged 3 to 18 Months Based on the Current Provision of Antiretroviral Therapy in Pregnant Women with HIV in Dr Soetomo Hospital Surabaya between January 2004 to December 2011

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ABSTRAK

*Penularan HIV vertikal dari ibu ke bayi adalah masalah global. Intervensi dalam pencegahan Mother To Child program Prevention of Transmission of HIV (PMTCT) memiliki tiga langkah utama yaitu penyediaan terapi antiretroviral pada ibu hamil, persalinan bedah caesar elektif dan mencegah ASI. Pemeriksaan ekspresi Human Immunodeficiency Syndrome-1 ribonucleic acid (HIV-1 RNA) dari bayi berusia 3 sampai 18 bulan merupakan pemeriksaan langkah diagnostik virus HIV dalam darah untuk menentukan terjadinya penularan. Melalui penyediaan antiretroviral (ARV) diharapkan mengurangi penularan dari ibu ke bayi. Tujuan penelitian ini adalah untuk membuktikan bahwa ekspresi HIV-1 RNA bayi berusia 3 sampai 18 bulan dari terapi ARV sejak diberikan usia kehamilan kurang dari atau sama dengan 28 minggu lebih rendah dari penyediaan ARV terapi selama 28 minggu. Penelitian dilakukan di poli Intermediate Care Unit dan Laboratorium Patologi Klinik RSUD dr. Soetomo Surabaya. Waktu penelitian adalah bulan Maret sampai Mei 2012. Penelitian ini merupakan penelitian analitik observasional dengan mengumpulkan data ibu hamil yang hidup dengan HIV periode Januari 2004 - Desember 2011 dan hasil dari HIV-1 RNA ekspresi bayi. Pengukuran bayi HIV-1 ekspresi RNA dilakukan dengan menggunakan Polymerase Chain Reaction (PCR) RNA menggunakan Cobas Amplicor jangkauan deteksi 400-750.000 salinan/ml. Diperoleh 33 sampel yang dibagi menjadi dua kelompok berdasarkan terapi antiretroviral saat ini, yaitu 14 (42.42%) dalam sediaan ARV untuk = 28 minggu dan 19 (57,58%) pada ARV diberikan dari usia kehamilan> 28 minggu. Semua sampel menunjukkan ekspresi RNA HIV-1 terdeteksi dengan kemungkinan bahwa perempuan hamil dengan HIV cenderung memiliki program intervensi yang sesuai dengan program Depkes 2004 dan WHO 2006. Sebagai kesimpulan, tidak ada perbedaan dalam ekspresi dari HIV-1 RNA bayi berusia 3 sampai 18 bulan berdasarkan ART saat ini pada ibu hamil dengan HIV. **(MOG 2011;19:134-139)***

ABSTRACT

*Vertical HIV transmission from mother to infant is a global problem. Intervention in the prevention of Mother To Child program Prevention of Transmission of HIV (PMTCT) has three main steps namely the provision of antiretroviral therapy in pregnant women, elective Caesarean section delivery and prevent breast milk (ASI). Examination of the expression of Human Immunodeficiency Syndrome-1 ribonucleic acid (HIV-1 RNA) of infants aged 3 to 18 months is a diagnostic step examination of the HIV virus in the blood to determine the occurrence of vertical transmission. The provision of antiretroviral (ARV) is expected to decrease transmission from mother to infant. The objective of this study was to prove that the expression of HIV-1 RNA of infants aged 3 to 18 months of ARV therapy since given gestational age less than or equal to 28 weeks is lower than the provision of ARV therapy over 28 weeks. The research was carried out in Intermediate Care Unit Department and Laboratory of Clinical Pathology dr. Soetomo Hospital Surabaya. The timing of the study is March through May 2012. This study is an observational analytic study by collecting data of pregnant women living with HIV in the period of January 2004 - December 2011 and the results of HIV-1 RNA expression of the baby. Measurement of HIV-1 RNA expression infant was conducted by using Polymerase Chain Reaction (PCR) RNA using the Cobas Amplicor detection range 400-750000 copies/ml. Thirty three samples were divided into two groups based on their current antiretroviral therapy, ie 14 (42.42%) in the provision of antiretrovirals for = 28 weeks and 19 (57.58%) in the ARV is administered from the age of pregnancy> 28 weeks. All samples showed the expression of HIV-1 RNA was detected with the likelihood that pregnant women with HIV tend to have a suitable intervention program MOH 2004 and WHO 2006. In conclusion, The expression of HIV-1 RNA in infants aged 3 are similar to that in infants aged 18 months. It is suggested that this study should be followed up prospectively, especially for infant diagnosed using antibody examination. **(MOG 2011;19:134-139)***

Keywords: *HIV-1 RNA expression infant, ARV, PMTCT,HIV*

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INTRODUCTION

There are more than 40 million people are infected with Human Immunodeficiency Syndrome (HIV), and 4.9 million new cases of HIV infection over the past two decades 1. Entering the 21st century, the perinatal HIV epidemic continues to grow worldwide. United Nations Acquired Immunodeficiency Syndrome (UNAIDS) estimates that 1-2 million children infected with HIV at the end of 1999. Some 570 000 children infected with HIV through Mother To Child Transmission of HIV (MTCT) during the year. That the data obtained from 5 million HIV incidence in adults in 1999, 46% of whom are women and most are in the reproductive age range. An estimated 2-4 million women give birth each year and 1600 newborns infected with HIV every day.[2]

MTCT is the most important source of transmission of HIV infection in the mother of his children. Recent interventions to reduce the risk of MTCT program is summarized in Prevention Mother To Child Transmission of HIV (PMTCT). Interventions include antiretroviral prophylaxis (during pregnancy, childbirth and early neonatal period), delivery by Caesarean section before labor and rupture of membranes, as well as avoidance of breast milk (ASI),/breastfeeding.[3]

Provision of antiretroviral (ARV) in pregnancy can reduce maternal plasma viral load, improve maternal Cluster Differentiation-4 (CD4) count lymphosite and prophylaxis for infants 4. The timing is right about the time of the mother-to-fetus transmission can improve the cost effectiveness of therapy. About one third of this transmission has been shown in some studies occurred at mid-gestation, whereas two-thirds of which occurred at the age of pregnancy and during labor.[5]

Prophylactic antiretroviral therapy are consistent with the recommendation World Health Organization (WHO) 2006, given to pregnant women infected with HIV at 28 weeks of gestation. It is based on several studies conducted in Thailand, Uganda and South Africa. The study has a span of time of administration of different drugs in terms of her pregnancy. So that the average time taken to initiate ARV therapy of some research. When to start antiretroviral therapy is associated with the greatest possible rate of transmission can occur either during the 28 weeks of gestation.[5,6,7]

Examination can be done to detect the success of prophylactic therapy in preventing vertical transmission is one of them is HIV viral load test. This test measures the amount of HIV virus in the blood. Measurement of HIV RNA in the blood can directly know the magnitude of viral replication. HIV Ribonucleic acid (RNA) can be measured by examination of Polymerase Chain Reaction (PCR).[8] In this study of HIV RNA PCR performed when infants 3-18 months old baby. Virological tests using PCR is an option, in infants with less than 18 months of age. This is because that at that age is an antibody, the bias will produce numbers. Because at that age infants still carries antibodies from the mother's immunoglobulin G (IgG) because this antibody has a molecular weight that can penetrate the placenta barrier. So in this age range most appropriate PCR to detect the transmission or not.[9,10,11] Constraints in the field led to a lack of data regarding the success of the PMTCT program at the Dr. Soetomo hospital. Research on the effectiveness of antiretroviral therapy in pregnant women with HIV who measured the expression of HIV-1 RNA of infants aged 3 to 18 this month, is expected to complete the data so that it helps decrease the success rate of vertical transmission. On this basis, the research was conducted.

MATERIALS AND METHODS

In this study we used the analytic observational methods. The research was conducted at the Intermediate Care Unit and Infectious Diseases (UPIPI), Department and Laboratory Medicine Clinical Pathology dr. Soetomo Hospital Surabaya from March until May 2012. The population in this study were all infants aged 3-18 months born to mothers with HIV who received antiretroviral therapy and is registered as a patient in poly UPIPI PMTCT dr. Soetomo hospital began in January 2004 December 2011. The samples were all infants aged 3-18 months born to mothers with HIV (+) who received antiretroviral therapy and PMTCT patients registered in hospitals UPIPI Outgoing Clinic dr. Soetomo hospital began in January 2004 - December 2011. We distinguish the samples into two infants aged 3-18 months who have had the results of HIV-1 RNA before and we will do an HIV-1 RNA at this time. This study used purposive sampling techniques of population studies affordable. Sample size was calculated based on the hypothesis test for two groups of the population proportion and a minimum number of samples obtained 29. Inclusion criteria: infants aged 3-18 months who are registered as patients and UPIPI outgoing clinic children born to mothers with HIV with antiretroviral treatment history of the Signed a Voluntary Counselling dr. Soetomo Hospital and Testing (VCT) and informed consent to participate in the study. Exclusion criteria: missing data and does not carrying on any medical record. End of test criteria: acquired damage to the blood samples that can not be processed further.

Sampling was carried through as many as 3 cc of venous blood and performed using sterile technique and

making the most of small needles and disposable. Blood specimen is inserted in a sterile vacutainer without anticoagulant K2EDTA/K3EDTA and whipped back and forth about 10 times and should not be frothy. Specimen tube sentifus mess around with the speed at 3000 rpm for 5-15 mins or 1500x g for 20 min at room temperature. Serum or plasma separated with sterile pipettes into a sterile tube by using gloves. Specimens are stored in a temperature of -20 C. RNA PCR using the Cobas Amplicor study of HIV-1 Monitor Test version 1.5 with the detection range 400-750000 HIV-1 RNA copies/ml.

The hypothesis of this study is the expression of HIV-1 RNA of infants aged 3 to 18 months is lower when administered antiretroviral therapy during pregnancy the mother is less than or equal to 28 weeks and the expression of HIV-1 RNA of infants aged 3 to 18 months was higher when treatment is given as maternal age over 28 weeks. The research data are recorded in the data collection form designed specifically for this study. Based on the objectives to be achieved then the processing and data analysis done with descriptive statistics and analytical with the computer program SPSS for Windows. In answer to the study hypothesis conducted Chi-square test statistic. Conduct feasibility obtained from the ethics commission for basic and clinical research in Dr. Soetomo Hospital Surabaya/Faculty of Medicine, University of Airlangga Surabaya.

RESULTS AND DISCUSSIONS

The overall population of 75 and a total sample of 35 with 2 samples included in the exclusion criteria because of incomplete data, so the sample size of 33. Table 1 indicates that the number of 14 (42.42%) HIV-1 RNA expression of infants aged 3-18 months to get a history of providing ARV therapy to pregnant mothers at the age of less than or equal to 28 weeks. At the beginning of ARV during pregnancy mothers over 28 weeks found the number 19 (57.58%) HIV-1 RNA expression is undetectable.

The age of pregnant women living with HIV an average of 27.12 ± 4.878 is the age of the youngest 17 years old and the oldest was 37 years old. Body Mass Index (BMI) we can not include data about the height because of incomplete so that only the weight of data being reported. Average body weight of pregnant women with HIV is 50.5 ± 9.8051 with the smallest weight was 29.5 kg and the largest is 70.0 kg. Birth weight on average was 2889.39 ± 334.887 with the lowest birth weight 2200 g and the largest is 3800 grams (Table 2).

Most maternal in the groups of CD4 = 200 cells copies/ml as much as 69.7%. Most are on stage as much as 51.52% stage 1, the regularity of drug taking by 81.82% are in regular groups. Mode of delivery by Caesarean section at most 93.94% and 93.94% of birth weight babies are at = 2500 g group (Table 3).

This study showed that there was no difference in the expression of HIV-1 RNA of infants aged 3 to 18 months based on the current provision of antiretroviral therapy in pregnant women with HIV in Dr. Soetomo hospital Surabaya from January 2004 to December 2011. The results contradict the hypothesis that there is. We tried to analyze this phenomenon by showing table 3.

The results of the highest maternal immune status was = 200 cells/mm3 (69.7%). Stadium is the largest of the lightest stage which is stage 1 (51.52%), most pregnant women living with HIV also take medication on a regular basis (81.82%), the way of labor is highest in Caesarean section (93.94%) and infants Most were born in the weight = 2500 grams (93.94%). Proportion of the existing data indicate that most pregnant women with HIV are in good condition the immune status, stage light, and alignment with the program that runs the Ministry of Health, 2004 and WHO 2006.[12,13] So it is not surprising that all samples show babies of HIV-1 RNA expression was undetected. Analysis of undetected HIV-1 RNA expression, we deepened by linking variable maternal immune status, disease stage and type of treatment regimen with the current administration to determine the role of undetected HIV-1 RNA in the samples.

No significant relationship found between immune status and the current provision of antiretrovirals (p = 0.084). Yet according to MOH recommendations 2004 and WHO 2006 when the provision of therapy depends on the stage and maternal immune status 12.13. However, the above table shows that there is alignment with the program CD4 <200 cells/mm3 largely began therapy at age = 28 weeks pregnant by 7 (21.21%) and CD4 = 200 cells/mm3 pregnancy begins at age> 28 weeks at 16 (48.49%). Presumably this could explain the undetected HIV-1 RNA expression in our samples. (Table 4).

There was relationship between the determination of a very meaningful time of therapy and disease stage (p = 0.001). Stage 1 begins when the drugs most women age> 28 weeks at 15 (45.45%), while stages 3 and 4 most of antiretrovirals started at age = 28 weeks pregnant at 5 (15.15%) and 7 (21.21 %). This is in accordance with the program, that the advanced-stage

HIV drugs are started at an early gestational age (Table 5).

There was relationship between the time had no meaning and types of ARV therapy regimen (p = 0.057), whereas it should depend on the type of regimen when treatment is given. When the regimen given at = 28 weeks gestation given the nature of therapeutic treatment consists of three different drugs (Highly Active Antiretroviral Therapy/HAART). When the regimen is given as gestation> 28 weeks of the therapy given is prolifactive consist of 1 or 2 different regimens alone.[12,13] Although there is no meaningful relationship but, from the above table types 1 and 2 different regimens, the largest being in the group of> 28 weeks of 9 (27.27%) and 3 (9.09%). Regimen consisting of 3 kinds of medicine were also highest in the group of antiretroviral drugs were started at age = 28 weeks pregnant by 11 (33.33%) (Table 6).

Table 1.Tabel between the variable expression of HIV-1 RNA as a baby and the mother of ARV

HIV-1 RNA expression infants	Maternal ARV begins at age = 28 weeks gestation	Maternal ARV begins at age > 28 minggu gestation
Detected	0	0
Undetected	14 (42.42%)	19 (57.58%)

Table 2. Table distribution characteristics of pregnant women with HIV and their babies

Categories	Mean	Minimum	Maximum	Deviation Standard	Total
Mother's Age (years old)	27.12	17	37	4.878	33
Mother's Weight (kgs)	50.500	29.5	70.0	9.8051	33
Infant's Weight (grams)	2889. 39	2200	3800	334.887	33

Table 3. Overview of HIV pregnant women and their babies with the HIV-1 RNA expression was detected which is distinguished by current antiretroviral therapy

Categories	Undetected HIV-1 RNA expression		Total
	Maternal ARV begins at = 28 weeks gestational age	Maternal ARV begins at > 28 weeks gestational age	
Mother:			
CD4:			
< 200 cells/mm3	21.21%	9.09%	30.3%
= 200 cells/mm3	21.21%	48.49%	69.7%
Stage:			
Stage 1	6.06%	45.46%	51.52%
Stage 2	15.15%	6.06%	21.21%
Stage 3	21.21%	6.06%	27.27%
Meidcation adherence:			
Regular	33.33%	48.49%	81.82%
Irregular	9.09%	9.09%	18.18%
Regiment:			
1 type	6.06%	27.27%	33.33%
2 types	3.03%	9.09%	12.12%
3 types	33.33%	21.22%	54.55%
Mode of deliver			
Caesarian sectio	36.36%	57.58%	81.82%
Per vaginam	6.06%	0%	
Infants:			
Birth Weight:			
< 2500 grams	0%	6.06%	6.06%
= 2500 grams	42.42%	51.52%	93.94%

Table 4. Table of variable immune status before mothers are given antiretroviral therapy and the time of ARV

Immune status of the mother / CD4 (cells/mm3) prior to ARV therapy is given.	Undetected HIV-1 RNA infants expression		P Value
	Maternal ARV begins at = 28 weeks gestational age	Maternal ARV begins at > 28 weeks gestational age	
< 200	7(70%*; 21.21%**)	3(30%*; 9.09%**)	0.084
= 200	7(30.43%*; 21.21%**)	16(69.57%*; 8.49%**)	

((*)the percentage of CD4 views of one group pre-treatment, (**) seen from the overall percentage of CD4 pre-therapy group)

Table 5. Table of variable disease stage of HIV pregnant women before ARV therapy and the time of ARV

HIV stage whenstarting ARV	Undetected HIV-1 RNA infant expression		P Value
	Maternal ARV beginsat = 28 weeks gestational age	Maternal ARV begins at >28 weeks gestational age	
Stage 1	2 (11.76%*; 6.06%**)	15(88.24%*; 45.45%**)	0.001
Stage 2	5(71.43%*; 15.15%**)	2(28.57%*; 6.06%**)	
Stage 3	7(77.78%*; 21.21%**)	2(22.22%*; 6.06%**)	

((*)percentage seen from a group of HIV disease stage when treatment begins; (**) percentage visible from the entire group of pregnant women with HIV disease stage when treatment begins)

Table 6. Table of regiment type variable and maternal ARV provision time

Therapy Regiment	Undetected HIV-1 RNA expression infant		P Value
	Maternal ARV begins at age = 28 weeks gestation	Maternal ARV begins at age > 28 weeks gestation	
1 type	2(18.18%*; 6.06%**)	9 (81.82%*; 27.27%**)	P= 0.057
2 types	1 (25%*; 3.03%**)	3 (75%*; 9.09%**)	
3 types	11 (61.11%*; 33.33%**)	7 (38.89%*; 21.22%**)	

((*) percentage of one group viewed ARV regiment; (**) percentage of the total group visits ARV regiment)

CONCLUSION

The expression of HIV-1 RNA in infants aged 3 are similar to that in infants aged 18 months. It is suggested that this study should be followed up prospectively, especially for infant diagnosed using antibody examination.

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