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# Triple antiretroviral therapy effectively eliminates HIV transmission from mother to child

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**Abstract :** Introduction: HIV transmissions can be reduced to a very low value by managing patient accurately. Every centers have modified their own standardized regimen for antiretroviral therapy.
Aim: To determine the HIV status after standardized triple antiretroviral therapy adapted in Haji Adam Malik Hospital.
Methods: This is an cohort-analytic study conducted in Haji Adam Malik hospital. Medical records of HIV-positive mother who delivered at Haji Adam Malik Hospital, starting in 2009-2014 were collected. They were all being given standardized antiretroviral therapy adapted in Haji Adam Malik Hospital. Diagnosis of HIV in children under the age of 18 months were done by PCR (Polymerase Chain Reaction). If the child has been aged ≥ 18 months, the method of diagnosis is Rapid Test.
Results: Of the 60 children examined, 11 children were aged <18 months and require PCR tests, while 49 others children were tested using rapid test. Of all children who tested PCR, no virus were detected. Similarly, in the examination of 49 children with a rapid test, all showed negative results.
Conclusion: The triple antiretroviral was effectively prevented the HIV transmission from mother to child.
**Keywords :** HIV, antiretroviral, transmission, pregnancy, fetal

## Introduction

UNAIDS estimates there are 35.9 to 44.3 million people living with HIV in worldwide. This number is growing about 15,000 patients per day.[1] The number of patients in South Asia and Southeast Asia are estimated at around 7.4 million in 2005. In Indonesia, HIV infection incidence has been increasing since 1999. In 2002, Data of Ministry of Health of Indonesia showed 90,000 and 130,000 cases of HIV infection. The amount is certainly still very far from the real number.[2]

Almost half of the 42 million people living with HIV are women of reproductive age. In addition, more than 2 million HIV-infected are pregnant womena and up to 90% of them are in developing countries, especially in Africa. The highest incidence of HIV infection are in East and Southern Africa.[3]

Transmission from mother to child can occur through intrauterine, intrapartum and during breastfeeding. The incidence of children with HIV was 330,000 in 2011, doubling of incidence in 2003, but 24% lower than the peak of 570,000 cases in 2009. PMTCT (Prevention of Mother to Child Transmission), can reduce transmission up to 90% using antiretroviral therapy (ART) for pregnant women and newborn child.[4]

Highly effective antiretroviral therapy (HAART) during pregnancy can reduce the HIV-1 MTCT rate to as low as 1% -2%, even in developing countries, and is now recommended for prevention of mother to child transmission (PMTCT) by the World Health Organization.Highly effective antiretroviral therapy (HAART) during pregnancy can reduce the HIV-1 MTCT rate to as low as 1%–2%, even in developing countries, and is now recommended for prevention of MTCT (PMTCT) by the World Health Organization.[5]

Haji Adam Malik Hospital is the center for HIV-positive pregnant women who were referred from various hospitals in Sumatera region. Treatment for HIV-positive pregnant women need a comprehensive collaboration between fetomaternal division with HIV unit that established since 2012. The goal for this program is to ensure patient received antiretroviral therapy, give education about the disease (omit breastfeeding, prefer caesarean section), prevent HIV transmission, and take back infant for follow up after the age of 18 months. The main problems encountered were patients came to hospital during active stage of labor. Mostly delivery occurred before the schedule date, which brought the need of emergency cesarean section. Then, after birth, only about 30% of these babies were coming regularly until the age of 18 months for follow up.

## Methods

This is an cohort-analytic study conducted in H. Adam Malik hospital. Medical records of HIV-positive mother who delivered at Haji Adam Malik Hospital, starting in 2009-2014 were collected.

In this study, will be investigated how the child's HIV status after a standardized antiretroviral therapy Haji Adam Malik Hospital. There are four drug regimen given to pregnant women. The first regimen: tenofovir, lamivudine, nevirapine with contraindications for patients with kidney disorders. The second regimen: tenofovir, lamivudine, efavirenz, preferably in patients with tuberculosis or central nervous system disorders. Three regimens: zidovudine, lamivudine, and nevirapine with contraindications anemia (Hb <10 g/dL) and CD4+ above 250/$mm^3$. Four regimens: zidovudine, lamivudine, and efavirenz. The first and second regimens given 2 times daily while the third and fourth regimen given 4 times daily. Cotrimoxazole is given to patients with CD4+ less than 200/$mm^3$. Newborns are given zidovudine to 6 weeks.

Diagnosis of HIV in children under the age of 18 months were done by PCR (Polymerase Chain Reaction). PCR was conducted in the laboratory Prodia Medan because Haji Adam Malik Hospital not have facilities for PCR. If the child has been aged ≥ 18 months, the method of diagnosis is rapid test.

## Results

There were 60 HIV-positive data that eligible for this study. Author collected blood samples from all infants from HIV-positive mothers in their visit to the hospital for follow up. The rest who did not show up were phoned and being asked to come for follow up. All the babies are not breastfed. Of the 60 infants, only three were born by spontaneous vaginal delivery. All babies born with normal weight (> 2500 g) and average 3164.5 ± 238.8 g.

**Table 1. Characteristics of newborns from HIV-positive mothers**

| Newborn characteristics | n | % |
|---|---|---|
| Gender | | |
| Male | 29 | 48.3 |
| Female | 31 | 51.7 |
| Mode of delivery | | |
| Vaginal | 3 | 0.05 |
| Abdominal | 57 | 0.95 |

Of the 60 children examined, 11 children were aged <18 months and require PCR tests, while 49 others children were tested using rapid test. Of all children who tested PCR, no virus were detected. Similarly, in the examination of 49 children with a rapid test, all showed negative results.

**Table 2. HIV test results of newborns**

| HIV test | n | % |
|---|---|---|
| PCR in children <18 months (n=11) | | |
| Virus detected | 0 | 0 |
| No virus detected | 11 | 100 |
| Rapid test in children ≥18 months (n=49) | | |
| Positive | 0 | 0 |
| Negative | 49 | 100 |

## Discussion

Tenofovir disoproxil fumarate (TDF) is a potent nucleotide analogue reverse transcriptase inhibitor (NRTI) that has excellent efficacy and tolerability profiles.[6]Baroncelli et al. (2009) did not find any obstetrics and fetal outcomes in pregnant women who received tenofovir.[7]Nevirapine is a HIV-1 specific non-nucleoside reverse transcriptase inhibitor that binds directly to the viral reverse transcriptase of HIV-1 to block polymerase activity by causing disruption of the enzymes catalytic site.[8]Lamivudine is a nucleoside reverse transcriptase inhibitor that is widely used for the treatment of HIV-1 infection in combination with other antiretrovirals. It is a highly effective agent that can be dosed once or twice daily due to its long intracellular half-life.[9]Efavirenz is a non-nucleoside reverse transcriptase inhibitor that in most treatment guidelines is recommended to be taken combined with two nucleoside analogue reverse transcriptase inhibitors.[10]After GS903 study showed that in 144 weeks comparison between tenofovir vs stavudine (plus lamivudin and efavirenz, 71 of 86 (83%) patients originally randomized to efavirenz plus tenofovir and lamivudine had VL of <400 copies/mL and 69/86 (80%) had a VL of <50 copies/mL, the regimen was being switched from stavudine to tenofovir (plus efavirenz and lamivudine) also showed maintained virological suppression and continued CD4 cell increases over 144 weeks.[11]Zidovudine is a nucleoside transcriptase inhibitor that compete with the endogenous nucleotides at the catalytic, i.e., substrate-binding, site of RT and are incorporated into the elongating proviral deoxyribonucleic acid (DNA) strand.[12]

The four line regimens are the same regimen as adapted bycurrent WHO guidelines recommendation: tenofovir + 3TC + nevirapine, tenofovir/FTC + nevirapine, tenofovir + 3TC + efavirenz, and tenofovir/FTC/efavirenz. The first regimen: tenofovir, lamivudine, nevirapine with contraindications for patients with kidney disorders. However, tenofovir + 3TC + nevirapine regimen showed high rates of failure in the latest study. Lapadula et al. have reported that regimens consisting of tenofovir, emtricitabine, and nevirapine are associated with a risk of early virologic failure in antiretroviral-naive, HIV-infected patients.The second regimen: tenofovir, lamivudine, efavirenz, preferably in patients with tuberculosis or central nervous system disorders. Three regimens: zidovudine, lamivudine, and nevirapine with contraindications anemia (Hb <10 g/dL) and CD4+ above 250/$mm^3$. Four regimens: zidovudine, lamivudine, and efavirenz. The first and second regimens given 2 times daily while the third and fourth regimen given 4 times daily. Cotrimoxazole is given to patients with CD4+ less than 200/$mm^3$. Newborns are given zidovudine to 6 weeks.[14]

The current WHO recommended regimen is as follows: where the pregnant woman does not yet need to start ART for therapeutic reasons, she should start Zidovudine (AZT) from 28 weeks or as soon as possible thereafter, be provided with single-dose Nevirapine (NVP) when entering labour, and be given AZT + 3TC for one week following delivery. Meanwhile, whether the mother was on the above or standard ART, the child should be given single dose NVP immediately after delivery and daily AZT until one week old.[14]

In this study, both two groups of 11 children were aged <18 months with PCR and 49 children with rapid test showed negative HIV status.This rate is similar to less than 2% the developed world where PMTCT have access to comprehensive testing, and counseling services and treatment.[15]Although inadequate continuum of care is the one of main problem that first observed in this study, surprisingly, no newborn suffered from HIV.[16]Author strongly recommend this regimen adaptation to other clinical settings. Further study on the long term effects of the antiretroviral drugs is needed.

## Conclusion

The triple antiretroviral was effectively prevented the HIV transmission from mother to child.

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