## **OBSTETRICS**

# Prevalence of HIV Seropositive pregnant women and their vertical transmission rate at Srinagarind Hospital

Phuchong Phalaruk MD\*, Chuanchom Sakondhavat MD\*, Srinaree Kaewrudee MD\*, Pope Kosalaraksa MD\*\*, Kesorn Lao-unka B.Sc MSN\*, Bhussaba Bungrathok B.Sc\*.

\* Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand \*\* Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

#### ABSTRACT

- **Objectives:** To assess the prevalence of HIV infection in pregnant women and to study HIV vertical transmission at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. Khon Kaen, Thailand.
- **Materials and Methods:** The data of all known HIV seropositive women attending the antenatal clinic and giving birth at Srinagarind Hospital in Khon Kaen Province during 1999-2008 were collected from their medical records. The inclusion criteria were the HIV infected pregnant women who were enrolled to our Prevention of HIV Perinatal Transmission Program and received the antiretroviral drugs for the prevention of HIV perinatal transmission. Moreover, all of the newborns received only formula feeding and their peripheral blood were tested for HIV by PCR technique at 6 weeks and 6 months after birth and for HIV-antibody (Ab) by Enzyme Immunoassay (EIA) at 18 months. The infants were concluded to be HIV infected by either at least 2 positive PCR or a positive HIV-Ab. After delivery, both mother and baby would be followed up for 2 years.
- **Results:** From 1999-2008, there were 30,926 women attended antenatal clinic and giving birth at Srinagarind Hospital. There were 28,497 (92.64%) whom received pre-test counseling and HIV testing, 154 (0.54%) were HIV seropositive. Their average age was 27.87 years, 51(32.12%) were primigravida. The average gestational age at birth was 38.10 weeks, 43 (27.92%) of the patients were delivered by cesarean section because of obstetric indications. One hundred and four children were follow-up according to schedule. The overall vertical transmission rate was 4.80%.
- **Conclusion:** The prevalence of HIV infection in pregnant women at Srinagarind Hospital was 0.54% and the vertical transmission rate was 4.80%. Compared with the national statistics, our HIV prevalence and vertical transmission rate are lower. However, comprehensive perinatal HIV prevention programs to reduce the vertical transmission rate of HIV closely to zero might be possible in the near future.

**Keywords:** HIV, pregnancy, vertical transmission rate.

#### Introduction

Since 1981, 65 million people have been infected with Human immunodeficiency virus (HIV) and 25 million have died of Acquired immunodeficiency syndrome (AIDS) related illnesses. In 2006, 4.3 million new infections were reported, as were 2.9 million AIDSrelated deaths that more than in any previous year. Today 33 million people are living with HIV and half of them are women and girls<sup>(1)</sup>.

Around the world, more than 2 million children were living with HIV, of whom 1,000 die from AIDSrelated illness every day. There were nearly 1,500 new HIV infections in children under 15 years old everyday. The majority of these children acquired their infections as a result of mother-to-child transmission during pregnancy, labor or breastfeeding<sup>(1,2)</sup>. Breastfeeding appears to double the risk of HIV transmission when compared with non-breastfeeding baby. In both developed and developing countries, the risk of a baby acquiring the virus from an infected mother ranged from 15-35 percent in the absence of preventive measured<sup>(1)</sup>.

In Thailand, HIV infection among women attending antenatal care services steadily increased from 0.8 percent in 1991 to 2.3 percent in 1995 and has dropped substantially to 0.7 percent since 2008<sup>(1)</sup>. Antiretroviral drugs (ARVs) can reduce the viral load and the rates of mother to child transmission. We have seen the use of ARVs for prevention of vertical transmission become the national standard of care in Thailand. The number of children who become perinatally HIV infected is being reduced every year.

The efficacy of monotherapy and combination of ARVs prophylaxis treatments of different duration and different drugs has reduced the vertical transmission rates to around 1-10 percents<sup>(3)</sup>. However, the usage of ARVs to treat both adults and children in now becoming a possibility in Thailand, but until now, access to these drugs has been limited. Combination therapies that can save the lives of HIV infected infants and their parents are still expensive but no longer out of reach.

In our prevention of HIV Perinatal Transmission Programs at Srinagarind Hospital which have been developed to reduce HIV vertical transmission since 1995. The first regimen was modified ACTG 076, Zidovudine (ZDV) was given to HIV pregnant women starting on week 14-36 of gestation and continued throughout pregnancy following an ACTG 076 except that during labor, intravenous ZDV was replaced by oral ZDV 300 mg given every 3 hours as a loading dose and ZDV syrup 2 mg/kg every 6 hours for 1 week orally for the newborns. According to the preliminary report of Sakondhavat C, et al, this regimen could reduce vertical transmission rate from 25.5% to 5.2%<sup>(4,5)</sup>.

During 2002-2006, subsequent protocol was following program for HIV prevention and treatment 2 (PHPT2). ZDV 300 mg were given orally twice a day starting on week 28 of gestation and continued throughout pregnancy. In the intrapartum period, 300 mg of ZDV plus a single dose of Nevirapine (NVP) 200 mg were given orally at the onset of labor and then followed by 300 mg of ZDV every 3 hours until delivery. Single dose NVP syrup 2 mg/kg and ZDV syrup 2 mg/ kg were given orally for the newborns as soon as possible after birth and every 6 hours for one week. Moreover, ZDV and 3TC were given to the mother for one week after giving birth for prevention of drug resistance. PHPT2 can reduce the vertical transmission rate to 2.3%<sup>(6-8)</sup>.

Highly active antiretroviral therapies (HAART) regimen, two drugs from Nucleoside Reverse Transcriptase Inhibitors group plus one drug from Non Nucleoside Reverse Transcriptase Inhibitors group or one drug from Protease Inhibitors group (ZDV + 3TC + NVP or ZDV + 3TC + PI) was introduced since 2006. ARVs were given starting on either week 14 or week 28 of gestation depended on the pregnant women's CD4 counts, if CD4 was below 250 cells/mm<sup>3</sup>, the treatment began at 14 weeks' gestation. If CD4 was 250 cells/mm<sup>3</sup> or more, the treatment stated at 28 weeks' gestation and continued throughout pregnancy. intrapartum and postpartum period (if NVP was provided). The newborns were given single dose NVP syrup 2 mg/kg plus ZDV syrup 2 mg/kg every 6 hours for one week. The latest regimen has ever been reported to be able to reduce vertical transmission rate to lower than 2%<sup>(9)</sup>. HAART regimen is used until present.

The objective of this study was to assess the prevalence of HIV infection in pregnant women and their vertical transmission rate at 18 months at Srinagarind Hospital.

#### **Material and Methods**

The study design was a retrospective descriptive study and was approved by the Ethics Committee at the Faculty of Medicine, Srinagarind Hospital, Khon Kaen University. The data of all known HIV seropositive pregnant women attending the antenatal clinic and giving birth at Srinagarind Hospital and their babies attending neonatal clinic during 1999-2008 were collected from their medical records.

The inclusion criteria were the HIV infected pregnant women who were enrolled to our Prevention of HIV Perinatal Transmission Program and received antiretroviral drugs for the prevention of HIV perinatal transmission. Moreover, all of the newborns received only formula feeding and their peripheral blood were tested for HIV by PCR technique at 6 weeks and 6 months after birth and for HIV-Ab by Enzyme Immunoassay (EIA) at 18 months. The infants were concluded to be HIV infected by either at least 2 positive PCR or a positive HIV-Ab. After delivery, both mother and baby would be followed up for 2 years. Babies with gestational age less than 24 weeks or birthweight less than 600 g were excluded from the study. The informed consent was obtained and HIV test was performed after pre-test counseling. ARVs were given to all seropositive

pregnant women for prevention of perinatal HIV transmission. In terms for ARVs used were modified ACTG 076, PHPT2 and HAART regimen respectively.

The data was analyzed using Microsoft Excel 2003 and Stata10 (Max, Min, Average, Mode, Median, count, percent).

#### Result

From 1999-2008, there were 30,926 women attended antenatal clinic and delivered at Srinagarind Hospital. There were 28,497 (92.64%) whom received pre-test counseling and HIV testing, 154 (0.54%) were HIV seropositive. Their mean age was 27.87 years, 51 cases (33.12%) were primigravida. Fifty cases (32.47%) had previously abortion, 5 cases (3.57%) had HBV co-infection and 4 (3.05%) were positive Venereal Disease Research Laboratory (VDRL). The mean gestational age at birth was 38.10 weeks, 43 cases (27.92%) were delivered by cesarean section because of obstetric indications (Table 1). The mean birthweight was 2,906.33 g and their mean APGAR scores were 8.43 and 9.71 at 1 and 5 minutes, respectively (Table 2). There were 104/154 (67.53%) children coming to follow-up on schedule, 14 from modified ACTG 076 group, 57 from PHPT2 group and 33 from HAART group. The overall vertical transmission rate was 4.80% (5/104). Seven percent (1/14) was infected in modified ACTG 076 group, 7.02% (4/57) was diagnosed in PHPT2 group and no one was diagnosed HIV seropositive in HARRT group (Table 3).

| Total                | HIV         |  |  |
|----------------------|-------------|--|--|
|                      | N=154       |  |  |
| Maternal age (years) |             |  |  |
| Max                  | 40          |  |  |
| Min                  | 18          |  |  |
| Mean                 | 27.87       |  |  |
| Gravidarum           |             |  |  |
| Primigravidarum      | 51(33.12%)  |  |  |
| Multigravidarum      | 103(66.88%) |  |  |
| Previous abortion    | 50(32.47%)  |  |  |

| Table 1. | Maternal | characteristics |
|----------|----------|-----------------|
|----------|----------|-----------------|

#### Table 1. Maternal characteristics (cont.)

| Total                       | HIV         |  |  |
|-----------------------------|-------------|--|--|
|                             | N=154       |  |  |
| Mean times of attending ANC | 8.98        |  |  |
| HBV                         |             |  |  |
| HBV testing                 | 140(90.91%) |  |  |
| Positive                    | 5(3.57%)    |  |  |
| VDRL                        |             |  |  |
| VDRL screening              | 131(85.06%) |  |  |
| Reactive                    | 4(3.05%)    |  |  |
| Mean GA at birth (wk)       | 38.10       |  |  |
| Delivery                    |             |  |  |
| Vaginal                     | 111(72.08%) |  |  |
| Cesarean section            | 43(27.92%)  |  |  |

GA = Gestational age

#### Table 2. Neonatal characteristics

| Total                | HIV        |  |
|----------------------|------------|--|
|                      | N=154      |  |
| Mean birthweight (g) | 2,906.33   |  |
| APGAR score at       |            |  |
| 1 minutes            | 8.43       |  |
| 5 minutes            | 9.71       |  |
| Fetal gender         |            |  |
| Male                 | 78(50.65%) |  |
| Female               | 76(49.35%) |  |

#### Table 3. Perinatal outcomes at 18 months

|                           | Number  | Modified ACTG 076 | PHPT 2 group | HAART group |
|---------------------------|---------|-------------------|--------------|-------------|
|                           |         | group             |              |             |
| Total children            | 154     | 32                | 82           | 40          |
| (%)                       | (100)   | (20.78)           | (53.25)      | (25.97)     |
| Follow-up children        | 104     | 14                | 57           | 33          |
| (%)                       | (67.53) | (43.75)           | (69.51)      | (82.50)     |
| HIV Vertical transmission | 5       | 1                 | 4            | 0           |
| (%)                       | (4.80)  | (7.14)            | (7.02)       | (0.00)      |

#### Discussion

According to Joint United Nations Program on HIV/AIDS (UNAIDS), Thai people in reproductive age (15-45 years) living with HIV was 0.9-2.1%, especially young women in 15-24 year (0.4-2.0%)<sup>(1)</sup>, which was compatible with Thai annual epidemiological surveillance report 2008, more than 2/3 of women living with HIV were in reproductive age<sup>(2)</sup>. The prevalence of HIV infection in pregnant women of this study was 0.54%, it is lower when compared to the national rates.

ARVs treatment of infected women during pregnancy, intrapartum and infants during the early postnatal period has been shown to significantly reduce perinatal HIV transmission rate. Modified ACTG 076 which ZDV was given to mothers and to babies significantly reduced HIV infection in babies at 18 months (vertical transmission rate 6.3% compare to our study 7.14%)<sup>(6)</sup>. PHPT2, HIV infected mothers received ZDV in the third trimester of pregnancy and babies received one week of ZDV therapy, a single dose of nevirapine (NVP) was then given to mothers in labor and to their babies soon after birth reduced. HIV vertical transmission rates to 2.3% (compare with our study 7.02%)<sup>(8)</sup>. HAART regimen's group, HIV infected mothers were receiving combination of 3 antiretroviral drugs during pregnancy and postpartum period and babies were receiving one week of ZDV and single dose of NVP, HIV-vertical transmission rates were 1-3% compare to our study, no newborn in this study was diagnosed HIV infection and may be the most effective method<sup>(9)</sup>. Nevertheless, in our study, an evaluation of various antiretroviral drugs give to HIV infected mothers and during labor with the same drugs given to their babies after birth, ZDV versus ZDV plus NVT did not result in significant difference in HIV vertical transmission rates at 18 months. Moreover, it was found that the overall vertical transmission rate was slightly lower (4.8%) when compared to the results of Sakondhavat et al's study (5.2%) undertaken in 1996-99 and also lower than the national vertical transmission rate (9-10%)<sup>(1,2)</sup>. Follow-up of children and fetal outcomes gradually improved over a decade, this shown effectiveness of our prevention program.

Prophylactic antiretroviral drugs seem to be effective and feasible in preventing HIV vertical transmission in our setting. We strongly advised not to breastfeed, all of the newborns received formula feeding. However, better outcomes could be expected if HIV sero-status were known for all childbearing women planning to become pregnant or at least for all pregnant women in the first trimester.

#### Conclusion

The prevalence of HIV infection in pregnant women at Srinagarind Hospital, Faculty of Medicine Khon Kaen University was 0.54%, and the vertical transmission rate at 18 months was 4.80%. Both are lower than the national rates. Comprehensive perinatal HIV prevention programs to reduce the vertical transmission rate of HIV closely to zero may be possible in the near future.

#### Acknowledgement

The authors would like to thank Faculty of Medicine, Khon Kaen University for the financial support of the research project. We also wish to thank all HIV infected pregnant women and staff members of the Division of Reproductive Health, Department of Obstetrics and Gynecology, Srinagarind Hospital.

#### References

- 1. UNAIDS. 2008 Report on the global AIDS epidemic. Mexico, UNAIDS. 2008:30–62.
- Ministry of Public Health. Annual report 2008: Annual Epidemiological Surveillance Report 2008. Bangkok : Thai veterans Publisher:77–86.
- Brocklehurst P. Interventions for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD000102. DOI: 10.1002/14651858. CD000102.
- Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med. 1994; 331:1173-80.
- Sakondhavat C, Kiatchooskul P, Kosalaraksa P, Intarakamhaeng S, Thinkhamrop J, Pinitsoomtorn P, et al. Prevention of HIV Transmission from Mother-to-child in Srinagarind hospital. J Med Assoc Thai 2001;84:1460– 66.

- Eshleman SH, Guay LA, Mwatha A, Brown E, Musoke P, Mmiro F, et al.. Comparison of mother-to-child transmission rates in Ugandan women with subtype A versus D HIV-1 who received single-dose nevirapine prophylaxis: HIV Network For Prevention Trials 012. J Acquir Immune Defic Syndr. 2005; 39:593-7.
- 7. Cressey TR, Jourdain G, Lallemant MJ, Kunkeaw S, Jackson JB, Musoke P, et al. Persistence of nevirapine exposure during the postpartum period after intrapartum single-dose nevirapine in addition to zidovudine prophylaxis for the prevention of mother-to-child transmission of HIV-1. J Acquir Immune Defic Syndr.

2005;38:283-8.

- Lallemant M, Jourdain G, Le Coeur S, Mary JY, Ngo-Giang-Huong N, Koetsawang S, et al. Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. N Engl J Med. 2004;351:217-28.
- Volmink J, Siegfried N, van der Merwe L, Brocklehurst P. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD003510. DOI: 10.1002/14651858.CD003510.pub2.

# ความชุกของการติดเชื้อเอชไอวีในสตรีตั้งครรภ์และอัตราการติดเชื้อจากมารดาสู่ทารก ในโรงพยาบาล ศรีนครินทร์

### ภุชงค์ ผลารักษ์, ชวนชม สกนธวัฒน์, ศรีนารี แก้วฤดี, ภพ โกศลารักษ์, เกสร เหล่าอรรคะ, บุษบา บุญกระโทก

**วัตถุประสงค์** : เพื่อศึกษาความชุกของการติดเชื้อเอชไอวีในสตรีตั้งครรภ์และอัตราการติดเชื้อจากมารดาสู่ทารก ในโรงพยาบาลศรี นครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น

**วิธีการวิจัย** : ใช้วิธีการสืบค้นประวัติและเก็บรวบรวมข้อมูลสตรีตั้งครรภ์ที่ติดเชื้อเอชไอวีที่มาฝากครรภ์และคลอดในโรงพยาบาลศรี นครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น ในช่วงปี พ.ศ. 2542-51 โดยเลือกสตรีตั้งครรภ์ที่เข้าโครงการการป้อง กันการติดเชื้อเอชไอวีจากมารดาสู่ทารก คือมารดาได้รับยาต้านไวรัสขณะตั้งครรภ์ ระหว่างคลอด และหลังคลอด บุตรได้รับยาต้านไวรัส หลังคลอดร่วมกับการงดดื่มนมมารดา รวมทั้งได้รับการตรวจเลือดเพื่อยืนยันการติดเชื้อเอชไอวี ด้วยวิธีพีซีอาร์ ที่อายุ 6 สัปดาห์และ 6 เดือน และตรวจหาภูมิต้านทานต่อเชื้อเอชไอวีเมื่ออายุ 18 เดือน หากผลการตรวจเป็นผลบวก 2 ครั้ง แสดงว่ามีการติดเชื้อเอชไอวี ทั้ง มารดาและบุตรจะได้รับการติดตามการรักษาอย่างต่อเนื่องเป็นเวลา 2 ปี

**ผลการวิจัย** : สตรีตั้งครรภ์ที่มาฝากครรภ์และคลอดในโรงพยาบาลศรีนครินทร์ ในระหว่างปี พ.ศ. 2542-51 มีจำนวนทั้งหมด 30,926 คน ได้รับการตรวจหาร่องรอยการติดเชื้อเอซไอวี จำนวน 28,651 คน (ร้อยละ 92.64) พบว่ามีสตรีตั้งครรภ์ ที่ติดเชื้อเอซไอวีทั้งหมด 154 คน (ร้อยละ 0.54) สตรีเหล่านี้มีอายุเฉลี่ย 27.87 ปี เป็นการตั้งครรภ์ครั้งแรก 51 คน (ร้อยละ 33.12) อายุครรภ์เฉลี่ย 38.10 สัปดาห์ อัตราการผ่าตัดคลอดบุตรทางหน้าท้องด้วยข้อบ่งชี้ทางสูติศาสตร์ จำนวน 43 คน (ร้อยละ 27.92) มีเด็กที่มาตรวจติดตามการรักษา 104 คน พบอัตราการติดเชื้อจากมารดาสู่ทารก จำนวน 5 คน (ร้อยละ 4.80)

**สรุป**: พบความซุกของการติดเซื้อเอซไอวีในสตรีตั้งครรภ์ ที่มาฝากครรภ์และคลอดในโรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น ร้อยละ 0.54 มีอัตราการติดเชื้อจากมารดาสู่ทารก ร้อยละ 4.80 ผลการศึกษาวิจัยนี้เมื่อเทียบ กับการศึกษาระดับซาติพบว่ามีอัตราที่ต่ำกว่า จึงมีการคาดหวังว่าการให้ยาต้านไวรัสในอนาคตอาจทำให้อัตราการติดเซื้อจากมารดา สู่ทารกลดลงจนเกือบเป็นศูนย์