Rapid Human Immunodeficiency Virus Diagnostic Test During the Intrapartum Period in Pregnant Women Who Did Not Receive Antenatal Care

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Abstract

The main barrier to implementation of antiretroviral drugs in HIV-infected pregnant women is the lack of antenatal care (ANC). From April 1999 to December 2001, the prevalence of pregnant women not receiving ANC and coming for delivery in Siriraj Hospital was 7.3 per cent (2,152/29,484) and the prevalence of HIV infection among this group was 5.7 per cent, substantially higher than that of 27332 pregnant women receiving ANC in Siriraj Hospital (2.2%). Besides developing interventions to increase use of ANC, the test for diagnosis of HIV infection during the intrapartum period should be rapid, inexpensive, highly sensitive and specific, easy to perform and results should be easy to interpret. The Determine Rapid Test for detection of HIV fulfills these criteria with 100 per cent sensitivity, 99.85 per cent specificity, 97.54 per cent positive predictive value, 100 per cent negative predictive value and 0.14 per cent false positive. To improve prevention of mother-to-child HIV transmission (PMTCT), the authors believe that this uncomplicated rapid HIV testing should be used during the intrapartum period to Thai-pregnant women who did not receive antenatal care and antiretroviral drugs might be offered as soon as possible for those testing HIV-positive and for their baby as chemoprophylaxis.

Key word : The Determine Rapid Test, Standard HIV Testing, Prevention of Mother-to-Child HIV Transmission (PMTCT)

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The use of zidovudine (ZVD) from 36 weeks' gestation until delivery has been found to reduce the risk of mother-infant human immunodeficiency virus transmission by half, from 18.9 per cent to 9.4 per cent, when used with infant formula to replace breastfeeding[1]. In Thailand, this short-course ZVD regimen has been implemented in a pilot project in two regions, i.e, regions 7 and 10, by the Ministry of Public Health. Based on the experience and success of these projects, the Department of Health began recommending and supporting a program of antenatal voluntary counseling and testing, short-course ZVD, and infant formula for HIV-infected pregnant women in all provinces of Thailand in 2000. All HIV-infected pregnant women are given 300 mg ZVD twice daily from 34 weeks' gestation until onset of labor then every 3 hours until delivery. Babies born to HIV-infected mothers are offered ZVD treatment (2 mg/kg every 6 hours) for 4 weeks [2]. In 1999, a clinical trial in Uganda demonstrated that intrapartum and a neonatal single-dose of Nevirapine (NVP) was safe and effective in reducing mother-to-child transmission, approximately 50 per cent lower than among the group receiving an intrapartum and brief neonatal regimen of ZVD[3].

Currently, the Public Health Service Task Force of the United States recommends that intrapartum and newborn antiretroviral regimens be administered to reduce perinatal HIV transmission if a woman does not receive ZVD as a component of her antenatal antiretroviral regimen. They should be counseled that potent combination antiretroviral regimens have substantial benefit for their own health and may provide enhanced protection against perinatal transmission[4]. However, the main barrier to implementation is the lack of antenatal care. Many pregnant women are not known to have HIV infection and come to delivery without antenatal care. The Determine rapid screening for HIV infection performed on-site by a test that does not require laboratory infrastructure or highly skilled personnel can help identify non-antenatal care pregnant women who may be infected with the virus and can facilitate immediate counseling to help prevent the individual from spreading the virus to their children[5,6].

To improve prevention of mother-to-child HIV transmission (PMTCT), the authors believe that this uncomplicated rapid HIV testing should be used during the intrapartum period to Thai-pregnant women who had not received antenatal care and antiretroviral drugs might be offered as soon as possible for those with a positive result and for their baby as chemoprophylaxis. This study aimed to determine the prevalence of pregnant women delivering without antenatal care in Siriraj Hospital and the prevalence of HIV-infection in this group as well as to evaluate a new rapid diagnostic test, the Determine test (Abbott Laboratories, Abbott Park, Ill.), which detects anti-HIV-1 and anti-HIV-2 antibodies based on immunochromatography and permits rapid detection of HIV infection in pregnant women. The authors performed the test with Determine HIV-1/2 on whole-blood samples from pregnant women who had not received antenatal care and coming for delivery in a septic-labor room of the Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, to determine the sensitivity, specificity and clinical utility of this test.

MATERIAL AND METHOD

The study was designed as a descriptive study at Siriraj Hospital from April 1999 to December 2001.

Standard routine HIV testing

A total of 27,332 pregnant women attending antenatal care were counseled and tested for anti-HIV. All sera/plasma were screened with the first test (ELISA, AxSYM, Abbott, USA). A negative result was considered as negative. Based on the criteria of algorithm of HIV testing from the WHO recommendation in 1997[7], any reactive sample was further investigated with the second and third assays (ELISA, Vironostika, Organon, Belguim and gelatin particle agglutination (GPA, Fujirebio, Japan). A concordance reactive result was considered as positive. In order to avoid any technical errors, a second blood test was recommended.

Rapid HIV testing

During this 3-year period, 2,152 pregnant women who came for delivery without prior antenatal care were counseled and EDTA blood was bedside tested with the Determine rapid HIV-1/2 test (Abbott Laboratories, USA), which is an immunochromatographic nitrocellulose format and based on the sandwich immunoassay technique[5]. All blood samples were transported to the Department of Microbiology for standard HIV testing in parallel. Plasma was used for anti-HIV testing as described above. The sensitivity and specificity of the Determine rapid HIV-1/2 test were evaluated and compared with the

results of standard HIV testing. Briefly, 1 drop (50 μL) of whole blood is placed on the sample application pad, followed by the addition of 1 drop of buffer. If a sample contains anti-HIV-1 and anti-HIV-2 antibodies, the antibodies first react with the antigen-selenium colloid conjugates. As the antibody-antigen selenium colloid complex flows past the capture site, the antibodies react with the antigens at the site, with formation of a visible red line within 15 minutes which considered as reactive. The test also contains a procedure control site, which confirms with validity of the assay by the formation of a visible red line.

Results

During 1999-2001, the frequency of pregnant women delivering without antenatal care in Siriraj Hospital was 7.3 per cent (2,152/29,484). The prevalence of HIV infection among the 27,332 pregnant women attending ANC in Siriraj Hospital was substantially lower than that of 2,152 pregnant women without ANC (2.2% *versus* 5.7%)

Rapid test showed 100 per cent sensitivity for detection of HIV with 99.85 per cent specificity, 97.54 per cent positive predictive value, 100 per cent negative predictive value and 0.14 per cent false positive.

DISCUSSION

During antenatal care (ANC), HIV counseling and testing are becoming routine in some parts of the world, including Thailand. Short-course antenatal ZVD regimens are now being used to prevent perinatal transmission from HIV-infected mothers to their children. To use them, however, the HIV-infected mothers are recognized through the ANC process, In this study the authors found that the prevalence of pregnant women not receiving ANC and coming to delivery in a septic labor room of Siriraj Hospital was 7.3 per cent and 5.7 per cent of this group had HIV infection. That means that the lack of ANC is an important barrier to preventing perinatal HIV transmission.

Besides ANC promotion, a rapid diagnostic test for HIV infection during intrapartum would be beneficial. In addition, this test should be inexpensive, highly sensitive and specific, easy to perform and results should be easy to interpret. The Determine rapid test for detection of HIV fulfilled these criteria with 100 per cent sensitivity, 99.85 per cent specificity, 97.54 per cent positive predictive value, 100 per cent negative predictive value and 0.14 per cent false positive rate. Comparable to a recent report, which showed that Determine HIV-1/2 had a 100 per cent sensitivity and 100 per cent specificity for detection of HIV on whole blood, serum, and plasma and the results completely agreed with those of PA, the latex agglutination test and ELISA[5]. Moreover, another recent report showed the Determine test to be extremely sensitive and specific even with samples from patients in the advanced stages of the disease, when the immune system is severely compromised. Even patients with CD-4 counts less than 10 cells/mm^3 were positive by the Determine test[6].

In comparison to the standard ELISA, Determine HIV-1/2 has several advantages. Determine HIV-1/2 is rapid, since results are available 15 minutes after sample application and does not require

Table 1. The prevalence of anti-HIV positive pregnant women receiving ANC and not receiving ANC.

Pregnant Women	Year	Number	No. Anti-HIV Positive	
				%
ANC	1999	9,996	230	2.3
	2000	9,188	196	2.1
	2001	8,148	164	2.0
Total			590	2.2
Without ANC	1999	617	45	7.3
	2000	781	43	5.5
	2001	754	34	4.5
Total			122	5.7

Table 2. Sensitivity and specificity of the rapid anti-HIV test (Determine) on samples positive or negative for HIV-1 by standard HIV testing.

Rapid anti-HIV test	Anti-HIV samples*		Total
	Positive	Negative	
Reactive	119	3	122
Negative	0	2,030	2,030
Total	119	2,033	2,152

* Samples were performed with standard HIV testing as described in material and method.

any specific instrumentation or any skill for reading the result. The other methods, particle agglutination assays (PAs), are also widely used since they do not require complex instrumentation. However, the particle agglutination assays (PAs) need 2 hours to achieve results according to the manufacturer's instructions and therefore are not appropriate for rapid emergency use, such as in the intrapartum period in pregnant women who had not received ANC. It has been noted that with rapid tests, negative results can be given to the patient at the time of testing. Eliminating the prohibition of breastfeeding during rooming-in. Although a positive test result requires confirmation by another test or Western blotting, the patients can receive immediate feedback on the likelihood of infection with HIV and can receive counseling and management which can effectively reduce perinatal-HIV transmission[8-10]. In 1999, the HIVNET 012 trial showed about 12 per cent of children born to HIV infected mothers who were breastfed were infected at 6-8 weeks and 13 per cent at 14-16 weeks of life after intrapartum and neonatal single dose nevirapine, 200 mg of nevirapine at onset of labor and 2 mg/kg to the infant at 48-72 hours[3].

Several effective antiretroviral regimens have recently been recommended in the United States for HIV-infected women in labor who have not received prior antiretroviral treatment. These include: 1) single dose nevirapine (NVP) at the onset of labor followed by a single dose of NVP for the newborn at age 48 hours; 2) oral ZDV and 3TC during labor, followed by 1 week of oral ZDV/3TC for the newborn; 3) intrapartum intravenous ZDV followed by 6 weeks of ZDV for the newborn; and 4) two doses NVP regimens combined with intrapartum intravenous ZDV and 6 weeks of ZDV for the newborn[4]. In addition, ZDV or ZDV in combination with other retroviral drugs should be administered to the newborn as soon as possible after delivery if their mothers have received no antiretroviral therapy during pregnancy or intrapartum. Under these circumstances, combined antiretroviral drug regimens during the intrapartum period and to the newborn within 72 hours after birth may be beneficial[11]. Generally, diagnosis and counseling are the cornerstones of prevention and care strategies for HIV infected individuals. Moreover, effective public health surveillance is essential to track the spread of HIV pandemic, guide research needs, and provide a focus for prevention activities[12]. A major challenge to the diagnosis of HIV infection and surveillance activities in developing countries may be attributed to the fact that many clinics or point-of-care facilities in these areas are poorly equipped and often lack diagnostic capabilities or the equipment needed to perform a standard enzyme-linked immunosorbent assay (ELISA), particle agglutination assays (PAs) and confirmatory Western blotting to identify those infected with HIV. Also, the individuals must often travel long distances to reach a health care facility, and the chances that the person will travel back to the clinic to receive the results may be slim due to transportation hardships. Considering the current worldwide emergency and the spread of HIV, the limitation of the methods described above warrants a rapid, simple low-cost, sensitive and specific test for the detection of anti-HIV antibodies. Thus, screening of samples by the rapid assay could serve as first-line diagnostic support with follow-up by the secondary method only for samples that appear to be positive upon initial testing. Because these tests are completed within 15 minutes, the patient benefits from a rapid result. A

negative result can be given to the patient at the time of testing, eliminating the need for a return visit. With a positive result, the patient can receive counseling which encourages adoption of risk reducing behaviors.

Currently, the authors are planning to develop new clinical practice guidelines to improve the prevention of mother-to-child HIV transmission (PMTCT). The rapid test will be used during the intrapartum period with all pregnant women who did not receive ANC. A combined antiretroviral drug regimen will be administered in cases having a positive rapid test.

SUMMARY

Because of the high frequency of pregnant women not receiving ANC and the high prevalence of HIV infection in this group, a rapid test for HIV infection is suitable for these women during the intrapartum period. Early active intervention for perinatal HIV transmission prevention can be performed in patients who have a reactive result. In this study, the Determine HIV 1/2 test proved to be an ideal test for the diagnosis of HIV infection because it was a rapid, inexpensive, highly sensitive and specific test. The test is also easy to perform. It may serve as a powerful tool for controlling the HIV pandemic in developing countries with limited laboratory infrastructures.

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การใช้ชุดทดสอบเอ็ชไอวีชนิดเร็วในสตรีขณะเจ็บครรภ์คลอดที่ไม่เคยฝากครรภ์มาก่อน

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ปัญหาสำคัญอันหนึ่งของการใช้ยาต้านไวรัสในสตรีตั้งครรภ์ที่ติดเชื้อเอ็ชไอวีเพื่อป้องกันการติดเชื้อจากมารดามายังทารกก็คือการไม่เคยฝากครรภ์ของมารดา ตั้งแต่เดือนเมษายน พ.ศ. 2541 ถึง เดือนธันวาคม พ.ศ. 2544 เราพบว่ามีสตรีตั้งครรภ์ที่มาคลอดบุตรที่โรงพยาบาลศิริราชโดยที่ไม่เคยฝากครรภ์มาก่อนถึงร้อยละ 7.3 และพบว่ามีการติดเชื้อเอ็ชไอวีในผู้ป่วยกลุ่มนี้ถึงร้อยละ 5.7 ซึ่งสูงกว่าในกลุ่มสตรีตั้งครรภ์ที่มาฝากครรภ์ (ร้อยละ 2.2) อย่างชัดเจน นอกจากการหาวิธีการเพื่อเพิ่มอัตราการฝากครรภ์แล้ว การตรวจเลือดหาการติดเชื้อเอ็ชไอวีในกลุ่มสตรีตั้งครรภ์ที่ไม่เคยฝากครรภ์มาก่อนขณะเจ็บครรภ์คลอดควรได้ผลเร็ว ราคาถูก ทำง่ายและให้ผลแม่นยำ แผ่นตรวจ Determine สำหรับเชื้อ เอ็ชไอวี 1 และ 2 สามารถสนองความต้องการได้ทั้งหมดด้วยความไว ร้อยละ 100 ความจำเพาะ ร้อยละ 99.85 ค่าทำนายผลบวกร้อยละ 97.54 ค่าทำนายผลลบ ร้อยละ 100 และผลบวกลวงร้อยละ 0.14 เพื่อเพิ่มการป้องกันการติดเชื้อจากมารดามายังทารก การใช้แผ่นตรวจแบบไวสำหรับเชื้อเอ็ชไอวี ในสตรีตั้งครรภ์ที่เจ็บครรภ์คลอดบุตรโดยที่ไม่เคยฝากครรภ์มาก่อน จะทำให้ผู้ป่วยและทารกแรกเกิดกลุ่มนี้สามารถได้รับยาต้านเชื้อไวรัสเร็วที่สุดเท่าที่ทำได้

คำสำคัญ : แผ่นตรวจสำหรับหาการติดเชื้อเอ็ชไอวี, การทดสอบภาวะติดเชื้อเอ็ชไอวีด้วยวิธีมาตรฐาน, การป้องกันการติดเชื้อจากมารดาสู่ทารก

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