

Occasional Survey

Mother-to-child Transmission of HIV: The Asian/Thai Experience

C PANCHAROEN, U THISYAKORN

Abstract

There are at least 6 million people living with HIV/AIDS in the Asia Pacific region. The numbers of HIV-infected women and children are increasing at an alarming rate. Important components that need to be addressed in order to successfully prevent mother-to-child transmission of HIV include voluntary and confidential counselling and testing, family planning, obstetric care, antiretroviral use and infant feeding. There are many services that can aid in the prevention of mother-to-child transmission of HIV and the care of HIV-infected mothers and their children. Each country needs to take into account its HIV/AIDS epidemiology, its infrastructure and the available resources. Providing services in a stepwise manner can aid in the achievement of prevention of mother-to-child transmission of HIV.

Key words

Asia; HIV; Mother-to-child

During the past decade, the incidence of paediatric AIDS has risen steadily and has become an increasing cause of morbidity and mortality during childhood worldwide. Although the largest number of HIV-infected persons derives from sub-Saharan Africa, the annual incidence of HIV infection in Asia is increasing so fast that causes alarm. As reported by the Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) in December 2000, HIV has already killed more than 20 million people worldwide since the beginning of the epidemic and it has infected more than 36 million people; almost half of them were women. There are at least 6 million people living with HIV/AIDS in the Asia Pacific region. The numbers of HIV-infected women and children are increasing at an alarming rate. Over one million children are HIV-infected while in the year 2000 alone, 600,000 children acquired HIV infection.¹

Epidemiology

The HIV/AIDS epidemic in Asia has grown from a handful of infections to become a major public health threat with wide ranging medical, social, and economic consequences. Gaining a foothold in injection drug users and commercial sex workers, HIV quickly spread to the clients of commercial sex workers and from them to their wives, girlfriends, and children. The result is a general population epidemic of frightening rapidity and magnitude. As with all natural disasters, it is inevitable that children will suffer disproportionately from this epidemic, both directly and indirectly. Since mother-to-child transmission of HIV is the most significant route of HIV infection in children, with increasing evidence of heterosexual transmission, the number of infected women and consequently their children is increasing. As paediatricians, we are very interested in ascertaining the incidence and prevalence of HIV-infected females of reproductive age in our communities. Unfortunately, reliable data are restricted to areas where these numbers have been specifically sought as research data. Using mathematical models, it has been demonstrated that once the seroprevalence exceeds 30% in women of reproductive age, the infant mortality will have increased to a point where it equals rates in the 1960s in developing countries which means that paediatric AIDS is

Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

C PANCHAROEN MD
U THISYAKORN MD

Correspondence to: Dr U THISYAKORN

Received April 9, 2001

now threatening much of the beneficial impact on infant mortality that has been achieved in these countries in the past 40 years.²

For many years, not enough was known about HIV transmission from mother-to-child to take steps to help HIV-infected women have uninfected babies. HIV may be passed from mother-to-child before, during, or after birth. The exact timing of transmission is the subject of extensive study because of its implications for counselling and the search for opportunities to interrupt the transmission process. Some children are infected in utero across the placenta, others are clearly infected during the birth process, and a small proportion are infected after birth through breastfeeding. Reported transmission rate of HIV from mother to infant varied from 20% to 40% in Asian countries. Higher transmission rate was observed when the HIV-infected mothers breast-fed their babies. The transmission rate has dropped by half after breastfeeding has been discouraged in HIV-infected mothers. However, most children who are at risk of acquiring HIV come from areas of the world where finding safe and economically feasible alternatives to breast milk is difficult. Strategies of infant feeding for HIV-infected mothers in those areas are urgently needed.

Breastfeeding by mothers known to be HIV-infected is actively discouraged in Thailand. Child mortality caused by infectious diseases is comparatively low in Thailand, consequently the discontinuation of breastfeeding is unlikely to result in substantial increases in infant disease-related mortality.^{3,4}

Without antiretroviral therapy, vertically HIV-infected children in Asia progress from initial HIV infection to the clinical AIDS at different rates and follow the bimodal pattern of clinical course like in the western countries, a smaller group who develops AIDS rapidly and dies within the first year or two of life, and a larger group who develop AIDS at slower rates closer to those seen in adults. As a consequence, survival of HIV-infected children can be much longer than is commonly perceived. Some child who was infected at birth started to have AIDS related symptoms and signs at the age of ten years.⁵ The common manifestations include failure to thrive, hepatosplenomegaly, pneumonia, diarrhoea, oral candidiasis, lymphadenopathy, skin rashes, encephalopathy, parotitis, persistent fever, lymphoid interstitial pneumonitis, and recurrent bacterial infections.² Antiretroviral therapy has shown beneficial effects in the affordable HIV-infected children. The main obstacle is the high cost of antiretroviral drugs that made them unavailable for most HIV-infected children who belong to the low-income families.⁶

HIV-infected children frequently experience many medical and psycho-developmental complications as a result of the infection. These lead in many cases to impaired development, multiple and prolonged hospitalizations and early death. The devastating impact is not limited only to the infected child. The family or the guardian will also be greatly affected, both psychologically and socio-economically, by the child's illness. The impact will eventually extend to the community in many ways. The community will be affected by the direct and indirect cost of the child's medical care. Household members will not be able to participate in the workforce at the same level, as they are obliged to take care of the sick child. The problems of discrimination and the curtailment of educational opportunities will ultimately arise. Therefore, interventions that can reduce the number of HIV-infected children are certainly worthwhile and will be of great benefit to the society.

Prevention of Mother-to-child Transmission of HIV

The success of the clinical trial of zidovudine in reducing the risk of maternal-infant HIV transmission (PACTG 076) has opened the door to a major preventive effort. In the PACTG 076 trial, HIV-infected pregnant women were given oral zidovudine between 14 and 34 weeks' gestation (median duration of treatment, 11 weeks). They also received zidovudine intravenously during labour. Their newborns received zidovudine for 6 weeks and were formula-fed. The rate of HIV transmission was reduced from 22.6% to 7.6%.⁷ This intervention was quickly adopted as a standard of care in most developed countries together with avoidance of breastfeeding in their newborn. These two measures, in combination with delivery by caesarean section, have contributed to the significant reduction of paediatric HIV/AIDS cases in those countries.⁸ However, because of its high cost and complexity, it is impossible to implement these strategies in most of the developing world. In Thailand, as in many other countries, studies to investigate the possible benefit of short-course zidovudine regimen in the prevention of vertical HIV transmission were carried out and it was found that the short-course zidovudine regimen is inferior to the PACTG 076 regimen.⁹ In 1996 The Thai Red Cross Society with the support of Princess Soamsawali and the Ministry of Public Health, initiated a donation campaign called "Save a child's life from AIDS". The key objectives were to prevent mother-to-child transmission of HIV by

procuring zidovudine for HIV-infected pregnant women through public donation and also to test its feasibility and acceptance; hospitals throughout the nation that were interested and had an adequate supporting infrastructure could request free zidovudine from The Thai Red Cross Society. In this programme, the HIV-infected pregnant women were given oral zidovudine anytime between 14 and 34 weeks of gestation, with the regimen somewhat different from the PACTG 076 regimen. In the PACTG 076 regimen, a woman would receive 100 milligrams of zidovudine five times daily during pregnancy. In this programme, the total dose of 500 milligrams zidovudine per day is given two times daily for better compliance. In addition, zidovudine was given intravenously during labour in the PACTG 076 study. However, giving medication intravenously can be quite complicated, especially in some community hospitals in rural Thailand. Therefore it was decided to give 300 milligrams zidovudine orally every 3 hours instead; it was found that the zidovudine level in the body remains quite comparable regardless of whether the medication is administered orally or intravenously. The newborn received zidovudine for 6 weeks and were formula-fed. The observation of this ongoing campaign in Thailand indicates that there is a need for such intervention in the hospitals nationwide. The results have shown that the treatment is indeed effective in a Thai setting. The model will encourage other hospitals to develop their infrastructure to enable them to adopt a similar approach. In addition the campaign has also served to stimulate public awareness of HIV and AIDS in reproductive health planning. Taken together, these measures will eventually lead to a nationwide implementation of an antiretroviral intervention programme for HIV-infected pregnant women.

Because the HIV/AIDS epidemic continues in Thailand, The Thai Red Cross foresees the necessity of maintaining the zidovudine donation programme. Several plans, with some modification, have been laid out for the continuation of the programme. A subgroup analysis of the programme showed that the transmission rate of women who received zidovudine less than or equal to 8 weeks before delivery was not statistically different from the transmission rate in those who received zidovudine more than 8 weeks before delivery. In response to this findings, by late 1999 The Thai Red Cross advised that antepartum zidovudine for HIV-infected pregnant women in this programme should be started at 32 weeks' gestation and be continued till labour. This will help saving the fund and the medication without compromising the effectiveness of the regimen, thus enabling the programme to provide the medication to more

HIV-infected women. The intrapartum and the neonatal components of this modified PACTG 076 regimen remain unchanged. Periodic assessments have taken place thereafter to assure that the transmission rate remains within an acceptable range. Since the medical knowledge in the field of HIV evolves rapidly, The Thai Red Cross recognizes that this programme may need to be frequently updated to provide the greatest benefit to patients.^{10,11} A study from Uganda (HIVNET 012) compared the safety and efficacy of nevirapine with zidovudine in the reduction of mother-to-child transmission of HIV. Both medications were well tolerated with no different adverse events in both groups. The transmission rate showed almost 50% reduction among mothers and infants who receive single dose nevirapine compared with those receiving the short-course zidovudine.¹² This information has led to a new intervention strategy in the developing world. As a result, nevirapine has been included in the WHO model list of essential drugs as a drug for decreasing mother-to-child transmission of HIV. While there is debate about toxicity of antiretroviral drugs and the effects they may have on the course of HIV infection in the mother, the evidence available today is that the benefits largely outweigh the risks linked to their use.¹ This new information has led The Thai Red Cross Society to develop a new intervention strategy. In the year 2000, nevirapine as described in HIVNET 012 study was incorporated into the programme's regimen. Both zidovudine and nevirapine will be offered to all participating HIV-infected pregnant women and their infants. Theoretically, using both medications together to tackle the virus may lead to a further reduction of transmission. This programme has demonstrated that the community can work effectively together to overcome the obstacle of the high cost of zidovudine. Donation of medication has proved feasible and can be used as one of the strategic tools to prevent mother-to-child transmission of HIV in less-developed countries. The Thai Red Cross has also been made a UNAIDS collaborating centre. This will expand the role of the organization in this region, the model of this programme can possibly be used as a demonstration or a prototype for other countries in this region. We believe that as long as HIV/AIDS remains a public health problem for Asia, the "community-to-community" programme of this kind must exist. It could be one of a few weapons that the society has to combat and control this deadly disease.

A recent study in Thailand showed that a relatively simple drug regimen – a short one-month course of zidovudine – given to HIV-infected pregnant women late in pregnancy together with – a short 3 days course of

zidovudine in the infant after birth is inferior to the long-long regimen starting in the mothers at 28 weeks' gestation, with 6 weeks of treatment in the infant and leads to a higher rate of perinatal HIV transmission. The study also suggests that longer treatment of the infant cannot substitute for longer treatment of the mothers.¹³ Several Asian countries have recently set up pilot projects to help HIV-infected women giving birth to healthy children, and are actively tackling some of the challenges involved. These experiences will also identify how to overcome the hurdles to implementing prevention programmes on a large scale in Asian countries. The pilot projects will also need to learn how to provide care and support, not just for the HIV-infected mother and her infant but for the other members of her family as well. The biggest challenge of all will be to expand coverage beyond the pilot projects to reach all HIV-infected pregnant women and their families. As part of planning ahead for this expansion, health systems will have to rise to the considerable challenge of improving infrastructure, training, motivating and retaining the necessary health staff, and improving distribution systems so that HIV test kits, medications and infant formula are consistently available to those who need them.

There are a wide range of services that can aid in the reduction of the transmission risk of HIV from mother-to-child. However, many countries are limited by a lack of available resources and infrastructure to implement such services. A stepwise approach enables each country to evaluate its capacity and prioritize and categorize the different services into steps of actions. Achievement of the first step will help building a firm ground for the more complex and sophisticated steps. Important components that need to be addressed in order to successfully prevent and reduce perinatal HIV transmission include voluntary and confidential counselling and testing, family planning, obstetric care, antiretroviral use and infant feeding. Each country needs to take into account its HIV/AIDS epidemiology, its infrastructure and the available resources. Providing services in a stepwise manner can aid in the achievement of prevention of mother-to-child transmission of HIV.

Since the rapid spread of HIV is by heterosexual contact which has led to the increase in mother-to-child transmission of HIV, public health education about risky behaviors in child bearing age people is the most important preventive strategy. Thailand's well-publicized success in curbing a rampant heterosexual epidemic has brought to light other routes of transmission against HIV which HIV prevention

programmes have been far less successful.¹⁴ HIV continues to spread virtually unchecked through the sharing of drug-injecting equipments and through unprotected sex between men. Many countries in Asia have yet to see a significant spread of HIV, despite evidence that many men regularly have sex outside of marriage. It may be just a matter of time before infections reach a critical level in populations with the highest risk behaviour and begin to spread more widely. Certainly, there is no room for complacency.¹

The HIV plaque has been added to war, hunger, and other forms of pestilence as a destroyer of the world's most vulnerable children. We as paediatricians cannot simply sit on the sidelines and observe as the number of those infected inexorably increases, with an increasing proportionate impact upon women and children. We must continue to work as child advocates. To achieve this end we must all maintain an updated knowledge base regarding all aspects of the HIV pandemic, even if we have not personally diagnosed a case, and must regard every case of HIV infection diagnosed in a child as a failure of our preventative measures in the adult population. We must be willing to set aside personal biases, to recognize the differences between cultural sensitivity and social responsibility, and to take on the added responsibility of providing a strong political voice on sensitive and controversial issues such as sexual practices. The world's children are counting on us.

Thailand has the advantage of going into this epidemic with its eyes wide open. No other country has had as complete a monitoring system or as early a warning of the problems to come. As children can be affected directly through HIV infection, and indirectly by the effects of HIV on their parents and by societal changes forced by the epidemic, they will disproportionately suffer the impacts of this disaster.

Conclusion

The problems of HIV infected and affected children can be drastically reduced by early and concerted efforts to address them. It will also require leadership, the cost of indecision and delay in acting will be high. Every additional HIV infection not prevented, every additional child allowed to enter prostitution, every child denied an education by discrimination will increase the ultimate economic and social cost to the country. These children are the country's future. The country's response to their problems will give an indication of how highly country values its future.⁶

References

1. UNAIDS Joint United Nations Program on HIV/AIDS/WHO. AIDS epidemic update. December 2000.
2. Pancharoen C, Thisyakorn U. The Pediatric AIDS in Asia. (in press Clin Infect Dis 2002)
3. Thisyakorn U, Paupunwatana S, Chotpitayasunondh T, Kanchanamayul V, Limpitikul W, Panpitpat C. Perinatal HIV infection in Thailand. International Symposium on Pediatric AIDS in Thailand: A Public Health and Social Dilemma. Cambridge: Harvard AIDS institute, 1995 p. 23-7.
4. Thisyakorn U. Breast feeding and perinatal HIV transmission in Thailand. SCN News 1998;17:10.
5. Lauinger JM, Beadle N, Thisyakorn U. 10-year-old boy with hemangiopericytoma and HIV infection. *Pediatr Infect Dis J* 2001;20:321-3.
6. Thisyakorn U. Pediatric HIV and AIDS in Thailand. In Brown T, Sittitirai W (eds). The impact of HIV on children in Thailand. Bangkok: Program on AIDS, Thai Red Cross Society 1995;13-27 and 73-87.
7. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1996;335:1621-9.
8. International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1: A meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1999;340:977-87.
9. Thisyakorn U, Ruxrungtham K, Phanuphak P. Risk reduction of HIV-1 vertical transmission: progress and implementation in Thailand. *HIV&AIDS Current Trends* 1998;4:1-3.
10. Thisyakorn U, Khongphatthanayothin M, Sirivichayakul S, et al. Thai Red Cross Zidovudine Donation Program to Prevent Vertical Transmission of HIV: The Effect of the Modified ACTG 076 Regimen. *AIDS* 2000;14:2921-7.
11. Rongkavilit C, Thisyakorn U, Phanuphak P. Prevention of mother-to-child transmission of HIV: Thai Red Cross zidovudine donation programme. UNAIDS Best Practice Collection. September 2000.
12. Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet* 1999;354:795-802.
13. Lallemand M, Jourdain G, Le Coeur S, et al. A trial of shortened zidovudine regimens to prevent mother-to-child transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;343:982-91.
14. Hanenberg R, Rojanapithayakorn W, Kunasol P, Sokal D. The impact of Thailand's HIV-control programme, as indicated by the decline of sexually transmitted diseases. *Lancet* 1994;344:243-5.