HIV/AIDS in Children

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Abstract

The incidence of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) in children has risen steadily over the years and has become an increasing cause of morbidity and mortality during childhood. More than 90% of all children with HIV infection acquired their infection at birth from HIV-infected mothers. With increasing evidence of heterosexual HIV transmission, the number of infected women and consequently their children is increasing. The transmission rate of HIV from mother to infant varies from 20% to 40%. Children can be affected directly through HIV infection and AIDS, and indirectly by the effects of their parents' HIV infection, including being orphaned, discrimination, infant abandonment and negative impact on children's education. Another concern regards children who are most vulnerable to HIV infection and AIDS, such as child prostitutes and children in difficult circumstances. Recommended actions include prevention of parental HIV infection, prevention of mother-to-child HIV transmission, addressing child prostitution, prevention of child labour and improving work conditions, assistance to street children, addressing discrimination, solving the problem of children orphaned by AIDS, reducing HIV-related child abandonment and creating new roles for schools in reducing negative social impact. Although the largest number of HIV-infected persons are from sub-Saharan Africa, the annual incidence of HIV infection in Asia is escalating alarmingly. As reported by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization in December 2001, HIV infection has already killed more than 20 million people worldwide since the beginning of the epidemic and has infected more than 40 million people; almost half of them were women. There are at least 7 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 1 million children are HIV-infected; in the year 2000 alone, 600,000 children acquired HIV infection.

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Epidemiology

The human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) epidemic in Asia has grown from a handful of cases to a major public health threat with wide-ranging medical, social and economic consequences. First gaining foothold among intravenous drug users and commercial sex workers, HIV quickly spreads to clients of the latter group and subsequently to their wives, girlfriends and children. The result is an epidemic of frightening proportion. 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, the increase in heterosexual transmission meant that 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, infant mortality will have increased to a point where it equals rates in the 1960s in developing countries; this means that paediatric AIDS is now threatening much of the beneficial impact on infant mortality achieved in these countries in the last 40 years. Other routes of HIV infection in children include sexual transmission, transmission through receipt of blood and blood products, and sharing of drug-injection equipment.[1]

Determining the timing of HIV transmission from mother to infant is the subject of extensive study because of its implications for counselling and the search for opportunities to interrupt the transmission process. It is generally accepted that approximately one-third of transmission in non-breast-

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feeding women occurs during gestation and the remaining two-thirds occur either very late in gestation or during labour. The risk of perinatal HIV transmission is higher for mothers with immunological and clinical indicators of advanced disease and with increased viral load. Elective caesarean delivery has been shown to enhance the protective effect of perinatal HIV transmission. Breast-feeding accounts for an additional 7% to 22% of transmission especially in countries where it is practised among HIV-infected women.[2] Reported transmission rate of HIV from mother to infant varies from 20% to 40% in Asian countries. Higher transmission rate was observed when HIV-infected mothers breastfed their babies. The transmission rate dropped by half after breastfeeding was discouraged in HIV-infected mothers. However, most children who are at risk of acquiring HIV come from areas where safe and economically feasible alternatives to breast milk are lacking. Strategies of infant feeding for HIV-infected mothers are urgently needed in those areas. Breast-feeding 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 increase in infant disease-related mortality.[3,4]

Without antiretroviral therapy, vertically HIV-infected children in Asia progress from initial HIV infection to clinical AIDS at different rates and follow the bimodel pattern of clinical course seen in western countries, whereby a small group develops AIDS rapidly and dies within the first year or two of life, while a larger group develop AIDS at slower rates close to those seen in adults. As a consequence, survival of HIV-infected children can be much longer than is commonly perceived. A child infected at birth could manifest AIDS-related signs and symptoms at the age of 10 years.[5] The common manifestations include failure to thrive, hepato-splenomegaly, pneumonia, diarrhoea, oral candidiasis, lymphadenopathy, skin rashes, encephalopathy, parotitis, persistent fever, lymphoid interstitial pneumonitis and recurrent bacterial infections.[3,6] Antiretroviral therapy has shown beneficial effects in HIV-infected children. The main obstacle is the high cost of antiretroviral drugs, making them unavailable to most HIV-infected children from low-income families.[7]

As a result of the infection, these infected children frequently experience many medical and psycho-developmental complications. In many cases, these lead to impaired development, multiple and prolonged hospitalisations and early death. The devastating impact is not limited only to the infected child. The family or guardians will also be greatly affected, both psychologically and socio-economically, by the child's illness. The impact will eventually extend to the community. The community will be affected by the direct and indirect costs of the child's medical care. Family members are unable to participate fully in the workforce, as they need to take care of the sick child. The problems of discrimination and 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 HIV Transmission

The success of clinical trials on zidovudine in reducing the risk of mother-to-child HIV transmission (PACTG 076) has paved the way for 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 results showed that the rate of HIV transmission was reduced from 22.6% to 7.6%.[8] This intervention was quickly adopted as a standard of care in most developed countries, together with avoidance of breast-feeding in newborns. These two measures, in combination with delivery by caesarean section, have contributed to the significant reduction of paediatric HIV/AIDS cases in those countries.[9] However, because of its high cost and complexity, it is impossible to implement these measures in most of the developing countries.

As in many other countries, Thailand also investigated the possible benefits of a short-course zidovudine regimen in the prevention of vertical HIV transmission. Studies were carried out and results showed it to be inferior to the PACTG 076 regimen.[10] A study in Thailand showed that a relatively simple drug regimen – a 1-month course of zidovudine was given to HIV-infected women late in their pregnancies, combined with a 3-day course of zidovudine in the infants after birth – is inferior to the longer regimen, whereby zidovudine is started in the mothers at 28 weeks of gestation, combined with 6 weeks of treatment in the infants. The study also suggested that longer treatment for the infant cannot be substituted with longer treatment for the mother.[11]

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 country that were interested and had adequate infrastructure could request for free zidovudine from the Thai Red Cross Society. In this programme, 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 be given 100 mg of zidovudine 5 times daily during pregnancy and intravenously during labor. However, in the Thai programme, the total dosage of 500 mg zidovudine per day was given twice daily for better compliance. In addition, as giving medication intravenously could be quite complicated, especially in some community hospitals in rural Thailand, it was decided that 300 mg zidovudine would be given orally every 3 hours instead. It was found that zidovudine levels remained quite comparable regardless of whether the medication is administered orally or intravenously. The newborns received zidovudine for 6 weeks and were formula-fed.

The results of this ongoing campaign in Thailand showed that such an intervention is much needed in hospitals throughout the country. The results have also shown that the treatment is effective in the Thai setting. This model will encourage other hospitals to develop their own infrastructure and to adopt a similar approach. In addition, the campaign has also raised 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 is still spreading throughout Thailand, the Thai Red Cross foresees the necessity of continuing the zidovudine donation programme. Several plans, with some modifications, have been laid out for the continuation of the programme. A subgroup analysis of the programme showed that the transmission rate in women who received zidovudine 8 weeks or less before delivery were not statistically different from those who received zidovudine more than 8 weeks before delivery. Acting on this finding, the Thai Red Cross, in late 1999, 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 to save costs without compromising the effectiveness of the regimen, thus enabling the programme to reach more HIV-infected pregnant women. The intrapartum and the neonatal components of this modified PACTG 076 regimen remain unchanged. Thereafter, periodic assessments were done to ensure that the transmission rate remains within an acceptable range. Since the field of HIV is evolving rapidly, the Thai Red Cross recognises that this programme may need to be frequently updated to provide the greatest benefit to patients.[12,13]

A study from Uganda (HIVNET 012) has 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 differing adverse events in both groups. The study showed an almost 50% reduction among mothers and infants who received single-dose nevirapine compared to those receiving short-course zidovudine.[14] This information has led to the development of a new intervention strategy in the developing world. As a result, nevirapine has been included in the World Health Organisation's (WHO) list of essential drugs to reduce mother-to-child transmission of HIV. While there is still debate on the 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.[15]

This new information has led the Thai Red Cross Society to develop a new intervention strategy. In the year 2000, nevirapine was incorporated into the programme's regimen. Both zidovudine and nevirapine were 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 new programme has demonstrated that the community can work effectively together to overcome the obstacle of the high cost of zidovudine. The donation of medication has been proven 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 Joint United Nations Programme on HIV/AIDS (UNAIDS) collaborating centre. This will expand its role in this region and the Thai programme could be used as a model for other countries in this region. As long as HIV/AIDS remains a public health problem for Asia, a "community-to-community" programme of this kind must exist. It can be one of the few weapons that society could use to combat and control this deadly disease.

Since the rapid spread of HIV is through heterosexual contact and this has led to the increase in mother-to-child transmission of HIV, public health education on risky behaviours in people of child-bearing age is the most important preventive measure. Thailand's well-publicised success in curbing a rampant heterosexual epidemic has brought to light other routes of HIV transmission, in which prevention programmes have been far less successful.[16] HIV infection continues to spread virtually unchecked through the sharing of drug-injecting equipment and through unprotected sex between men. However, many countries in Asia have yet to see a significant increase in HIV infection, despite evidence that many men regularly have sex outside marriage. It may be just a matter of time before infections reach a critical level in populations with high-risk behaviours and begin to spread more widely. Certainly,

there is no room for complacency.[15]

The HIV plague has been added to war, hunger and other forms of pestilence as a destroyer of the world's most vulnerable children. As paediatricians, we simply cannot sit on the sidelines and observe as the number of infected cases increases inexorably, with a proportionate increase in the impact on women and children. We must continue to work as child advocates; hence, we must update our knowledge base with regards to 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 recognise the difference 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 suffer disproportionately the impact of this diaster.

Conclusion

The problems of HIV-infected and affected children can be drastically reduced by early and concerted efforts to address them. Strong leadership is required, as the costs of indecision and procrastination will be high. Each new case of HIV infection, each additional child entering prostitution, each child denied an education by discrimination will only add to the country's economic and social burden. These children are the country's future; the country's response to their problems will give an indication of how highly it values its future.[7]

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