INTRODUCTION

HIV infection in children continues to be a growing challenge in India with an estimated 100,000 infected women giving births to about 30,000 infected infants every year(1). The irony of these statistics is that mother-to-child transmission of HIV is largely a preventable infection; however the implementation of preventive strategies in a diverse country like India is exceedingly complex. The face of pediatric HIV has changed irrevocably with the availability of potent antiretroviral treatment (ART) and accessible diagnostic monitoring. The Indian Government’s action in 2006 to enhance the ART rollout for children has breathed new life and hope into the lives of children living with HIV. These children are now less likely to suffer from early mortality and myriad opportunistic infections. These successes, however, are accompanied by several challenges such as difficulty in maintaining good adherence to a lifelong regimen, managing long term adverse effects, development of resistance and treatment failure, and rehabilitation of these children into society. The ensuing sections deal with key issues related to prevention and treatment of childhood HIV in India.

PERINATALLY TRANSMITTED HIV

Prevention

In general, most infected infants are born to mothers who are unaware of their status. The National AIDS Control Organization’s (NACO) current efforts to improve access to universal opt-out testing of pregnant women during the antenatal period, and to enhance the use of integrated counseling and testing centers (ICTCs) throughout the nation can improve efficacy in diagnosis of asymptomatic individuals(2). A 25-year longitudinal analysis of the ‘Prevention of Parent-to-Child Transmission’ (PPTCT) program in Zimbabwe, concluded that reduction in vertical transmission in recent years was predominantly attributable to declining maternal HIV prevalence(3). The use of single-dose nevirapine has been found to be effective and feasible in India, but the specter of development of drug resistance and subsequent high risk of treatment failure in mothers who later start full ART looms large and cannot be disregarded(4). A recent meta analysis showed a high prevalence of resistance among mothers and infected infants who received single-dose nevirapine, and that this risk may be somewhat alleviated when other anti-retroviral drugs are given simultaneously(5). Although 3-drug ART for PPTCT is the standard of care in the developed world, concerns of feasibility and compliance preclude the use of this strategy on a National scale in India and other developing nations. These issues, as well as the availability of more effective short-course prophylactic regimens(6) should lead to a careful reconsideration of the ideal cost-effective PPTCT strategy in India.

Postnatal follow-up and testing

The increasing levels of antenatal coverage reported by NACO offer an opportunity to integrate HIV-prevention and treatment services with routine antenatal, postnatal and adolescent care. Early diagnosis of HIV infection status in exposed children is the first step towards improving pediatric HIV care in developing countries. The preferred test in the
setting of persisting maternal HIV antibodies is HIV-1 DNA PCR, which has a sensitivity of 98% and a specificity of 99%, even in resource-limited settings where HIV subtype C is predominant(7). To achieve a balance between cost and accuracy, the WHO recently recommended a testing strategy that uses a virological test in infants at 4-6 weeks of age or at the earliest opportunity thereafter(8). The advantages of early diagnosis of HIV infection by this strategy in perinatally exposed infants are: (i) timely treatment of asymptomatic HIV infected infants, (ii) sound decisions related to infant feeding choices and cotrimoxazole prophylaxis, (iii) enhanced postnatal follow up of infants and better evaluation of effectiveness of the PPTCT program, and (iv) alleviation of anxiety among parents and improvement of overall quality of life in affected families. Thus, making accessible a reliable virological test for early diagnosis of HIV infection in perinatally exposed infants should remain a priority area for NACO.

**Infant feeding choices**

Although avoidance of breastfeeding for prevention of postnatal HIV transmission is the norm in the developed world, the choice of infant feeding is not so straightforward in resource-limited settings. Breastfeeding is the accepted tradition and more importantly, the benefits of breastfeeding in such setting should not be understated. The knowledge that mixed feeding is associated with a greater risk of vertical HIV transmission compared to exclusive breastfeeding needs consistent emphasis in daily practice(9). Recent data from Africa have shown that replacement feeding is considerably more expensive, and shows no advantage over breastfeeding when considering HIV free survival of infants up to 2 years(10,11). Moreover, new strategies where antiretroviral drugs were given to the mother and breastfeeding infant postnatally have shown encouraging results in reducing breastfeeding related HIV transmission(12,13). The recent SWEN Study, which included over 700 mother-infant pairs in India, concluded that daily nevirapine given to breastfeeding infants for 6 weeks was safe and successful in reducing the risk of postnatal HIV transmission and death when evaluated at 6 weeks of age(14). Although the protective effect was less visible at 6 months of age, these results should catalyze the government to re-evaluate our PPTCT guidelines and support research to optimize protection in breastfeeding infants when access to acceptable, feasible, affordable, safe and sustainable replacement feeding is not available.

**ART in Children**

With the widespread use of ART, there has been a shift from dealing with ‘death and serious illness’ to ‘living with a chronic illness’. The ‘National Pediatric ART Initiative’ launched by NACO in November 2006 uses a novel multi-pronged approach including provision of pediatric fixed dose combination (FDC) drugs, use of simplified body weight-stratified dosing tools to support prescription of ART, establishment of National guidelines, and training of physicians from the public and private sectors(15). As of May 2008, over 10,000 children are currently receiving ART, an exponential increase from 1,800 children in October 2006(15). A longitudinal analysis of a cohort of 295 children on ART according to NACO guidelines in Tamil Nadu indicated that the one-year survival rate was 90%(16), which was comparable to results in both resource-rich and resource-limited settings(17,18). The strategy of FDC pills for children as part of the National program has been found to be effective and acceptable to caregivers and children(19,20). The adequacy of current dosing strategies in children weighing less than 6 kg, malnourished children and those taking simultaneous anti-tubercular drugs however, are areas of concern requiring further research(21-23). Renewed attention to develop appropriate formulations for these groups of children will further strengthen the efforts in improving the lives of infected children.

The ideal timing of ART initiation in children is another debatable issue. The pathogenesis of HIV infection in children differs from that of adults, as the virus affects an immature immune system that is more vulnerable to destruction(24). The recommendations of starting ART only when the threshold of advanced disease stage or severe immunodeficiency has been crossed is viewed by some as “too late” to effectively halt the rapid progression of disease in children with perinatally
acquired HIV infection(25). On the other hand, issues related to compliance, availability, cost and adverse effects have been cited as reasons to defer therapy until absolutely necessary. For infants younger than 12 months of age, the risk of progression is higher than that for older children, and is independent of surrogate markers such as CD4 percentages and viral load(26). The randomized controlled CHER study has supported this observation by demonstrating that mortality could be reduced by 75% when treatment is initiated within 3 months of age in perinatally infected asymptomatic infants(27). This evidence led WHO to revise the guidelines, favoring ART initiation in all infected infants regardless of their disease stage(8).

Adherence and disclosure

Optimal viral suppression ideally requires an ART adherence rate of >95%(28). However, studies in children have reported adherence estimates of 50% to 80%, with the higher range of estimates reported from lower-income settings(29-31). Adherence is a complex behavior involving education, motivation and acceptance, and needs continuous reinforcement and nurturing of the healthcare provider-patient relationship. The complexity may be increased in children due to reliance on caregivers who themselves might be ill, or caregivers who are not the children’s own parents. Poor availability of pediatric formulations and poor palatability are also reasons unique to children. The use of FDC ART in India has eased medication schedules tremendously and are likely to facilitate adherence.

One of the strongest correlates of good adherence is complete disclosure of HIV status by caregivers to children(32). When children have supportive caregivers, are aware of their HIV status, and know that the drugs they are taking will help prolong life, they become self-motivated to stick to their medication schedules, and are even able to overcome external adherence challenges(33). A recent surveillance among HIV-infected Thai schoolchildren (median age of 9 years) receiving ART reported that less than one third knew about their infection(34). A pattern of inaccurate disclosure was prevalent where children were told that they had a non-HIV related health problem. The situation is likely to be similar in India, but studies are needed to understand the patterns and barriers to disclosure among children. Disclosure principles to assist parents and providers have been included in the NACO pediatric treatment guidelines. However, a good assessment of the applicability and actual implementation of these principles is warranted.

IMMUNIZATIONS

Adequate immunization contributes substantially towards reduction in morbidity, and is a critical component of HIV care in children. The WHO Panel concluded that all killed vaccines used in the Universal Immunization Program schedule are safe and can be used in HIV infected children(35). Live virus vaccines such as measles and oral polio vaccine are also relatively safe and may be used with slightly differing recommendations(35). BCG vaccine is no longer recommended for children who are known to be HIV-infected, even if asymptomatic following concerns of increased risk of disseminated BCG disease among vaccinated HIV-infected infants in Africa(36,37). Keeping in mind the benefits of potentially preventing severe tuberculosis, the validity of this recommendation should be confirmed in a low-HIV prevalence country like India. Clear evidence-based policies on use of optional vaccines among HIV-infected children in India will be valuable.

HIV AND ADOLESCENTS

Young people have often been described as being at the center of the HIV epidemic worldwide(38). In India too, a large proportion of new infections occur among youth aged between 15 and 24 years. High-risk behavior often begins during adolescence, and prevention messages are likely to be most effective in this age group. A decline in HIV prevalence in several countries has been associated with a reported change in high-risk behavior among younger age groups suggesting that adolescents and youth represent the greatest potential force to be targeted with appropriate preventive interventions(38).

The physical, cognitive and emotional changes occurring among adolescents enhance their vulnerability to the ill-effects of chronic HIV. Despite cultural expectations of dependence, their
need for autonomy and independence often translates into refusal to take medications or undergo routine tests(39). Disclosure is a particular challenge as fear of rejection from peers occupies a large part of the psyche of the adolescent. School life is frequently disrupted due to unstable home environments, medical illness or behavioral acting out. Because of confidentiality issues, care providers need to be proactive regarding school attendance and must include support services outside of the school environment for the child and family. The process of transitioning care from pediatric to adult doctors should be initiated in the pre-teen years and continued over several years(40). A multidisciplinary team with expertise in the area of adolescent health should be developed to address the youth’s unasked concerns regarding body image, sexuality and moral codes. Adolescents should be given information about their own bodies, including why their growth may be slow, what can be expected from antiretroviral therapy and how they can practice safe sex. Each health encounter should be an opportunity to discuss issues that will eventually help them develop self-awareness, self-appreciation and self-respect. HIV-infected youths need a sense of hope and control over their disease: the confidence that they can get married, gain employment and integrate into society meaningfully. A conceptual framework for developing a comprehensive and effective program geared towards adolescents living with HIV in India is urgently needed.

Conclusions

The recent developments in the care of children living with HIV in India are encouraging. The problems of high prevalence of malnutrition, stigma and coinfections such as tuberculosis need to be addressed by integrating antiretroviral treatment programs with other related health services. Critical areas that need further research include developing low-cost diagnostic tests for earlier identification of HIV infection in infants and disease monitoring, exploring innovative methods of achieving maximal viral suppression and designing optimal ways to re-integrate adolescents into regular society. National support in developing large cohesive multi-site cohorts designed to facilitate consistent patient follow-up is a pressing need in India. Building on the existing country-wide network of centers taking care of children with HIV will facilitate additional insights into the medical and psychosocial evolution of childhood HIV in India, and development of specific interventions to further improve lives.

Funding: None.
Competing interests: None stated.

References


