EDITORIAL

A Silver Lining in the HIV/AIDS Cloud

K Rajeshwari

From Department of Pediatrics, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi 110002.
rajeshwari.dr@gmail.com

Medical science has overcome insurmountable challenges. The physician's indomitable will and the potency of modern medicine have conquered the most intractable of illnesses. There are; however, a few adversaries that remain unsubdued. Of these, the most formidable is HIV/AIDS. India is one of its foremost victims. And amongst India's population, the mother and child are the most affected. Transmission of HIV from mother-to-child is a grim manifestation of this. Medicine; however, is relentless in its pursuit. The 'Prevention of Parent-to-Child Transmission of HIV (PPTCT) Programme', under the aegis of the National AIDS Control Organization (NACO) is a fine example of medicine's tenaciousness, to first bring down, and then finally eliminate the spread of HIV in India.

There is a large global evidence-base that substantial reduction in new pediatric infections can be achieved as a result of high coverage with highly effective interventions for PPTCT [1]. In 2013, the World Health Organization (WHO) published new guidelines which recommended providing life-long triple anti-retroviral therapy (ART) for all pregnant women living with HIV, irrespective of the CD4 cell count [2]; this new option termed (B+), would result in significant reduction in transmission of mother to child infections and would be helpful in maximising coverage for those needing treatment for their own health and long-term survival. This strategy would also prevent 'stopping and starting ART' with repeat pregnancies, providing early protection against mother to child transmission in future pregnancies, reducing the risk of transmission to sero-discordant male partners of these women, and reducing the emergence of drug resistance. Option B+ also offered other advantages, which included simplification of choice of ART regimen, and service delivery and harmonization with ongoing ART programmes.

The cost of antiretroviral drugs was a major determinant in a countries' choice of a particular drug regimen for PPTCT. In 2009, the average cost of ART offered under Option B was three to five times higher than the cost of providing single dose Nevirapine to the mother and child at delivery. However, by the end of 2011, this differential had diminished to two times higher. The cost of formulations of tenofovir with lamivudine and efavirenz has also decreased by 30% over the past three years [3]. The cost of these drugs is expected to fall further in future.

About 14,000 babies infected with HIV are born to an estimated 38,000 HIV-infected pregnant women in India. Mother to child transmission of HIV, which occurs during pregnancy, childbirth, or through breastfeeding, accounts for 4.7 percent of overall HIV transmission in the country (NACO Annual Report, 2013).It is the most important route of HIV-transmission among children in India. It is essential that these infected pregnant women are provided the package of PPTCT services to reduce transmission of HIV to the baby. The real challenge lies in reaching all pregnant women accessing antenatal care (ANC) services, at all health service delivery points, and to reach early in pregnancy, especially in line with the WHO guidelines that require women to attend ANC as early as possible.

In India, NACO has adopted the PPTCT component as an important service under National Aids Control Program (NACP) to respond to the challenge of controlling and reversing the HIV epidemic. PPTCT, that started in 2002, has witnessed a significant scale-up of HIV counselling, testing and treatment.The PPTCT used a single dose Nevirapine as the drug of choice which had the potential to reduce the risk of transmission to 12%-15%. Later, based on the WHO guidelines, NACO in September 2012, rolled out the triple drug ARV regimen (option B) in the 4 southern high prevalence states of Andhra Pradesh, Telangana, Karnataka and Tamil Nadu. This was later expanded to the entire country. Based on the new guidelines, NACO advocates initiating lifelong ART (triple drug regimen) for all pregnant and breast-feeding women living with HIV, regardless of CD4 count or WHO clinical stage, for their own health and also to prevent vertical HIV transmission [4].

In this issue of *Indian Pediatrics*, the exact transmission rates of HIV infection among pregnant women attending an ART centre in Delhi and the follow up of the infants at a Pediatric Centre of Excellence at Kalawati Saran Children's Hospital has been published [5].The study included mothers who had received single dose Nevirapine as preventive strategy for PMTCT as well as those receiving triple therapy as option B+. The overall transmission rate of HIV described in the study is 2% and an overall ARV cover in HIV-positive mothers of 94%. On analyzing the data before and after the change in PPTCT guidelines, no significant difference was found in terms of HIV-free survival or HIV transmission rate. Of the 155 infants, 10 (6.5%) died before 18 months of age. Of these, one had positive and three had negative HIV DNA-PCR at the age of 6 weeks (all 3 on exclusive replacement feeds), while the rest died before their HIV status could be ascertained. Out of the four children who were tested at 6 weeks only, one was positive and three were negative. They were apparently on replacement feeding and thus were perhaps uninfected. The fate of the other 6 is not known. It is possible that inclusion of these infants also in the final analysis (if their 18-month status was known) would have yielded a higher rate of HIV transmission.

It appears that single dose nevirapine was as effective as option B+ inprevention of HIV transmission in this study. Whether the triple therapy would have conferred various health benefits to the mother and birthweight of those children would have been better than those who received only single dose of nevirapine, needs further exploration. At 18 months age, 14% HIV-uninfected infants were wasted, 28% stunted, and 3% had microcephaly in this study. It is not known whether the mothers of these infants were on triple therapy or not. Recent evidence from trials in Botswana [6] revealed that both weight-for-age and length-for-age were significantly lower in HIV-exposed infants exposed to ART *in utero* compared to those that were only exposed to maternal single drug prophylaxis. It remains unclear whether these differences have a short term impact or whether they predispose the child for subsequent poorer growth, chronic disease and neurocognitive dysfunction [7]. The long term effects of antiretroviral drugs on the growing brain need further exploration.

At present, the benefits of ART in reducing vertical transmission and improving maternal health greatly outweigh the potential adverse effects of ART exposure to children [8]. However, as PMTCT coverage increases, the number of uninfected infants exposed to antiretroviral therapy (ARV) *in utero* or through breastfeeding will likewise increase, making it critical to continue monitoring for adverse effects.

As Hippocrates said wisely, *"Healing is a matter of time, but it is sometimes also a matter of opportunity."* An opportunity now beckons. Let this serve as a clarion call to physicians to pool their capabilities, knowledge and resources and engage with their patients with renewed vigour, enthusiasm and hope.The time starts now.

Funding*: None;* Competing interests*: None stated.*

REFERENCES

1. World Health Organization (2010) Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access. Available: *http://whqlibdoc.who.int/publications/2010/9789241599818_ eng.pdf.* Accessed on 15 December, 2019.
2. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach. Geneva: World Health Organization; 2013 Jun. Available: *https://apps.who.int/iris/bitstream/handle/10665/85321/9789241505727_eng.pdf.* Accessed on 15 December, 2019.
3. World Health Organization. Programmatic Update: Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. Executive summary, April 2012. Available from: *https://www.who.int/hiv/pub/pmtct_update.pdf.* Accessed on December 20, 2019.
4. National AIDS Control Organization. Updated Guidelines for Prevention of Parent to Child Transmission of HIV using multi drug anti-retroviral regimen in India, December 2013. Available from: *http://naco.gov.in/sites/default/files/National_Guidelines_for_PPTCT_0.pdf.* Accessed on December 20, 2019.
5. Baijal N, Seth A, Singh S, Sharma G, Kumar P, Chandra J. HIV-free survival at the age of 18 months in children born to women with HIV infection: A retrospective cohort study. Indian Pediatr. 2020;57:34-8.
6. Powis K, Smeateon L, Fawzi W, Ogwu A, Machakaire E, Souda S, *et al*. In utero HAART exposure associated with decreased growth among HIV-exposed uninfected breast fed infantsin Botswana. In Proceedings of 5th International Workshop on HIV Pediatrics, Kuala Lumpur, Malaysia. 2013 June 28-29. Reviews in Antiviral Therapy in Infectious Diseases; 2013_7. Abstract 011.
7. Foster C, Lyall H. HIV and mitochondrial toxicity in children. J Antimicrob Chemother. 2008;61:8-12
8. Chikhungu LC, Bispo S, Rollins N, Siegfried N, Newell ML. HIV-free survival at 12-24 months in breastfed infants of HIV-infected women on antiretroviral treatment. Trop Med Int Health. 2016;21:820-8.