



Mother to Child Transmission of the Human Immunodeficiency Virus

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The acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus has a major worldwide impact on health, culture, demographics and economics [1], with more than 35 million deaths since the beginning of the epidemic, including 2 million (370,000 of them children) during 2007 [2]. According to the recent United Nations AIDS data, there are about 33 million people, including 2.3 million children, living with HIV/AIDS today (two-thirds of them in Sub-Saharan Africa). During 2007, about 2.7 million people became newly infected with HIV, including 0.5 million children who were mainly infected by perinatal transmission of the virus [2,3]. It is estimated that every day 7000 people become newly infected with HIV with over 1000 children infected daily with HIV as a result of mother to child HIV transmission [2,4]. Based on the last (2006) Israeli Ministry of Health report there are about 3940 people (63% males, 37% females) currently living with HIV/AIDS in Israel, including 100 children [5].

HIV is vertically transmitted from mothers to their newborns [6-8]. In the absence of any antiretroviral therapy the rate of HIV-MTCT is 30–40% [8]. In contrast, with the appropriate treatment (to the mothers and to their newborns) the rate of HIV-MTCT has been dramatically diminished – to less than 2% [9]. Currently, complete prevention of HIV-MTCT is a realistic goal [6]. Mothers with high viral load and low CD4 cells count at the time of delivery, with hepatitis C co-infection and with premature rupture of membranes, are more likely to transmit HIV infection to their children [10]. Most HIV transmissions take place near the time of or during delivery and after birth due to breast-feeding [11-14]. In cases of *in utero* HIV-MTCT, it occurs in the third trimester, mostly within 60 days before delivery [13]. Accordingly, the HIV-MTCT prevention programs are based on the treatment of all pregnant women (regardless of their CD4 counts), using highly active antiretroviral therapy starting at week 16 to 22 of pregnancy, during labor (zidovudine, Retrovir®) intravenously to the mother and cesarean section, except when HIV RNA < 50 copies/ml at weeks 34–36), and postpartum (Retrovir) orally for 6 weeks, starting within 6 hours of birth to the newborn, and avoidance of breast-feeding) [15-17]. To eliminate HIV-MTCT, all

components of the prevention program should be included. Thus, an early HIV diagnosis (at least 14–20 weeks before delivery) is essential for all pregnant women with HIV.

The HAART regimen in pregnancy should be the same as in non-pregnant patients. Currently, monotherapy with zidovudine (Retrovir) is not recommended for treatment of HIV pregnant women, though it should be a part of the HAART regimen. Efavirenz (Stocrin®) and the combination of didanosine (ddI – Videx®) and Stavudine (d4T – Zerit®) are contraindicated during pregnancy. Nevirapine (NVP – Viramune®) should not be initiated in pregnancy since it is associated with toxicity in women with CD4 counts above 250 cells/mm³ [18]. The protease inhibitors are currently the preferred third drug in the HAART regimen for HIV pregnant women, especially ritonavir (Norvir®)-boosted lopinavir (LPV/r; Kaletra®) or ritonavir-boosted saquinavir (SQV/r; Invirase®) [4,18].

The risk of HIV-MTCT increases with breast-feeding. Thus, it is avoided in the western world (including Israel) and formula feeding is recommended instead [4,10,18]. However, in developing countries, breast-feeding is the optimal source of nutrition and protects newborns from life-threatening infections [2]. Moreover, the avoidance of breast-feeding in the latter setting may have negative cultural and psychological effects on HIV-infected mothers [10]. Recently, Kumwenda et al. [19] reported that HIV prophylaxis with HAART treatment to the breast-fed children throughout the breast-feeding period (14 weeks) significantly reduced the HIV-MTCT rate [19]. Thus, in developing countries the latter approach (HIV prophylaxis throughout the entire breast-feeding period) may be beneficial.

In this issue of the journal, Elchalal et al. [20] report the HIV-MTCT rate in 35 HIV-positive women (88% of Ethiopian origin) who gave birth to 45 infants during the years 1996–2006 in the Jerusalem area. In 5 women (14%), HIV diagnosis was made only after delivery. The HIV-MTCT rate in the entire group was 8.6%, with a significantly higher transmission rate (40%) in women with post-delivery HIV diagnosis, emphasizing the importance of early HIV diagnosis for the prevention of HIV-MTCT. The relatively

HIV/MCT = mother to child HIV transmission

HAART = highly active antiretroviral therapy

high rate of transmission in the Jerusalem cohort appears to be due to the lack of any antiretroviral treatment during pregnancy (in women with known HIV) and during/after delivery in mothers who were diagnosed with HIV following delivery. Nevertheless, it should be noted that the current recommended treatment for HIV during pregnancy is a complete HAART regimen [4,18] rather than zidovudine monotherapy that was offered to the patients in the Jerusalem cohort. In addition, Elchalal and team offered elective cesarean section to all HIV pregnant women regardless of their viral load at the time of delivery, though this is neither indicated nor beneficial in women with low viral load (< 50 copies/ml) at weeks 34–36 [4,17].

Last year, at the first Israeli HIV meeting, Agmon-Levine reported an overall rate of 3.6% of HIV-MTCT in 300 pregnancies of 241 HIV-infected women who were treated in six AIDS centers in Israel [Agmon-Levine and Stoegeer, unpublished observations]. As was observed by Elchalal and colleagues [20], late HIV diagnosis was significantly associated with higher rates of viral transmission, emphasizing the need for screening and early HIV diagnosis of pregnant women as a major part of the HIV-MTCT prevention program in order to eliminate HIV-MTCT and to prevent pediatric HIV/AIDS.

To conclude, elimination of HIV-MTCT is a realistic goal in Israel. In order to achieve that goal, all parts of the HIV-MTCT prevention program (screening and early diagnosis, HAART to all pregnant women, treatment of mothers and newborns during and after delivery, and the avoidance of breast-feeding) are mandatory and should be strictly performed by a coordinated team of health care workers, family physicians, pediatricians, gynecologists and HIV experts.

References

- Cotton DJ. AIDS in women. In: Merigan TC Jr, Bartlett JG, Bolognesi D, eds. *AIDS Medicine*. 2nd edn. Baltimore, Maryland: Williams & Wilkins, 1999:151–62.
- Report on the Global AIDS Epidemic: 2008. Geneva: Joint United Nations programme on HIV/AIDS (UNAIDS) and the World Health Organization, 2008.
- Vocks-Hauck M. Pregnancy and HIV. In: Hoffmann C, Rockstroh JK, Kamps BS, eds. *HIV Medicine 2007*. 15th edn. Paris: Flying Publisher, 2007:353–68.
- European AIDS Clinical Society (EACS) Guidelines for the Clinical Management and Treatment of HIV Infected Adults in Europe. Paris, France, June 2008. (Accessed August 25, 2008, at <http://www.eacs.eu/guide/index.htm>).
- Chemtob D. HIV/AIDS in Israel, Epidemiological Periodic Report 1981-2006. Ministry of Health. Public Health Services Department of Tuberculosis & AIDS. Jerusalem, Israel December 2007. (Accessed August 25, 2008, at <http://www.health.gov.il/Download/pages/PeriodicReport2007final.pdf>).
- Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS. How many child deaths can we prevent this year? *Lancet* 2003;362:65–71.
- Roustit M, Jlaiel M, Leclercq P, Stanke-Labesque F. Pharmacokinetics and therapeutic drug monitoring of antiretrovirals in pregnant women. *Br J Clin Pharmacol* 2008;66(2):179–95.
- Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173–80.
- Cooper ER, Nugent RP, Diaz C, et al. After AIDS clinical trial 076: the changing pattern of zidovudine use during pregnancy, and the subsequent reduction in the vertical transmission of human immunodeficiency virus in a cohort of infected women and their infants. *J Infect Dis* 1996;174:1207–11.
- Tess BH, Rodrigues LC, Newell ML, Dunn DT, Lago TD. Breastfeeding, genetic, obstetric and other risk factors associated with mother-to-child transmission of HIV-1 in Sao Paulo State, Brazil: Sao Paulo Collaborative Study for Vertical Transmission of HIV-1. *AIDS* 1998;26:513–20.
- Tuomala RE, O'Driscoll PT, Bremer JW, et al. Cell-associated genital tract virus and vertical transmission of human immunodeficiency virus type 1 in antiretroviral-experienced women. *J Infect Dis* 2003;187(3):375–84.
- John-Stewart G, Mbori-Ngacha D, Ekpini R, et al. Breast-feeding and transmission of HIV-1. *J Acquir Immune Defic Syndr* 2004;35:196–202.
- Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and Infants Transmission Study Group. *N Engl J Med* 1999;341(6):394–402.
- Ceballos A, de Los Angeles Pando M, Liberatore D, et al. Efficacy of strategies to reduce mother-to-child HIV-1 transmission in Argentina, 1993-2000. *J Acquir Immune Defic Syndr* 2002;31(3):348–53.
- Watts DH. Management of human immunodeficiency virus infection in pregnancy. *N Engl J Med* 2002;346:1879–91.
- Mandelbrot L, Landreau-Mascaro A, Rekacewicz C, et al. Lamivudine-zidovudine combination for prevention of maternal-infant transmission of HIV-1. *JAMA* 2001;285:2129–31.
- The European Mode of Delivery Collaboration. Elective cesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999;353:1035–9.
- Hammer SM, Eron JJ Jr, Reiss P, et al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. *JAMA* 2008;300(5):555–70.
- Kumwenda NI, Hoover DR, Mofenson LM, et al. Extended antiretroviral prophylaxis to reduce breast-milk HIV-1 transmission. *N Engl J Med* 2008;359(2):119–29.
- Elchalal U, Avgil M, Goslitzer T, et al. Mother to child transmission of human immunodeficiency virus: the Jerusalem experience, 1996–2006. *IMAJ* 2008;10:667–71.

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