

# EDITORIAL

## Recent advances in prevention of mother to child (PMTCT) of HIV

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In Africa alone, over 1600 infants become infected with human immunodeficiency virus (HIV) each day despite the advances in prevention of mother to child transmission (PMTCT). WHO recommends the 4 pronged approach to PMTCT that includes primary prevention of HIV, prevention of unintended pregnancies in HIV infected women, PMTCT and care and support for HIV infected women, infants and families. The complete PMTCT package includes comprehensive antenatal (ANC) care, modified obstetric practices, antiretroviral therapy and infant feeding counseling and support. This editorial will focus mainly on the advances made in antiretroviral regimens for PMTCT.

The first major breakthrough for PMTCT was in 1994 when US/ French researchers proved that zidovudine (AZT) in pregnancy could reduce vertical transmission. The ACTG 076 study demonstrated that zidovudine (AZT) starting at 14 weeks gestation, intravenous in labor and for 6 weeks to the infant postnatally reduced vertical transmission by 67%<sup>1</sup>. Subsequently shorter regimens using AZT from 36 weeks gestation with or without dosing of the infant demonstrated 50% reduction in HIV transmission albeit less in breastfeeding populations<sup>2, 3</sup>. The most simple and feasible regimen to date is the HIVNET 012 regimen where mothers received a single 200mg tablet of nevirapine (NVP) at the onset of labor and the infant's received a single 2mg/kg/dose dose of NVP syrup within 72 hours of delivery. This regimen demonstrated a 47% reduction in HIV transmission at 6 weeks of age<sup>4</sup>. Recent data from Thailand have shown a further and significant reduction in transmission when single dose NVP to the mother and her infant was added to the standard AZT regimen starting at 28 weeks gestation. There was an 80% reduction in transmission in a Thai non-breastfeeding population with transmission rates of 2-3 % at 6 weeks postpartum<sup>5</sup>. The same regimen in a breastfeeding population in West Africa demonstrated vertical transmission rates of 5-6 % at the same time point<sup>6</sup>. Taha et al report modest benefit of postnatal NVP combined with AZT in infants who were identified at delivery<sup>7</sup>. Therefore infants born to HIV infected women and identified at delivery will benefit from postnatal prophylaxis. In the SIMBA study mothers received AZT and DDI starting at 36 weeks and the infants were randomized to NVP or 3TC prophylaxis during

breastfeeding. The study demonstrated a significant reduction in breast milk HIV transmission in both arms<sup>8</sup>. However, concerns were raised about the extrapolation of this study in breastfeeding populations, in view of the shorter breastfeeding period (mean 3.5 months), baseline CD4 count and viral load at delivery in the study mothers.

Since the HIVNET 012 study results were released many countries in resource limited setting implemented NVP for PMTCT with varying degrees of success. Emergence of NVP resistant mutations after single dose NVP have made the success of HIVNET 012 controversial in many circles. Some experts do not recommend use of NVP for PMTCT, since it may reduce the effectiveness of non-nucleoside reverse transcriptase inhibitors (NNRTI's) in future HAART regimens. In HIVNET 012, twenty percent of the mothers and 46% of the infected infants had resistant mutations at 6 weeks but they had faded 15-18 months later<sup>9</sup>. Most mothers had the common K103N mutation and the majority of infants had the Y181C mutation demonstrating no transfer of the resistant virus from mother to infant in that study. Preliminary data from Thailand suggested that women who had been exposed to single dose NVP for PMTCT were less likely to achieve undetectable viral load after 6 months on an NVP based HAART regimen. Fifty percent and 70% of the women exposed and not exposed to sdNVP respectively had undetectable viral load (< 50 copies/ml) after 6 months of HAART<sup>10</sup>. However, this difference was not noted in women who had received sdNVP more than 6 months prior to initiation of HAART. It is not completely clear what the clinical impact will be and studies are planned to try and address this important question. WHO still recommends that until more data is available sdNVP is one of the effective options for PMTCT in resource constrained settings<sup>11</sup>.

One cannot discuss PMTCT in Africa and not address the difficult issue of breast milk transmission. Breastfeeding still remains the most feasible option for feeding infants in most resource-constrained settings with the risk of HIV transmission through breast milk ranging from 14 -29%<sup>12</sup>. The only randomized controlled trial of vertical transmission in infants who were breastfeeding versus formula feeding demonstrated the increased risk of HIV transmission through breastfeeding. The attributable risk of breast milk transmission was as high as 44% in that study and breast milk transmission occurred in the first 6 months of life (75%). However, more recently data from Zambia suggest that most breast milk transmission may occur after 6 months of age<sup>13</sup>. Multiple studies have shown reduced breast milk transmission when infants are exclusively breast fed as opposed to mixed fed. Formula feeding in resource poor settings may reduce mother to child HIV transmission but remains difficult for many women and may potentially increase the risk of diarrhoea,

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malnutrition and death in infants. Therefore infant feeding counseling has to be strengthened and appropriate guidance and support provided for the mother to provide the best infant feeding in her context.

Currently studies are underway to reduce HIV transmission through breastfeeding by using NVP prophylaxis for periods ranging from 6 weeks to 6 months of age. Hyperimmune HIV globulin to mothers at 37 weeks gestation and soon after delivery to the infant is also being investigated to determine its effect on breast milk transmission.

In developed countries the use of HAART in pregnancy has reduced MTCT to less than 5%. In a resource constrained setting WHO recommends HAART in pregnancy for women at highest risk of MTCT. These include women with WHO clinical category III and IV and or CD4 count less than 200 cells/mm<sup>3</sup>. For those women who do not require HAART for their own health different PMTCT regimens can be provided according to the national guidelines. Further areas of research include: the need to determine the effectiveness of HAART in pregnant and lactating women in Africa, measurement of antiretroviral drug levels in the breast milk of women on HAART, the impact of single dose NVP for PMTCT on future response to HAART regimens containing Non nucleoside Reverse Transcriptase Inhibitors (NNRTIs) and observing the impact of early cessation of breastfeeding and infant replacement feeding in resource limited settings.

This issue of *African Health Sciences* includes two important articles, community effectiveness of PMTCT and the role of partners and stakeholders in the community. Documentation of the effectiveness of PMTCT programs at community level is limited and the need to partner with others in order to strengthen the services is a priority. Bajunirwe et al examines the effectiveness of perinatal AZT or single dose NVP in Uganda and compares the vertical transmission rates in women from 3 PMTCT centers to those of naïve women<sup>14</sup>. Effectiveness of NVP or AZT in the PMTCT program in Uganda had not been evaluated at the community level and despite this study's limitations, Bajunirwe et al were able to demonstrate the benefit of antiretroviral therapy in PMTCT at selected hospitals in Kampala, Uganda. Both AZT and NVP reduced vertical transmission to 16-17% while the women without ARV exposure had vertical transmission rate as high as 37% at 6 weeks of infant age. Tadesse found that 321 women attending antenatal clinics in 11 public health clinics and the university teaching hospital obtained most of their PMTCT information from the radio, health workers and religious groups<sup>15</sup>. Most women planned to breastfeed for more than 6 months and not breastfeeding an infant was perceived negatively. As pointed out by the writers wanting to test for HIV does not always reflect actual testing for HIV when the opportunity arises. Therefore despite high rates of those wanting to test and disclose in the above study, in practice most Africa women are not able to disclose to their spouse. From this study and many others,

male involvement in reproductive health and PMTCT remains a problem for most African countries. The media and health workers provide most of the essential information on PMTCT and therefore a concerted effort to increase communication through these and other relevant fora is critical.

PMTCT remains a critical area for scale up in Africa, where despite multiple programs, the number of HIV infected pregnant women who access them is less than 5%. There is still an urgent need to expand and scale up services in resource poor settings and prevent further infections in children. Efforts to increase the level of HIV testing in ANC, acceptance of PMTCT services, disclosure to partners and couple testing remain a priority. Increased community sensitization, counseling, treatment and support of women identified as HIV infected should improve acceptance of PMTCT services in Africa and subsequently reduce paediatric HIV.

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