Perinatal HIV and Option B+

The prevalence of HIV among pregnant women using public health services in South Africa is well documented.[1] The prevalence rose steeply from 1990 through to 2003. Subsequently a plateau phase has been observed, with the national prevalence at 29 - 30%.

An important cross-sectional and service-based survey by Goga *et al.* in 2010 and 2011 reported remarkable success in reducing perinatal mother-to-child transmission (PMTCT) rates[2] (and 'Effectiveness of the National Prevention of Mother-to-Child Transmission (PMTCT) Programme in South Africa: 2011 National SAPMTCT Survey Results', released by Minister Aaron Motsoaledi on 19 July 2012). Infants between 4 and 8 weeks of age attending primary or community health clinics were included in the study, irrespective of knowledge of maternal HIV status. HIV enzyme-linked immunosorbent assay tests were performed on dried blood spot heel-prick samples, and if positive HIV DNA polymerase chain reaction tests were done. The prevalences of HIV among the mothers and the transmission rates at 6 weeks could be determined. The researchers included 10 000 infants in each sample. The national transmission rates were 3.5% (95% confidence interval (CI) 2.9 - 4.1) and 2.7% (95% CI 2.1 - 3.2) in 2010 and 2011, respectively.

In contrast to the success in reducing mother-to-child transmission (MTCT) of HIV, maternal mortality in South Africa has increased by 200% over the past 20 years.[3] The 2005 - 2007 *Saving Mothers Report* showed that for the first time maternal deaths due to indirect obstetric causes have increased to account for a bigger portion of deaths (49.7%) than direct obstetric causes (45.9%).[4] This reflects the increase in maternal deaths due to AIDS. The trend continues with the 2008 - 2010 *Saving Mothers Report*, which shows an increase in institutional maternal death ratios from 151.8 to 176.2/100 000 live births.[5]

Relevant questions to be asked at the present phase of the evolving pandemic are whether all HIV-positive pregnant women should be commenced on highly active antiretroviral therapy (HAART). The World Health Organization (WHO) produced a programmatic update in April 2012.[6] Option B+ is suggested as a programme with substantial clinical and programmatic advantages. In Option B+ all HIV-positive pregnant women will be commenced on a single-pill fixed-dose HAART regimen containing tenofovir, lamivudine and efavirenz (EFV). The cost is reasonable, and will be about US$180 annually. Arguments in favour of this public health measure are:

- A contribution towards a global scale-up of PMTCT and eliminating paediatric HIV
- A significant reduction in HIV infection in discordant couples
- Increased country experience with operational and programme implementation of Options A and B
- Simplification and optimisation of the use of antiretrovirals (ARVs) with a standardised first-line treatment regimen.

Schouten *et al.* motivate that in countries such as Malawi, minimal access to CD4 count analysis limits rapid expansion of antiretroviral therapy (ART).[7] In addition, mortality among HIV-positive women with high CD4 counts in Zimbabwe within 24 months of delivery is increased 6-fold compared with HIV-negative women.[8]

Ford *et al.* published a systematic review and meta-analysis on the safety of EFV in the first trimester.[9] The risk ratio of birth defects when EFV-based were compared with non-EFV-based regimens was 0.85 (95% CI 0.61 - 1.20). The methodological quality of the studies included was judged to be moderate and the unlikely but possible bias to be due to selective abortion following EFV use, mentioned as a limitation of the analysis. There is, however, recent evidence that more safety information is required before resorting to a public health approach to PMTCT. Knapp *et al.* reported a prospective observational study of infants with *in utero* exposure to ARVs.[10] A panel of physicians blinded for ARV exposure reviewed clinical case reports of infants with congenital abnormalities. The only significant association between an ARV and congenital abnormalities following a multivariate logistic regression analysis was EFV exposure in the first trimester. Of the 47 infants with first-trimester exposure to EFV, 6 (12.8%) had congenital abnormalities. Siberry *et al.* reported that infants exposed to an antenatal tenofovir-containing HAART regimen had slightly but significantly lower length-for-age and head circumference at 1 year of age.[11] Pharmacological surveillance at least will be required, especially for women who fall pregnant while on an EFV-based HAART regimen.

Experienced clinicians confirm that MTCT of HIV is commonest when women do not attend antenatal clinics, do not adhere to ART, or develop resistance to the drugs. Maternal morbidity and mortality are also mostly confined to women with severely impaired immunity and often also co-morbidity in the group mentioned above, or with advanced disease or co-morbidity that are not detected until complications occur. Option B+ will stretch the resources of the public health service and weaken the ability of health workers to identify the group at high risk of transmission and maternal morbidity and mortality.

A large collaborative study is currently being conducted to investigate the global public health PMTCT as well as maternal and infant health questions (the protocols are available on request from the PROMISE Operations Center, email promise.ops@fstrf.org). Funded by the American National Institutes of Health (NIH) through the International Maternal Paediatric Adolescent Clinical Trials group (IMPAACT), the Promoting Maternal and Infant Survival Everywhere (PROMISE) study comprises separate clinical research arms for women who intend to breastfeed and formula-feed their infants. The antepartum component of the study will randomise women with CD4 counts ≥350 cells/μl to continue antenatal zidovudine (AZT), and during labour AZT and nevirapine, or to receive HAART.

- The breastfeeding arm will include 3 400 mother-infant pairs and will be conducted in 3 cities in South Africa, and in India, Malawi, Tanzania, Uganda and Zimbabwe.
- The formula-feeding arm will include 1 000 mother-infant pairs and will be conducted in 2 cities in South Africa as well as in India.

The postpartum component of the study will randomise women who were on HAART during pregnancy to stop or continue HAART following cessation of breastfeeding or delivery (formula-feeding arm). The women will be followed up for 2 years to assess the effect of continuing or stopping HAART on their health.

Countries affected by the global HIV pandemic have moved from despair to hope over the past 20 years as knowledge and skills to combat the disease have rapidly increased. The gains towards preventing MTCT of HIV are remarkable, even in lesser-resourced countries. The way forward for perinatal ARV use should, as in the past, be guided by sound scientific evidence.

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Owing to the rapidly increasing number of submissions to SAJOG, *Professor Leon Snyman has been appointed Section Editor for Gynaecology for the journal. Professor Snyman, of the Department of Obstetrics and Gynaecology at the University of Pretoria, is a sub-specialist in Gynaecological Oncology and takes a keen interest in laparoscopic surgery. He will be an enormous help in improving the throughput of submissions to the journal.* – Editor