

## Editorial

### TWO FRONT BURNERS ON THE AFRICAN MORBIDITY MORTALITY SCALE

The present issue of the Western Nigeria Journal of Medical Sciences contains a review article on The Human Immunodeficiency Virus (HIV) infection and an investigative paper on Home Management of Malaria. These are two preventable diseases which have remained scourges in many sub-Saharan African populations. Decades ago, malaria and HIV infections together with tuberculosis, measles, acute respiratory infections and diarrhoeal disorders were classified by the G8 / G7 leaders in collaboration with WHO, UNICEF. Etc as diseases of poverty and targeted for massive effort<sup>1</sup>.

Ezechi et al have written a review on the Prevention of Mother to Child Transmission of HIV infection. This is a subject of immense importance because the vast majority of childhood HIV infections take place via the mother to child vertical route plus the fact that HIV/AIDS burden in Nigeria is the third largest in the entire world after India and South Africa. Estimates run into 2.86 million for the infected and 1.5 million for cumulative deaths<sup>2,3</sup>. It is obvious that the way to control HIV/AIDS in children is to prevent it in adults.

Malaria is a persisting old problem. Since over two decades ago, it had been known to contribute 41% to total underfives morbidity and 30% to total underfives deaths in Nigeria. Even now the malaria situation has not improved much. 40% of the world population mostly in the developing countries is at risk of malaria with 300 to 500 million yearly infections and estimated 1- 2 million deaths. Ninety percent of malaria cases and deaths are among the underfives children in Africa.

The plans of WHO for global eradication have given way to the less definitive plans of campaigns and controls. In the mean time, vectors have developed resistance to insecticides and parasites to chemotherapeutic agents. The ROLLBACK MALARIA strategy initiated by WHO, UNICEF, UNDP and the world bank in 1998<sup>1,4,5</sup> is a package comprising of focus on the highest risk group of mothers and children, preventive treatment of pregnant women, access to rapid diagnosis and treatment at village/community level, better use of existing control tools, interventions like integrated childhood illness management to reduce malaria deaths, improved surveillance and multiple prevention measures including insecticides bed nets and vector control. Double chemotherapy was introduced to combat rising prevalence of resistance to drugs.

However, today, malaria remains a scourge in Nigeria and similar poor resource countries. The paper by Oyedeji et al on the home management of malaria shows some of the reasons why this is so. If we are able, somehow to combine prompt and correct home treatment of malaria with its preventive measures, we could achieve better control.

Unless we are able to turn policy at the governmental and the sponsoring health agencies levels to practice at the village/community and home levels, we can be accused of professing prevention very much but practicing it very little. Principally too, we must address the underlying poor socio economic conditions which have turned HIV and malaria infections to diseases of poverty. After all, it has been stated that poverty of the spirit and of resources remains the antecedent risk factor for preventable disease<sup>6</sup>.

Of course, the future break through to the discovery of effective and affordable vaccines to these infections is the real hope; but should the suffering and deaths continue while we wait for the vaccines?

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## Editorial

### References

1. Eva Ombaka Massive Effort against Diseases of Poverty. Contact 2001, 173; 3-5
2. Ezechi O. C., Ekong E, Kanki P, Murphy R. HAART treatment outcome in Nigerians with low baseline CD4 cell counts. Proceedings of the Presidential Emergency plan for AIDS relief. Annual meeting June 12-16 2006; South Africa Abstract No 483.
3. Federal Ministry of Health (FMOH) Nigeria. National guideline for HIV/AIDS treatment and care in adolescents and adults. FMOH, Nigeria May 2007
4. Rolling back Malaria The World Health Report 1999 WHO Geneva P 49
5. Facts and Figures about Malaria in Africa WHO Newsletter WHO Lagos June 2000 Vol. 16 (2)
6. Braithwaite R. I, Lythcott N. Community empowerment as a strategy for health promotion for black and other minority populations. JAMA 1989; 261 : 282-3

## INVITED ARTICLE

### Prevention of Mother-To-Child Transmission of HIV Infection : a review

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#### Background

Nigerian HIV/AIDS disease burden is the third largest worldwide, behind India and South Africa, with estimated cumulative death of 1.5 million people, 2.86 million infected persons and more than two million children orphaned<sup>1,2</sup>. The high burden of the disease continues to constitute a major public health concern for the country. The epidemic has impacted all segments of the society, but most especially women in their most productive and reproductive years. Over the years, an epidemic, once dominated by infected males, has become progressively feminised. In Sub Saharan Africa, where about two-thirds of global disease burden resides, 61% of adults living with HIV are women<sup>3</sup>. In Nigeria, approximately 60% of adults living with HIV/AIDS are women<sup>4</sup>. The increasing HIV prevalence among women also showed an increase in mother-to-child transmission of HIV. Until 2004, over 4.3 million children have succumbed to the AIDS epidemic worldwide and in 2004 an estimated 700,000 children under the age of 15 years became infected with HIV<sup>3</sup>. The vast majority (>90%) acquired the infection through mother-to-child transmission (MTCT). In the absence of any intervention, rates of MTCT of HIV can vary from 15 to 30 per cent in the developed countries and can reach as high as 30 to 45 per cent in developing countries. This difference is mainly attributable to infant feeding practices in the developing world<sup>5,6</sup>.

Currently 95 per cent of vertical transmission occurs in the developing countries and the challenge in these settings is to find the most cost-effective and feasible intervention to prevent MTCT. The transmission of HIV from an infected mother to her child can be reduced to less than 2 per cent by intensive interventions that include combination therapy of potent antiretrovirals, obstetrical interventions including elective caesarean section at 38 week and complete avoidance of breastfeeding<sup>6</sup>.<sup>11</sup> Mother to child transmission of HIV is tragic and should be drastically reduced, particularly in resource poor settings, where fragile and poorly funded health systems hamper care and prevention efforts<sup>12</sup>. The impact of the disease is best captured

by data suggesting that at least one third of HIV infected children in developing countries die within their first years of life. MTCT has become a critical child's health problem in Africa. It contributes to severe morbidity and significant mortality and equally undermines the impact of programmes that had significantly reduced child mortality in previous decades<sup>12,13</sup>. The development of successful and specific MTCT prevention intervention/strategies that reduces this transmission to less than 2% has been one of the greatest successes in AIDS research. Prevention of mother-to-child-transmission of HIV infection is a politically and scientifically accepted approach to reduce the impact of HIV, especially on the children<sup>14</sup>.

We discuss in this paper the mechanisms of mother to child transmission, factors associated with it, magnitude of MTCT in Nigeria, care of HIV positive pregnant mother and her infant, and the strategies to prevent mother to child transmission including infant feeding option in the context of HIV.

#### HIV and Women

Considered a small part of the HIV epidemic even a decade ago, AIDS in women is now properly understood as a global health crisis of horrific proportions. The demographic characteristics of those affected by the epidemic have changed dramatically since the first cases were reported in 1981. Unlike the early days of the HIV and AIDS epidemic in the United States, when the affected population consisted overwhelmingly of homosexual men, leading some to assume incorrectly that the epidemic would remain contained within the gay population, today new cases of HIV infection result predominantly from heterosexual contact and MTCT, with a disproportionate representation of women flocks<sup>16,17</sup>. UNAIDS estimates that 18.5 million women have HIV/AIDS, roughly equal to the burden among men. In Sub Saharan Africa alone, 15 million women are estimated to be HIV infected<sup>3</sup>. Without the availability of antiretroviral therapy, these women have vastly shortened lives and are living behind a generation of orphans, many of whom will also be

HIV infected if proven and effective PMTCT strategies are not universally implemented. Currently, almost half of the new HIV infections in the reproductive age group are women<sup>3</sup>. In Nigeria, women make up an ever-increasing proportion of HIV/AIDS cases. According to 2005 estimates, approximately 60% of reported HIV/AIDS cases now occur in women. However, compared with men, less information is available for them on the natural history of HIV disease, and they continue to frequently experience reduced access to proper diagnosis, treatment, and antiretroviral therapy<sup>2,4,18</sup>. In Nigeria unprotected heterosexual intercourse is the primary risk factor for HIV infection in adolescent and adult women. More than 90% of all infected Nigerian women get the virus from a male sex partner; the remainder become infected through transfusion with HIV infected blood and use of unsterilised sharps and instruments. Intravenous drug use is not a common mode of HIV transmission among Nigerian women.

The increasing HIV disease burden in Nigerian women may suggest a high risky behaviour among the women. However, available evidence shows otherwise<sup>19</sup>. There are various factors that make women vulnerable to HIV infection. Available evidence shows that the risk of becoming infected with HIV and STI during unprotected vaginal intercourse is 2-4 times higher for women than men<sup>4,20</sup>. The factors responsible include biologic factors of large vaginal mucosa surface area, higher viral concentration in the semen compared to vaginal secretions, immature cervix and scanty vaginal secretion in young women and the almost asymptomatic nature of STIs in women. Socioeconomic factors fueling the epidemic in women includes economic and societal approved dependency on men, polygamy, widow inheritance, wife hospitality and practices in which first daughters do not get married but raise children for the family. Other factors are gender inequality, poor education, discrimination against the girl child, female genital mutilation, early marriage, women traffic, sexual harassment, violence, stigma and various forms of discrimination.

To reduce the vulnerability of women to HIV infection, it is important to empower women through education, legislation against practices that put women at risk and political commitment.

#### Effect of Pregnancy on HIV Disease

Though both HIV and pregnancy cause immune suppression, there appears to be no serious deleterious effect of pregnancy on HIV, provided the infection is early and asymptomatic<sup>21</sup>. Studies in the United States and Europe have shown no effect of pregnancy on the progression of HIV disease<sup>22-25</sup>. The largest study included women with known date of seroconversion and reported that the adjusted relative risk of progression from HIV infection to the acquired immunodeficiency syndrome (AIDS) associated with pregnancy was 0.7 (95 percent confidence interval, 0.4 to 1.2)<sup>22,25</sup>.

Reports from developing countries suggest that progression accelerates with pregnancy, but it is difficult to interpret such reports because the samples are small and the studies are subject to selection bias related to the presence of indications for testing<sup>26-28</sup>.

The vast majority of HIV infected women are in their childbearing years and fertility does not seem to be impaired except in the end stage severe immunodeficiency state<sup>18,29</sup>.

Plasma HIV viral load and CD4 count are the laboratory markers for HIV infection. CD4 count range in healthy adults is 500-1500 cells/mm<sup>3</sup>. In all women, the absolute CD4 count decreases to 543±169 cells/mm<sup>3</sup> during pregnancy irrespective of whether they are HIV positive or negative<sup>30</sup>. In its report, Centre for Disease Control and Prevention concluded that maternal morbidity and mortality are not increased by pregnancy in seropositive but otherwise asymptomatic women<sup>31</sup>.

#### Effect of HIV on Pregnancy

Reports from developed countries shows that HIV has little or no effect on pregnancy outcome<sup>32,33</sup>, however studies in developing countries have shown greater frequencies of preterm birth, low birth weight, intrauterine growth restriction, and stillbirth among the infants of HIV-infected women than among those of similar groups of women who were HIV-negative<sup>32,34</sup>. No studies have indicated that there is an increase in the frequency of birth defects related to HIV infection, and the theory that there is a syndrome of malformation related to HIV infection has not been proved<sup>32,35</sup>. The observation recorded in developed countries may be due to multiple factors of high base line immunity, adequate antenatal care, early diagnosis and antiretroviral therapy<sup>21</sup>.



### Mother To Child Transmission of HIV(MTCT)

Mother to child transmission remains the main mode of acquisition of HIV infection in children. The number of children living with HIV infection is estimated at 1.3 million with 3.8 million deaths since the epidemic began<sup>3</sup>. Each year approximately 2.4 million infected women give birth and 1800 infants acquire HIV infection every day. MTCT can occur *in utero*, *intra partum*, or *post partum* through breast feeding<sup>36</sup>. However it is important to note that the exact timing of HIV transmission from mother to the child is not known with certainty<sup>27</sup>. Some fetuses are infected in utero, others in late gestation or during delivery or during puerperium via breast milk in lactating mothers. The relative proportion of transmission that occurs intrapartum versus intrauterine remains controversial<sup>27</sup>. However data from polymerase chain reaction studies have confirmed the rarity of MTCT in early pregnancy<sup>12</sup>. The current hypothesis is based on experimental and clinical observations that support these three different periods of transmission<sup>27,37</sup>. Bryson and colleagues have proposed a working definition to determine the timing of MTCT<sup>38</sup>. A child is classified as having been infected during pregnancy if the HIV genome is detected within 48 hours of delivery by polymerase chain reaction or viral culture, and during delivery if those diagnostic tests were negative in a sample taken during the first 48 hours after delivery, but become positive in subsequent samples taken within 7 to 90 days of delivery.

In HIV positive women who do not breastfeed, it is estimated that without intervention, over 80% of HIV transmission from mother to child occur late in the third trimester (from 36 weeks), during labour and at delivery, with fewer than 2% of transmissions occurring during the first and second trimesters<sup>14,36</sup>. In regions where HIV-infected women are likely to breastfeed, as much as 44 percent of HIV infection of infants can be attributed to breastfeeding<sup>39</sup>.

The risk of mother to child transmission varies between 15 and 20% in non breastfeeding women and between 25 and 50% in breastfeeding women in the absence of any intervention<sup>40,41</sup>. Interventions such as antiretroviral therapy, caesarean section and avoidance of breastfeeding can reduce the risk of MTCT HIV transmission from 25 to 30% to less than 2%<sup>6,7,8,11,12,30,40</sup>.

**MTCT during pregnancy:** The sperm and the ovum lack the CD4 receptor and therefore cannot be

infected by HIV<sup>12</sup>. This implies that at fertilisation, the resulting zygote does not contain the HIV genome. In most HIV infected women, HIV does not cross the placenta from mother to fetus.; instead, the placenta acts as a physical barrier that shields the developing fetus from circulating viruses in the mother's blood<sup>12,42</sup>. This protection from the placenta may break down, however, if the mother has a placental infection during pregnancy or develops a high level of HIV virus during pregnancy<sup>12</sup>.

**MTCT during labour and delivery:** Infants of HIV positive mothers are at great risk of becoming infected with HIV during childbirth. During this period, 10-20% of newborns will acquire HIV infection if no steps are taken to prevent transmission. Most infants who become infected during labour and delivery do so by sucking, imbibing, or aspirating maternal blood or cervical secretions that contain HIV<sup>12</sup>.

**MTCT postpartum(breastfeeding):** HIV is present in breastmilk, although in viral concentrations significantly lower than those found in blood<sup>12,43</sup>. Studies using animal models suggest that cell free HIV in breast milk could infect cells of the intestinal mucosa<sup>44,45</sup>. M cells, which are specialised epithelial cells found in the Peyer's patches of the intestinal mucosa, may allow infectious agents such as HIV to cross the intact mucosa by engulfing and transporting the pathogens and presenting it to macrophages that indent the serosal surfaces of the M cells<sup>46</sup>. According to Dunn DT and colleagues, on the average, about 15% of babies born to HIV positive mother will become infected through prolonged breastfeeding. This transmission risk is doubled when the mother becomes infected while breastfeeding<sup>47</sup>. Seventy five percent of infections among breastfed infants occurs before six months of age<sup>12,39</sup>.

Breastfeeding is one of the major reasons for the wide differences in MTCT rates between developed and African countries, Nigeria inclusive<sup>40,48</sup>.

### Risk factors for MTCT

Several factors have been shown to be associated with transmission of HIV from mother to child<sup>48,49,50,51,53</sup>.

For the purposes of this review these risk factors have been grouped under maternal, viral, obstetrics or fetal factors.

**Maternal Factors:** The presence of AIDS-defining illnesses or acute HIV disease, which correlates with

a high level of viremia and lower CD4+ cell counts, is associated with higher risk of MTCT<sup>12</sup>. Several studies have shown that women with concomitant maternal illness and disease (malaria, sexually transmitted infections, bacterial vaginosis, syphilis)<sup>12,65-68</sup>, and certain habits (unprotected sex with multiple sexual partners, substance abuse, and cigarette smoking)<sup>12,69,70</sup> are more likely to transmit HIV to their babies.

The use of antiretroviral drugs during pregnancy substantially reduces MTCT of HIV, be it monotherapy, double therapy, or highly active antiretroviral therapy (HAART)<sup>12</sup>. However regimens like HAART, that optimally reduces viral load are more effective in preventing MTCT<sup>71,72,73</sup>. MTCT rate less than 2% have been reported in women who received HAART during pregnancy<sup>7,12</sup>.

**Maternal HIV-1 plasma viral load:** Garcia et al<sup>53</sup> followed 552 HIV-infected pregnant women, of whom 321 used no ART. They reported that perinatal transmission rates were 0% when HIV-1 RNA was less than 1000 copies/ml, and increased stepwise as maternal VL increased: 20.0% with HIV-1 VL 1000±10 000 copies/ml; 24.1% with HIV-1 VL 10 001±50 000 copies/ml; 31.6% with VL 50 001±100 000 copies/ml; and 63.3% with VL 4100 000 copies/ml. There was no VL above which transmission was always observed<sup>51</sup>. Although maternal VL seems paramount at predicting transmission, Sperling et al<sup>54</sup> showed that perinatal transmission, albeit at an extremely low rate, did occur in mothers in the lowest VL quartile, and even if VL was below the quantitative limit of the assay used. Because no upper or lower threshold can be described, VL data, although useful in assessing risk, cannot definitively predict whether transmission will or will not occur. Low maternal CD4+ cell counts at the time of delivery have been associated with increased risk of transmission<sup>50,51</sup>. However, this association was established before the availability of VL measurements. A low CD4+ cell count may be a surrogate marker of high maternal viral burden<sup>51</sup>. In this regard, the most important predictive factor is maternal HIV-1 plasma viral load<sup>49,50,51,52,53,54</sup>. The higher the maternal VL, the greater the likelihood of vertical HIV transmission.

**Obstetric factors:** Prolonged rupture of fetal membranes (defined as rupture of fetal membrane for more than 4 hours), which increases newborn exposure to maternal blood/body fluids, has been

shown to increase the risk of vertical transmission<sup>51,55</sup>. Other obstetric factors, such as placental abruption, use of fetal scalp electrodes, performing an episiotomy, labor-induced vaginal lacerations, chorioamnionitis, and presence of ulcerative sexually transmitted diseases in the maternal genital tract may similarly expose the newborn to maternal blood or secretions<sup>51,56-58</sup>. Procedures such as amniocentesis and chorionic villus sampling, which are usually performed during the first or second trimester, may also be a risk factor for intrapartum transmission<sup>50,51,57,58</sup>. Although these obstetric factors/complications are important, they only contribute to the mode by which HIV is most often transmitted, namely labor and a spontaneous vaginal delivery. High levels of HIV in cervicovaginal fluid have been shown<sup>51,60</sup> to increase the risk of vertical HIV transmission. Chuachoowong et al<sup>60</sup> found that short-course antepartum zidovudine administration decreased cervicovaginal HIV RNA levels and reduced the rate of perinatal transmission.

Elective CS performed before the rupture of membranes and labour has also been studied as a means to circumvent the risk posed by vaginal delivery<sup>51,61,63</sup>. A meta-analysis by the International Perinatal HIV Group<sup>51,61</sup> of 15 prospective cohort studies examined mode of delivery and the risk of vertical HIV transmission in approximately 8000 HIV-infected pregnant women. The results showed a significantly lower risk of vertical transmission after an elective CS compared with either a vaginal delivery or CS performed after membranes had ruptured. Even though ART reduced transmission rates to 7.3% in HIV-infected mothers who did not undergo elective CS, mothers who had an elective CS and took ART had a rate of transmission of only 2%. These results are impressive, but were accumulated prior to the use of highly active antiretroviral therapy (HAART) during pregnancy<sup>51</sup>. However at VL less than 1000 copies/ml, CS do not confer any advantage over vaginal delivery<sup>7</sup>. Considering the fact that HIV infected pregnant women have higher rates of postoperative complications and infections, particularly when such procedures are performed in resource-poor nations<sup>51,59</sup>, universal prescription of CS may not be acceptable on the basis of risk benefit ratio. The usefulness of elective CS in countries where potent ART options are available may be reserved for those HIV-infected pregnant women who have VLs

greater than 1000copies/ml at the time of delivery<sup>7,51</sup>.

**Infant factors:** Prematurity is a risk factor for increased transmission probably due to thin skin, susceptible mucous membranes, immature immune functions, genetic susceptibility and low levels of maternal antibodies in the premature infant.

**Breastfeeding:** The major postpartum risk of HIV transmission is breastfeeding. Nduati and colleagues<sup>39</sup> from Kenya studied the effect of breastfeeding and formula feeding on the rates of mother to child HIV transmission among ART pregnant women. In the study they found that 61(31%) of 197 infants became HIV seropositive in the breastfeeding arm compared with 31(15.2%) of 204 infants who were given formula. This difference was statistically significant. Also noted was the fact that more than half of the overall risk difference was observed by 6 weeks of life, with additional continuous risk over the remaining 22 months of the study. The results from this and other studies<sup>47,51,63</sup> provide compelling evidence for the risk of HIV transmission with breastfeeding. In industrialized countries this important risk factor has been effectively curtailed by advising all HIV-infected mothers not to breastfeed their offspring<sup>7,51</sup>. Such an injunction is more difficult to implement in resource poor countries, where ready, affordable provision of formula coupled with access to a clean water supply remains problematic outside the purview of clinical trials.

In the postnatal period breast feeding in the presence of cracked nipples or mastitis, feeding by both breast feeds and top feeds, continuation of breastfeeds for prolonged periods of time, seroconversion of the mother during postnatal period, high viral load, low CD4 cell count, all increase the risk of transmission of HIV<sup>6,7,64</sup>.

Very important in MTCT are other background factors of sociocultural factors, gender violence and inequality, stigma and discrimination, poor attitude of health workers and poor knowledge of the health workers, access to ARV drug, placental infections including malaria and status of malaria prevention programme in the country.

### Magnitude of MTCT in Nigeria

Nigeria is home to over 150 million people, with females representing approximately half of the population. Majority of these females are within the reproductive age group. The 2005 HIV sentinel surveillance reported the HIV prevalence among pregnant women as 4.4%<sup>48</sup>. Approximately 300,000

of the 6 million pregnancies occurring in Nigeria annually are in HIV positive women; putting about 300,000 infants at the risk of HIV either during pregnancy, labour/delivery and post delivery through breastfeeding<sup>7,48</sup>. Without any intervention, 65-117 of 500 of the HIV exposed babies in Nigeria will become HIV positive<sup>7,48</sup>. Considering the fact that paediatric HIV infection is the future of HIV, it will be almost impossible to control HIV in Nigeria if nothing is done to prevent these new infections.

### Strategies for prevention of mother to child transmission.

The WHO<sup>74,75</sup> four-pronged strategy for preventing mother to child transmission of HIV infection addresses a broad range of HIV-related prevention, care, and treatment and support needs of pregnant women, mothers, their children and families. This comprehensive approach includes the following four elements:

**1. The primary prevention of HIV infection among women, especially young women.** Avoiding infection in parents-to-be will help to prevent HIV transmission to infants and young children, as well as help towards other prevention goals. HIV prevention needs to be directed at a broad range of women at risk and their partners. As primary HIV infection during pregnancy and breast feeding poses an increased threat of MTCT, HIV prevention efforts should address the needs of pregnant and lactating women, especially in high prevalence areas. In addition, special effort should be made to prevent future infection among women diagnosed HIV-negative especially in antenatal care settings.

**2. The prevention of unintended pregnancies among HIV-infected women.** This includes the strengthening of reproductive health (including family planning) services for all women, including those who are infected, enabling them to make informed decisions about their future reproductive life, including when to seek appropriate support and services to prevent unintended pregnancies. Most HIV-infected women in the developing world do not know their serostatus. Increased availability of counseling and testing services would enable them to obtain essential care and support services, including family planning and reproductive health services, in order that they can make informed decisions about their future reproductive lives.

**3. Provision of specific interventions to reduce HIV transmission from HIV infected women to their infants.** For HIV-positive women who do

become pregnant, WHO has identified a package of interventions to prevent the transmission of HIV infection from mother to her infant. It includes the use of antiretroviral drug regimens for HIV-infected pregnant women and their newborns, safe obstetric practices and counseling and support for HIV-infected pregnant women on infant feeding options.

### 4. Provision of treatment, care and support for HIV-infected mothers, their infants and family.

There should be full integration of care and support into ongoing efforts to improve maternal and child health services which should be tailored to the needs of women for safe and effective antenatal, obstetric and reproductive health services. This also includes sexual and reproductive health interventions for HIV-infected women and other care for HIV-infected women and for children born to HIV-infected mothers.

**PMTCT Specific Interventions.** The specific interventions that have been proven to reduce mother to child transmission of HIV virus include;

**a. Provision of essential obstetric care.** The only sure way of detecting and providing care for HIV positive women is to universally provide care for all women during pregnancy. The integration of HIV comprehensive care into all obstetric services at all level is the only sure way of identifying HIV positive women. In antenatal and labor ward settings, the Nigerian PMTCT guidelines recommends universal HIV counselling and testing, with the opportunity to decline<sup>48</sup>. This is followed by one-on-one post-test counseling and is associated with a high uptake of testing<sup>4,7,12</sup>. Availability of rapid testing allows women to be tested and receive their HIV test results at the first prenatal visit<sup>12</sup>. When HIV status is known, mothers can be evaluated for ART eligibility and offered ART treatment and prophylaxis as indicated<sup>4,12,48</sup>. Antenatal care for HIV positive women is essentially the same as for HIV negative women; however women at late stage of HIV disease may need specialist care like all other pregnant women with medical illness. HIV negative women should be provided HIV prevention services towards ensuring that they remain negative during and after pregnancy. Those women found negative during the antenatal period should be retested during late pregnancy and or in labour. Three doses of malaria intermittent preventive treatment using sulfadoxidine pyrimethamine should be provided for HIV positive women after the 13th week.

**b. HIV testing and counseling.** PMTCT services should be integrated into the primary health

care systems. All women accessing antenatal care should be offered adequate counseling which should include a well delivered counseling and testing for HIV screening at first visit. They should also be counseled on the need for antiretroviral prophylaxis if positive and ineligible for ART, or counseling for ARV if eligible as well as safe delivery and infant breast feeding options<sup>74,75,76</sup>.

### c. Antiretroviral treatment and prophylaxis

The use of antiretroviral drugs during pregnancy is important for PMTCT and should follow the national guidelines for ART and prophylaxis<sup>2,4,48,74,75,77</sup>. For women diagnosed with HIV during pregnancy and eligible for treatment with ARVs, treatment should be initiated as soon as possible. Commencement of treatment may be delayed until after the first trimester because of nausea and vomiting associated with not only the pregnancy but with some of the ARV drugs. Equally some of these drugs are still not in the market and their risk of teratogenicity have not been conclusively excluded. However, when the woman is severely ill, the benefits of treatment outweigh any potential risk to the foetus. Efavirenz (EFV), an antiretroviral drug that is considered potentially teratogenic is not recommended until after the first trimester of pregnancy and should be avoided in women of childbearing age unless effective contraception can be ensured. Women who do not need treatment (ie, women who are not "eligible" for treatment based on the National guidelines), should be offered ARV as prophylaxis to prevent MTCT using either Zidovudine alone from 28 weeks or zidovudine and lamivudine from 34 weeks if seen after 33 weeks. These drugs should be continued for 5-7 days after delivery. Single dose nevirapine should be added in labour. For women seen first or diagnosis made first in labour single dose nevirapine should be given and zidovudine and lamivudine for 5-7 days<sup>48,77</sup>.

**d. Safe delivery practices:** Interventions that can reduce MTCT during labour and delivery include the following:

1. Administration of ARV treatment and prophylaxis during labour in accordance with national protocols.
2. Use of good infection prevention practices for all patient care.
3. Application of universal safety precautionary measures, which include the use of protective gear, safe use and disposal of sharps, sterilization of equipment, and safe disposal of contaminated materials.



4. Minimizing cervical examinations, performed only when absolutely necessary and with appropriate clean technique.
  5. Prevention of prolonged labour through active management of labour.
  6. Avoidance of invasive foetal monitoring methods, instrumental deliveries, routine artificial rupture of membrane and traumatic delivery and routine use of episiotomy.
  7. Prevention of postpartum haemorrhage and adoption of safe blood transfusion practices.
  8. Adopt safe and appropriate delivery methods. safe . Cesarean section, when performed before the onset of labour or membrane rupture, has been associated with reduced MTCT. Generally the choice of elective cesarean should be based on the viral load of the woman before delivery and availability of expertise needed for the surgery and safety of the procedure in the environment. For women with viral load of = 1000copies/ml elective CS confers no benefit over vaginal delivery.
- e. Safe infant-feeding practices:** A consensus statement on HIV and infant feeding has been adopted by all relevant United Nations departments and agencies, following a technical consultation in Geneva, Switzerland, in October 2006 organized by WHO<sup>78</sup>. Its main recommendations include that the most appropriate infant feeding option for an HIV-infected mother should continue to depend on her individual circumstances, including her health status and the local situation, but should take greater consideration of the health services available and the counselling and support she is likely to receive. When replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS), avoidance of all breastfeeding by HIV-infected women is recommended. Exclusive breastfeeding is only recommended for HIV-infected women if replacement feeding is not AFASS and only for the first few months of life. If an HIV-infected woman chooses to breastfeed, she must be cognizant that breastfeeding is not without risk to the infant. However, the risk of HIV infection must be balanced with the risks associated with replacement feeding, and this must be done for each HIV-infected woman on an individual basis. Women need support to choose and adhere to the best option for them. Governments and others should provide this support, and also take action in the priority areas described in the UN HIV and infant feeding framework for priority action.
- f. Care of the HIV exposed Child. Expansion of PMTCT services will lead to the identification of HIV exposed infants and provide opportunity for early intervention and care. The immediate care of the newborn exposed to HIV should follow standard practice. Regardless of the mother's HIV status at delivery all infants should<sup>48</sup>;
    - i. Have their mouth and nostrils wiped with gauze at delivery of the head.
    - ii. Be handled with latex gloves until maternal blood and secretions are washed off.
    - iii. Have the cord clamped and cut under cover of a lightly wrapped gauze swab to avoid blood spurting.
    - iv. Be kept warm
    - v. Be washed with warm chlorhexidine solution or wiped dry with a towel or surgical cloth to remove maternal body fluids.
    - vi. Be suctioned if indicated using mechanical/electrical suction unit at pressure below 100mmHg or bulb suction. Mouth operated suction is contraindicated.
    - vii. Have vitamin K administered, ensuring injection safety.

It is important at this point to find out and support the mother's feeding choice and support her. All babies born to HIV positive mothers are exposed to HIV infection and should receive post exposure prophylaxis, given as single dose nevirapine 2 mg/kg body weight as soon as possible after delivery but within 72 hours, plus zidovudine 4 mg/kg body weight 12 hourly for 6 weeks<sup>48</sup>.

**Establishing the HIV status of HIV exposed baby**  
Determining the status of children exposed to HIV during pregnancy, labour or postpartum is an important part of follow up services in PMTCT programmes. HIV testing and counselling should therefore be part of follow up care of these children. In the first 18 months of life, methods of HIV testing that rely on the detection of the HIV virus or products are required as HIV antibody testing may not reliably confirm the true HIV status of the infant. Screening of infant less than 18 months should be done using DNAPCR from the age of 6 weeks. This can be done either on a whole blood sample or a dried blood spot (DBS) on a filter paper. Breast-feeding babies who tested negative to DNA PCR

should have a repeat test after 6 weeks of cessation of breast-feeding.

#### Barrier to PMTCT

Significant progress has been achieved in prevention of HIV MTCT. However, experiences in many countries suggested that ARV prophylaxis for PMTCT alone had only limited impact<sup>4,7,12,79</sup>. Even in facilities where ARV prophylaxis was available, still a number of pregnant women would drop out at different steps of the health care process<sup>79,80</sup>. Many countries reported low uptake of HIV testing. The most important barrier to use the services was found to be fear of stigma and discrimination among HIV positive pregnant women<sup>7,12,81-84</sup>. Poor counselling or lack of counselling meant that HIV positive pregnant women lacked awareness on PMTCT opportunities, which limited their access to these services<sup>85,86</sup>. Worryingly some studies revealed that health staff were unwilling to provide appropriate care for HIV positive pregnant women, often because of their own fear or lack of knowledge<sup>87-89</sup>. Socioeconomic practices, low status of women and nondisclosures are other barriers to effective implementation of PMTCT strategies.

#### Conclusion

Mother-to-child transmission of HIV is a global problem. While MTCT rates less than 2% have been achieved in developed countries, rates from developing countries are still embarrassingly high. The differences in rates are as a result of challenges of choice, availability, affordability of antiretroviral agents, issue of infant feeding choices, stigma and discrimination, non disclosure and other sociocultural factors. It is therefore evident that to achieve the same MTCT rate reported from developed countries, these challenges and barriers should be given same priority as the medical interventions. The challenge is to find the most cost-effective and feasible intervention to achieve zero per cent transmission of HIV from an infected mother to her child while addressing the other sociocultural factors.

#### Acknowledgements

We thank our colleagues at the Clinical Sciences Division and Human Virology Laboratory, Nigerian Institute of Medical Research, Lagos for their commitment, dedication and perseverance as the burden of Nigerians accessing care at our facilities keep increasing daily. To the HIV positive pregnant women and their offspring your now familiar celebrations of a HIV negative DNA PCR results have kept us going despite the mounting challenges.

#### Reference

1. Ezechi OC, Ekong E, Kanki P, Murphy R.. HAART treatment outcome in Nigerians with low baseline CD4 cell counts. Proceedings of the The Presidential Emergency Plan for AIDS Relief Annual Meeting June 12-16 2006 Durban, South Africa. Abstract No 483.
2. Federal Ministry of Health (FMoH), Nigeria. National Guideline for HIV/AIDS treatment and care in adolescents and adults. FMoH, Nigeria May 2007.
3. UNAIDS. AIDS Epidemic Update. Geneva: UNAIDS December 2007.
4. Nigerian Institute of Medical Research (NIMR), Nigeria. Prevention of mother to child transmission of HIV. In: Training manuals for Doctors on the use of antiretroviral drugs in Nigeria. First Edition. Pg 60-74.
5. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, *et al.* Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA* 2000; 283 : 1175-82.
6. Merchant RH, & Lala MM. Prevention of mother-to-child transmission of HIV - An overview. *Indian Journal of Medical Research* 121:489-501.
7. Ezechi OC, Njemanze O, Gab-Okafor C, Onwujekwe DI, Odunukwe NN, Ezeobi PM *et al.* Success of outreach PMTCT programming. Proceedings of the AIDS Conference, Toronto Canada 2006. Abstract No WOPDB021.
8. Cooper ER, Charurat M, Mofenson L, Hanson IC, Pitt J, Diaz C, *et al.* Combination antiretroviral strategies for the treatment of

- pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr* 2002; 29 : 484-94.
9. European Collaborative Study. HIV-infected pregnant women and vertical transmission in Europe since 1986. *AIDS* 2001; 15 : 761-70.
  10. Dorenbaum A, Cunningham CK, Gelber RD, Culnane M, Mofenson L, Britto P, et al. Two-dose intrapartum/newborn nevirapine and standard antiretroviral therapy to reduce perinatal HIV transmission: a randomized trial. *JAMA* 2002; 288 : 189-98.
  11. Merchant RH, Damania K, Gilada IS, Bhagwat RV, Karkare JS, Oswal JS, et al. Strategy for preventing vertical transmission of HIV: Bombay experience. *Indian Pediatr* 2001; 38 : 132-8)
  12. Adewole IF, Odutolu O, Sagay SS. Prevention of mother-to-child transmission of HIV . In: Adeyi O, Kanki PJ, Odutolu O , Idoko JA(editors) *AIDS in Nigeria- A nation on the threshold*. Harvard Series on population and international health. Cambridge MA. Pg 349-384.
  13. Dabis F, Leroy V, Casteborn K et al. Preventing of mother-to-child transmission of HIV-1 in Africa in the year 2000. *AIDS* 2000;14:1017-1026).
  14. Nguyen TA, Oosterhoff P, Ngoc YP, Wright P, Hardon A . Barriers to access prevention of mother-to-child transmission for HIV positive women in a well-resourced setting in Vietnam. *AIDS Research and Therapy* 2008, 5:7;5-7.
  15. Musoke P M. and Miiro F.A. Prevention of HIV mother to child transmission: a review. *AIDS Rev* 2000; 2: 263-274.
  16. Fauci AS. The AIDS Epidemic : Considerations for the 21st Century. *The New England Journal of Medicine*. 1999;341(14):1046-1050.
  17. HIV/AIDS surveillance report. Vol. 10. No. 2. Atlanta: Center for Disease Control and Prevention, 1998:1-43.
  18. Ezechi OC, Jogo A, Njemanze O, Gab-Okafor C, Onwujekwe DI, Odunukwe NN, Ezeobi PM et al . Effect of HIV infection and immunosuppression on the menstrual function of Nigerian women. Proceedings of the 4th IAS conference on HIV Pathogenesis, Treatment and Prevention. 22-25 July Sydney, Australia. Abstract No MOPDB02.
  19. Ezechi OC. Sexual behaviour and contraceptive practices of Nigerian living with HIV/AIDS. MPH Dissertation . University of Lagos, Lagos Nigeria. 2006.
  20. Nicolosi A, Correa Leite ML, Musicco M et al . The efficiency of male to female and female to male sexual transmission of the HIV- A study of 730 stable couples. *Epidemiology*. 1994;5:570-574.
  21. Onakewhor JUE. HIV/AIDS in pregnancy. In: Okpere E(editor) *Clinical Obstetrics*. First edition. Uniben press. Benin City .2003:100-115.
  22. Saada M, Le Chenadec J, Berrebi A, et al. Pregnancy and progression to AIDS: results of the French prospective cohorts. *AIDS* 2000;14:2355-60.
  23. Burns DN, Landesman S, Minkoff H, et al. The influence of pregnancy on human immunodeficiency virus type 1 infection: antepartum and postpartum changes in human immunodeficiency virus type 1 viral load. *Am J Obstet Gynecol* 1998;178:355-9.
  24. Weisser M, Rudin C, Bategay M, et al. Does pregnancy influence the course of HIV infection? Evidence from two large Swiss cohort studies. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;15:404-10.
  25. Watts DH. Management of Human Immunodeficiency Virus in pregnancy. *N Engl J Med*. 2002; 346 (24): 1879-1891.
  26. Deschamps MM, Pape JW, Desvarieux M, et al. A prospective study of HIV-seropositive asymptomatic women of childbearing age in a developing country. *J Acquir Immune Defic Syndr* 1993;6:446-551.
  27. Kumar RM, Uduman SA, Khurrana AK. Impact of pregnancy on maternal AIDS. *J Reprod Med* 1997;42:429-34.
  28. Ezechi OC, Onwujekwe DI, Adu RA. Planning pregnancy in HIV positive couples: Exploring the available options . *Medipharma Journal* 2006; 4:5-9.
  29. Salham S. Women and HIV Infection including mother to Child transmission. In: *Women and HIV*. First Edition. Jaypee Brothers. New Delhi .2003;92-117.
  30. Tripathi R, Tyagi S, Chanchal . HIV in Obstetrics and Gynaecology. In Gandhi G, Mehta S, Batra S (editors). *Infections in Obstetrics and Gynaecology*. First Edition. Jaypee Brothers .New Delhi .2006;35-55.
  31. Center for Disease Control and Prevention (CDC). Guideline for treatment of sexual transmitted diseases. *Morbidity and Mortality Weekly Report* .1998;47:1-5.
  32. Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *Br J Obstet Gynaecol* 1998;105:836-48.
  33. Bucceri A, Luchini L, Rancilio L, et al. Pregnancy outcome among HIV positive and negative intravenous drug users. *Eur J Obstet Gynecol Reprod Biol* 1997;72:169-74.
  34. Leroy V, Ladner J, Nyiraziraje M, et al. Effect of HIV-1 infection on pregnancy outcome in women in Kigali, Rwanda, 1992-1994. *AIDS* 1998; 12:643-50.
  35. Embree JE, Braddick M, Datta P, et al. Lack of correlation of maternal human immunodeficiency virus infection with neonatal malformations. *Pediatr Infect Dis J* 1989;8:700-4.
  36. Garcia PM, Kalish LA, Pitt J, Minkoff H, Quinn TC, Burchett SK et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and infants Transmission Study Group. *New England Journal Medicine* 1999;341:394-402.
  37. Mofenson LM. Epidemiology and determinants of vertical HIV transmission. *Semin Pediatric infect Dis*. 1994:252-256.
  38. Bryson Y, Luzuriga K, Wara D. Proposed definitions for inutero versus intrapartum transmission of HIV-1. *New England Journal of Medicine*. 1999;327:1246-1247.
  39. Nduati R, John G, Mbori-Ngacha D, et al. Effect of breast-feeding and formula feeding on transmission of HIV-1: a randomized clinical trial. *JAMA*. 2000;283:1167-1174.
  40. Ezechi OC et al : Breastfeeding Practices among Nigerian women of known and unknown HIV status . Proceedings of the Conference on HIV Transmission. Washington USA 17-22 July 2007. Abstract No 024.
  41. Working Group on MTCT of HIV. Rates of MTCT of HIV-1 in Africa, America and Europe: results from 13 perinatal studies. *Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology*. 1995;8:506-510.
  42. Semba RD. Overview of the potential role of vitamin A in mother to child transmission of HIV-1. *Acta Paediatr Suppl*. 1997;421:107-112.
  43. Preble EA, Piwoz EG. Prevention of Mother to child transmission of HIV in Africa: Practical Guidance for the Programs> Support for Analysis and Research in Africa(SARA) Project. Washington, DC: Academy for Educational Development.2001.
  44. Baba TW, Kock J, Mittler M et al . Mucosal infection of neonatal rhesus monkeys with cell free SI V. *AIDS Res Human Retroviruses*. 1994;10:351-357.
  45. Sellon RK, Jordan HL, Kennedy-Stokkopf SK, Tompkins MB, Tompkins WAF. Feline immunodeficiency virus can be experimentally transmitted via milk during acute maternal infection. *Virology*. 1994;8:3380-3385.
  46. Featherstone C. M cells: portals to the mucosal immune system. *Lancet* 1997;350:1230-1235.
  47. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of HIV 1 transmission through breastfeeding. *Lancet* 1992;340:585-588.
  48. Federal Ministry of Health(FMoH), Nigeria. National Guideline on Prevention of Mother to child transmission of HIV(PMTCT). FMoH, Nigeria July 2007.
  49. Mofenson LM. Interaction between timing of perinatal human immunodeficiency virus infection and the design of preventive and therapeutic interventions. *Acta Paediatr Suppl* 1997;421:1-9.
  50. Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. *N Engl J Med* 1999;341:385-393.
  51. McGowan JP, Shah SS: Management of HIV



- infection during pregnancy. *Current Opinion in Obstetrics and Gynecology* 2000, 12:357-367
52. Dickover RE, Garratty E, Herman SA, et al. Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission. *JAMA* 1996; 275:599-605.
  53. Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. *N Engl J Med* 1999; 341:394-402.
  54. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. *N Engl J Med* 1996; 335:1621-1629.
  55. Kuhn L, Steketee RW, Weedon J, et al. Distinct risk factors for intrauterine and intrapartum human immunodeficiency virus transmission and consequences for disease progression in infected children. *J Infect Dis* 1999; 179:52±58.
  56. Landesman SH, Kalish LA, Burns DN, et al. Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. *N Engl J Med* 1996; 334:1617±1623.
  57. Van Dyke RB, Korber BT, Popek E, et al. The ariel project: a prospective cohort study of maternal-child transmission of human immunodeficiency virus type 1 in the era of maternal antiretroviral therapy. *J Infect Dis* 1999; 179:319±328.
  58. Wabwire-Mangen F, Gray RH, Mmiro FA, et al. Placental membrane inflammation and risks of maternal-to-child transmission of HIV-1 in Uganda. *J Acquir Immun Defic Syndr* 1999; 22:379-385.
  59. Semprini AE, Castagna C, Ravizza M, et al. The incidence of complications after caesarian section in 156 HIV-positive women. *AIDS* 1995; 9:913-917.
  60. Chuachoowong R, Shaffer N, Siriwasin W, et al. Short-course antenatal zidovudine reduces both cervicovaginal human immunodeficiency virus type 1 RNA levels and risk of perinatal transmission. *J Infect Dis* 2000; 181:99-106.
  61. The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1. *N Engl J Med* 1999; 340:977-987.
  62. The European Mode of Delivery Collaboration. Elective caesarian-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999; 353:1035-1039.
  63. Kreiss J. Breast feeding and vertical transmission of HIV-1. *Acta Paediatr Suppl* 1997; 421:113-117.
  64. Leroy V, Newell ML, Dabis F, Feckham C, Van de Perre P, Bulterys M, et al. International multicentre pooled analysis of late postnatal mother-to-child transmission of HIV-1 infection. Ghent International Working Group on Mother-to-Child transmission of HIV. *Lancet* 1998; 352: 597-600.
  65. Ayouba A, Nerrienet E, Menu E. Mother-to-child transmission of HIV-1 in relation to season in Yaounde, Cameroon. *Am J Trop Med Hyg*, 2003; 69(4): 447449.
  66. Cohen J. Mother's malaria appears to enhance spread of AIDS virus. *Science*, 2003; 302:1311.
  67. Plummer FA. Heterosexual transmission of human immunodeficiency virus type-1 (HIV): interactions of conventional sexually transmitted diseases, hormonal contraception and HIV-1. *AIDS Res Hum Retroviruses*, 1998; 14(Suppl 1):S5S10.
  68. Taha T, Kumwenda N, Liomba G, et al. Heterosexual and perinatal transmission of HIV-1: association with bacterial vaginosis (BV). XII International Conference on AIDS, Geneva, Switzerland, June 28 July 3, 1998 (abstract 527/23347).
  69. Bulterys M, Landesman S, Burns DN, Rubinstein A, Goedert J. Sexual behavior and injection drug use during pregnancy and vertical transmission of HIV-1. *J Acquir Immune Defic Syndr Hum Retrovirol*, 1997; 15: 7682.
  70. Turner BJ, Hauck WW, Fanning R, Markson LE. Cigarette smoking and maternal-child HIV transmission. *J Acquir Immune Defic Syndr Hum Retrovirol*, 1997; 14:327337.
  71. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. *N Engl J Med*, 1996; 335:1621-1629.
  72. Blattner W, Cooper E, Charurat M, et al. Effectiveness of potent antiretroviral therapies on reducing perinatal transmission of HIV-1. *XIII International AIDS Conference*, Durban, South Africa, July 9-14, 2000 (abstract LbOr4).
  73. Chuachoowong R, Shaffer N, Siriwasin W, et al. Short-course antenatal zidovudine reduces both cervicovaginal human immunodeficiency virus type 1 levels and risk of perinatal transmission. *J Infect Dis*, 2000; 181:99-106.
  74. WHO; Prevention of Mother-To-Child Transmission (PMTCT) Briefing Note; WHO, Geneva, October 1st, 2007.
  75. WHO/HHS-CDC PMTCT Generic Training Package (GTP)- Officially launched in 2004.
  76. Pai NP, Tulsy JP, Cohan D, Colford JM, Reingold AL. Rapid point-of-care HIV testing in pregnant women: a systematic review and meta-analysis *Tropical Medicine and International Health*. 2007; 12 (2 ): pp162173
  77. APIN Plus protocol
  78. WHO. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access: recommendations for a public health approach. WHO, Geneva, Switzerland; 2006.
  79. Nguyen TA, Oosterhoff P, Ngoc YP, Wright P, Hardon A. Barriers to access prevention of mother-to-child transmission for HIV positive women in a well-resourced setting in Vietnam. *AIDS Research and Therapy* 2008, 5(7):1-12.
  80. World Health Organization: Strategic Approaches to the Prevention of HIV Infection in Infants: report of a WHO meeting. 2003. <http://www.who.int/hiv/pub/mtct/en/StrategicApproachesE.pdf>.
  81. Gridassova O. The stigmatization of the pregnant HIV infected women is the major factor of MTCT [abstract]. *Antivir Ther* 2003, 8(1):S500-S501.
  82. Painter TM, Diaby KL, Matia DM, Lin LS, Sibailly TS, Kouassi MK, Ekpini ER, Roels TH, Wiktor SZ. Women's reasons for not participating in follow up visits before starting short course antiretroviral prophylaxis for prevention of mother to child transmission of HIV: qualitative interview study. *BMJ* 2004; 329(7465):543.
  83. Busza JR. Promoting the Positive: Responses to Stigma and Discrimination in Southeast Asia. *AIDS Care* 2001, 13(4):441-456.
  84. Rogers A, Meundi A, Amma A, Rao A, Shetty P, Antony J, Sebastian D, Shetty P, Shetty AK. HIV-related Knowledge, Attitude, Perceived Benefits, And Risks of HIV Testing Among Pregnant Women In Rural Southern India. *AIDS Patient Care STDS* 2006, 20(11):803-811.
  85. Hyodo C, Tanaka T, Kobayashi M: Factors affecting attitudes toward mother-to-child transmission of HIV among pregnant women in a maternal and child hospital in Thailand. *Int J STD AIDS* 2000, 11(6):406-409.
  86. Koniz-Booher P, Burkhalter B, de Wagt A, Iliff P, Willumsen J: HIV and Infant Feeding: A Compilation of Programmatic Evidence. Quality Assurance Project (QAP), University Research Co., LLC (URC); 2004.
  87. Morch E, Thu Anh N, Ha DQ, Hanh NTT: Rapid assessment of the PMTCT program. Hanoi: Vietnam Ministry of Health; 2006.
  88. Stringer JS, Stringer EM, Phanuphak P: Prevention of mother-to child transmission of HIV in Thailand: Physicians' attitudes on Zidovudine use, pregnancy termination, and willingness to provide care. *J Acquir Immune Defic Syndr* 1999, 21(3):217-222.
  89. Parameswari S, Shaffi A, Viswanath R: MTCT training programme for village health nurses (VHN) in Namakkal District, South India. *Proceedings of the 3rd International Conference on Global Strategies for the Prevention of HIV Transmission from Mothers to Infants: 13-19 June 2001; Kampala, Uganda* 2001