

There are an estimated 12-15 million HIV infected women worldwide, the majority of whom are in their reproductive years. A total of 1800 HIV infected children are born in the world each day.

The following 2 situations arise.

1. HIV +ve woman becoming pregnant.
2. A pregnant lady detected to be HIV +ve.

All pregnant women should receive counseling regarding the benefits and risks of HIV screening and be encouraged to undergo voluntary HIV serologic testing. Despite favorable trial results many developing countries are unsure of the appropriateness of implementing antenatal screening and prevention programs for vertical transmission of HIV. Identification of HIV infection in pregnant women, if combined with uptake of interventions, reduces the risk of mother to child transmission. The lifetime costs of care for a child infected with HIV have been estimated at £178 300. Screening pregnant women for HIV can avert this cost and lead to gains in life years for both mothers and children.

The World Health Organization (WHO) recommends a four-pronged approach to the prevention of mother to child transmission.

- A. Preventing new infections in parents-to-be
- B. Preventing unwanted pregnancies in HIV infected women
- C. Preventing MTCT (Mother To Child Transmission)
- D. Appropriate treatment and care.

The major reduction in the prevention of MTCT of HIV has come from three strategies to prevent transmission in pregnancy and to infants.

1. ART
2. Elective cesarean section
3. Modifications of infant feeding.

Issues to Consider in Caring for HIV – Seropositive Pregnant Women

1. Impact of pregnancy – on maternal HIV disease and therapy options
2. Perinatal transmission – the risk and means of reduction
3. Impact of HIV – on pregnancy outcome and obstetric care
4. Infant follow-up – Early diagnosis and opportunistic infection prophylaxis.

Impact of Pregnancy on Maternal Health and Therapy of HIV –

- A. Possibility of a shortened life expectancy
- B. Disease progression – no clear data available
- C. Symptoms – Fatigue, nausea and vomiting, dyspnea, headaches and skin lesions are common in pregnancy regardless of HIV status.
- D. Drug therapy.

Perinatal Transmission (MTCT - Mother To Child Transmission)

It may occur in following ways.

1. *In utero*, via transplacental passage: 30-40%
2. During labor and delivery: 50%
3. Breastfeeding: 5-32%

The incidence is higher in developing countries compared to developed countries. This may be related to a number of factors, e.g. breastfeeding, nutritional deficiencies and/or coexisting infections other than HIV-1, absence of adequate prenatal care, and increased rate of premature deliveries.

Factors associated with an increased risk of transmission:

- a. Maternal HIV viral load - Rates of transmission increases with increasing viral load.
- b. Antiretroviral therapy (ART) - ART of the mother during pregnancy and labor has been very effective in reducing the risk of transmission to the infant.
- c. Lower CD4+ count - confers an increased risk.
- d. Other maternal factors - like cigarette smoking and older maternal age have been associated with an increased risk.
- e. Obstetric factors – Premature rupture of the amniotic membranes, Chorioamnionitis and placental membrane inflammation are associated with an Increased risk of transmission.
- f. Prematurity - Delivery at < 34 weeks is associated with an increased risk of infant infection.
- g. Mode of delivery - Elective cesarean section may reduce perinatal transmission.

ANTIRETROVIRAL THERAPY

The treatment options will depend, first, upon the clinical stage of disease of the mother, determining whether she requires ART for her own health, or a prophylactic regimen to reduce the risk of MTCT, and second, on the availability of ARV regimens.

Women Who Require ART for their Own Health

Ideally, HIV infected women should achieve an undetectable viral load prior to conception to virtually eliminate the risk of HIV transmission. HAART use in pregnancy has been associated with low rates of toxicity, although higher rates of preterm delivery have been reported. Those women already on ARV treatment who become pregnant should continue with a HAART regimen, although the drugs used may need to be adjusted. While the primary purpose of this treatment is to benefit the mother, it will also significantly reduce the risk of MTCT, and improvements in maternal health can also improve child survival. On the evidence available to date, the benefits of ART during pregnancy outweigh the potential side effects or risks to mother or baby.

Sufficient data exist to reassure that Zidovudine, Lamivudine, Nevirapine, Abacavir and Nelfinavir are not teratogenic. There have been reports of a possible association between NRTI containing ARV regimens, and the development of mitochondrial toxicity in the newborn and mother. There are concerns over the use of Efavirenz in pregnancy due to a small number of reports of neural tube defects and the Dandy-Walker malformation. Hence US FDA has classified it as a Pregnancy Category D drug. Stavudine and Didanosine should not be used together in pregnant women, unless the potential benefits outweigh the risks, due to an increased risk of lactic acidosis. PIs have been associated with worsening of DM, gestational diabetes and hyperglycemia in women receiving PI regimens during pregnancy. Nelfinavir related GI symptoms are significantly more likely during pregnancy. Given the diabetogenic state of pregnancy and the potential complications of PIs, women receiving HAART during pregnancy should be monitored carefully for obstetric complications, and glucose levels should be monitored with the use of PIs in pregnancy.

Women for whom HAART is not yet indicated

HAART regimens, started after the first trimester of pregnancy and stopped after delivery, have been recommended for all HIV +ve pregnant women for the prevention of MTCT, regardless of their need to continue with post-pregnancy treatment. It aims to provide maximal viral suppression, maximum reduction in the risk of transmission and to minimize the risk of selection of resistant virus.

Although all ARVs may have side effects, there has been accumulating evidence of an increased risk of hepatic adverse events, which may be fatal and are often associated with rash, in particular about NVP containing HAART regimens, particularly in women with higher CD4+ counts (>250 cells/mm³). Reports on NVP related toxicity in pregnancy vary.

As per ART guidelines of API (2005-06), in mothers (with CD4 counts >250/mm³) who can afford and therapy can be closely monitored, a combination of standard 3 drug ART is recommended for reducing risk of MTCT. This option termed as START (Short-term antiretroviral therapy) intends to treat mothers with standard three drugs ART throughout the duration of pregnancy (except first trimester) and discontinuing shortly after delivery. The advantage of this approach is achieving maximal suppression of HIV and prevention of ARV resistance development, which would not compromise mother's future therapeutic options.

ARV Regimens

1. Nevirapine only regimen: For the majority of HIV +ve women in the poorest settings, the only available treatment option is a single-dose NVP regimen. A single dose NVP to the mother at the onset of labor will reduce transmission rate to 10-15% at 6 weeks. There have been some suggestions that NVP should be provided to all pregnant women without the need for testing.
2. Combination regimens: One study has suggested that women previously exposed to NVP for PMTCT are less likely to suppress the virus to below 50 copies/ml at 6 months on NVP containing HAART regimens. Combination short-course regimens, where the maternal and infant NVP doses are added to a base regimen of zidovudine alone or in combination with 3TC for 4-7 days postpartum, may reduce transmission to below 5%. Combining a NVP dose to mother and infant with zidovudine has become the WHO recommended regimen for those women who do not require ongoing HAART therapy.

Other Issues in Management of the Pregnant HIV +ve Patient

- Investigations-
 - Tuberculin skin testing
 - TORCH titre
 - VDRL test
 - PAP smear
 - Cervical cultures for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.
 - Repeated lymphocyte subset testing should be done every 3 months if CD4+ count at baseline

Table 1: Recommended zidovudine dosages to reduce perinatal HIV transmission

Antepartum Therapy

- Begin after 14 weeks' gestation: Zidovudine, 100 mg orally five times per day.

Intrapartum Therapy

- Intravenous zidovudine, 2 mg per kg loading dose over 30 to 60 minutes, followed by 1 mg per kg per hour drip until cord is clamped.
- If delivery is anticipated within 30 minutes of time of arrival, a diluted bolus of zidovudine can be given (maximum concentration: 4 mg per ml).
- If intravenous zidovudine is unavailable, an oral loading dose of 400 mg followed by 200 mg every two hours may be considered, although efficacy has not been studied.
- In patients undergoing induction of labor, zidovudine should be given when induction begins.
- In patients undergoing elective cesarean section, zidovudine should be started four hours before surgery.

was <500 cells/mm³ to assess need for PCP prophylaxis.

- PCP prophylaxis and treatment of other opportunistic infections- The guidelines are same as in non-pregnant women.
- Psychosocial needs should be met with.
- Gynaec follow-up
- Infant follow-up.

Thus, HIV and pregnancy together is a complex situation and should be handled with a multi-disciplinary prong.

SUGGESTED READING

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