

HIV in Pregnancy

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Global Epidemiology of HIV

- Globally women and children are the fastest growing group of HIV positive individuals.
- Where the incidence of transmission of HIV by heterosexual contact is high there is an associated high incidence of vertical transmission and infection of infants.

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Risk of HIV Vertical Transmission

- HIV infection currently has very high mortality rate approaching 100%.
- Prevention of transmission is our only mechanism for decreasing the morbidity and mortality of HIV infection.
- Effective interventions to significantly decrease vertical transmission can be implemented.

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Risk Factors for Vertical Transmission

- Maternal immunity
- Biological factors of the infecting virus
- Obstetric factors related to delivery
- Levels of maternal virus

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HIV and Pregnancy

- Pregnancy does not have any significant effect on HIV disease progression
- HIV infection does not have any significant effect on pregnancy outcome

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Role of HIV load in Vertical Transmission

- Many studies show a direct relationship between viral load, cell-free and cell associated, and vertical transmission.
- Other studies do not show a direct relationship between viral load and transmission.
- Studies show anti-retrovirals decrease transmission.

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Treatment of HIV Positive Pregnant Women

- Two main objectives:
 - decrease viral load and decrease risk of vertical transmission
 - Increase CD4 count and decrease risk of opportunistic infections.

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Screening for HIV in Pregnancy

- Screening for an infectious disease in pregnancy only of value if there is a effective preventative or therapeutic intervention.
- Screening for HIV in pregnancy is indicated in selected circumstances.

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Who to screen for HIV infection?

- Initial assumption was that “at risk” women could be identified for screening.
- Screening only “at risk” women may miss 40 to 80% of HIV positive women when high sero-prevalence.

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How to Screen?

- Public Health Perspective on Screening
 - Offering routine screening should be based of HIV prevalence.
 - Routine screening appropriate if $> 1:1000$ women infected
 - False positives occur in about 1:1000 tests thus $> 50\%$ of screening tests will be false positives if HIV prevalence $< 1:1000$.

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Interventions

- Prevent transmission to infant in labour
 - role of antiretrovirals
 - role of caesarean section
 - role of breast feeding

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Reducing the Risk of Vertical Transmission of HIV

- Reducing the HIV level in genital secretions through the use of local disinfectants
- Reducing the viral level in mother through the use of antiretroviral agents
- Treating the infant with antiretroviral therapy prophylactically
- HIV vaccination to prevent infection.

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Optimal obstetrical practices to reduce Transmission.

- Preventing premature birth
- Preventing rupture of membranes more than four hours before delivery
- Preventing chorioamnionitis
- Caesarean Section may decrease risk of transmission
- Post-partum transmission can be prevented by the avoidance of breastfeeding

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Mode of Delivery

- Management of labour and delivery should focus on minimising the risk for both perinatal transmission of HIV and the potential for maternal and neonatal complications.
- Caesarean section performed before the onset of labour and with HIV viral load >1000 copies / mL.

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Breast feeding and HIV transmission.

- Prolonged breast feeding is estimated to cause one-third to half of new infant HIV infections worldwide
- In third world if exclusively breast feeding promoted then it should also be followed with early weaning

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Initial Studies with Antiretrovirals

- In 1994 the ACTG 076 study, a randomised, double-blind, placebo controlled trial of the safety and efficacy of AZT, found that administration of AZT in pregnancy, delivery and to the neonate for 6 weeks reduced the mother-to child transmission of HIV by two thirds.

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ACTG 076 - Protocol

- Zidovudine 100 mg five times daily orally during pregnancy.
- Zidovudine 2mg/Kg/ is hour then 1mg/Kg/IVI until delivery.
- Zidovudine 2 mg /Kg / dose four times daily orally to infant for 6 weeks starting within 12 hours of birth.

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ACTG 076 - Result

- 402 infant mother pairs evaluated for rate of vertical transmission:
 - AZT = 7.6% (CI 4.3 - 12.3%)
 - Placebo = 22.6% (CI 17.0 - 29.0%) ($p < 0.001$).

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Role of Nevirapine

- Single dose Nevirapine may have a role
 - in resource poor countries
 - for mothers who present late
 - mothers who have issues with compliance

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Nevirapine

- Single dose nevirapine had deleterious effect on later nevirapine therapy in mother due to long half-life of the drug and the selection of nevirapine-resistant mutants.
- Thai study of on post-partum women who had received nevirapine after prolonged antepartum AZT monotherapy.

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HIV phenotype

- Two HIV phenotypes defined by co-receptor usage which can be transmitted from mother to child.
- Advanced infection get shift from NSI (CCR5) to SI (CXCR4) variants which appear in spite of or because of AZT.

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Nevirapine

- Shift under AZT pressure to “rapid/high” (SI) phenotype could result in a greater degree and extent of diversity of nevirapine resistance compared with patients on other monotherapy.
- Stravudine (d4T) induces resistance at a slower rate than AZT.
- Effect of stravudine on balance of SI an NSI phenotype unknown.

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Nevirapine

- Addition of single-dose nevirapine to AZT therapy of mother with infants receiving nevirapine showed:
 - Nevirapine-Nevirapine = 1.1% (CI 0.3-2.2)
 - Nevirapine-placebo = 1.9% (CI 0.9-3.0)
 - Placebo-Placebo = 6.3% (CI 3.8-8.9)
- No effect on maternal viral load
No side-effects

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Combined AZT and 3TC

- Short course therapy with AZT and 3TC
 - 36/40 AZT & 3TC – baby 6/52 AZT = 5.7%
 - 40/40 AZT & 3TC – baby 6/52 AZT = 8.9%
 - Placebo = 15.3%

Long term breast feeding increased infection rate in all groups by 18 months of age.

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Summary Recommendations

- Mother on HAART to suppress viral load and increase CD4
- Baby treated with AZT 6/52
- Role of 3TC in baby unclear but may be indicated if high maternal viral load or resistance mutations
- Nevirapine should not be used alone, only with AZT/3TC so as not to compromise infants further care if infected with HIV.
- Elective caesarean section may be indicated.

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