IN THE NAME OF GOD

HIV and Pregnancy

Fact sheet
Updated November 2017

- HIV continues to be a major global public health issue, having claimed more than 35 million lives so far. In 2016, 1.0 million people died from HIV-related causes globally.
- There were approximately 36.7 million people living with HIV at the end of 2016 with 1.8 million people becoming newly infected in 2016 globally.
- 54% of adults and 43% of children living with HIV are currently receiving lifelong antiretroviral therapy (ART).

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- Global ART coverage for pregnant and breastfeeding women living with HIV is high at 76% .
- The WHO African Region is the most affected region, with 25.6 million people living with HIV in 2016. The African region also accounts for almost two thirds of the global total of new HIV infections.
- HIV infection is often diagnosed through rapid diagnostic tests (RDTs), which detect the presence or absence of HIV antibodies.

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- Key populations are groups who are at increased risk of HIV irrespective of epidemic type or local context. They include: √ *men who have sex with men*, √ *people who inject drugs*,√ *people in prisons and other closed settings*,√ *sex workers and their clients*, and √*transgender people*.
- Key populations often have legal and social issues related to their behaviours that increase vulnerability to HIV and reduce access to testing and treatment programmes.
- In 2015, an estimated 44% of new infections occurred among key populations and their partners.

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- There is no cure for HIV infection. However, effective antiretroviral (ARV) drugs can control the virus and help prevent transmission so that people with HIV, and those at substantial risk, can enjoy healthy, long and productive lives.
- It is estimated that currently only 70% of people with HIV know their status. To reach the target of 90%, an additional 7.5 million people need to access HIV testing services. In mid-2017, 20.9 million people living with HIV were receiving antiretroviral therapy (ART) globally.
- Between 2000 and 2016, new HIV infections fell by 39%, and HIV-related deaths fell by one third with 13.1 million lives saved due to ART in the same period. This achievement was the result of great efforts by national HIV programmes supported by civil society and a range of development partners.

HIV Infection in Women

- When AIDS first was recognized in 1981 it was considered to be a disease of men who have sex with men (MSM) and of injection drug users
- With the rapid increase in the number of women infected with HIV has come an increased understanding of the potential for heterosexual transmission of HIV infection
- Human immunodeficiency virus (HIV) infection is now a profound impact on the health of women worldwide
- By the end of 2011, more than 50% of the people living with HIV infection were women

HIV Infection in Women

- HIV Infection in Women is one of the most important health problem because:
  - Being a man or a woman has a significant impact on health, women and girls face increased vulnerability to HIV/AIDS
  - HIV infection in women can facilitate the spread of infection
  - HIV infection in women can transmit the infection to children

Then we talk about HIV infection in pregnancy

Preconception Counseling and Care for HIV-Infected Women of Childbearing Age

- The goals of preconception care for women living with HIV:
  - Prevent unintended pregnancy
  - Optimize maternal health before pregnancy
  - Improve maternal and fetal outcomes in pregnancy
  - Prevent perinatal transmission
  - Prevent HIV transmission to an HIV-uninfected sexual partner when trying to conceive

Timing of Transmission

- HIV can be transmitted from an HIV-infected woman to her child:
  - During intrauterine gestation
  - At delivery
  - In the postpartum period through breast-feeding
- The investigators estimated that 92% of all instances of transmission occurred during the last 2 months of pregnancy and that 65% occurred during the intrapartum period

Potential Factors Influencing Mother-to-Child Transmission of HIV

- Maternal Factors
- Fetal or Placental Factors
- Labor or Birth Canal Factors
- Immune Factors
  - Humoral
  - Cell Mediated

Potential Factors Influencing Mother-to-Child Transmission of HIV

- **Maternal Factors:**
  - Advanced HIV disease, as measured by:
    - Clinical staging
    - Low CD4+ lymphocyte count
    - Higher viral loads
    - p24 antigenemia
  - Primary HIV infection
  - Viral phenotype: syncytium inducing
  - Viral genotype: virulent mutant strain of HIV
  - Coinfection with other sexually transmitted diseases
  - First-born twins
  - Obstetric events
    - Vaginal delivery
    - Invasive procedures or fetal monitoring during labor
    - Prolonged premature rupture of membranes (>4 hr)
  - Older maternal age
  - Cigarette smoking and illicit drug use during pregnancy
  - Breast-feeding
  - Unprotected sexual intercourse with multiple partners

Potential Factors Influencing Mother-to-Child Transmission of HIV

- **Fetal or Placental Factors:**
  - Chorioamnionitis
  - Prematurity
  - Low birth weight
- **Labor or Birth Canal Factors:**
  - Cervicovaginal viral load
  - Local HIV-specific immune response
  - Maternal-fetal transfusion of blood

Potential Factors Influencing Mother-to-Child Transmission of HIV

- **Immune Factors:**
  - Humoral:
    - Neutralizing antibody
    - Antibody-dependent cellular cytotoxicity
    - gp120 V3 loop antibody
    - MHC concordance and homozygosity
    - Maternal human leukocyte antigen A*2301
  - Cell Mediated:
    - Cytotoxic T lymphocytes
    - CD8 suppression
    - Mucosal immunity

Impact of Pregnancy on HIV Infection

- Pregnancy is immunosuppressive conditions:
  - The number of CD4+ cells decreases
  - The CD4+ percentage remains relatively stable
  - HIV viral loads remain relatively stable throughout pregnancy without treatment
- In developed countries large studies failed to show that pregnancy accelerates HIV replication or disease progression
- In developing countries data suggest that there may be a progression of HIV disease in pregnancy under certain conditions
- Differences in the impact of pregnancy on HIV infection across geographic areas may reflect differences in potential confounding issues, such as:
  - Poverty and nutrition,
  - Greater likelihood of advanced HIV disease at the time of pregnancy
  - Impact of additional infectious diseases

Impact of HIV Infection on Pregnancy

- Because infection with HIV early in pregnancy is uncommon, embryopathy does not seem to be a major problem
- HIV infection appears to be associated with increased adverse pregnancy outcomes, and it is not clear whether ART exacerbates this increased risk
- In South Africa, a recent report noted that the maternal mortality ratio in HIV-infected women was about 10 times higher than in uninfected women, in a setting where few women were receiving ART
- In developed countries maternal HIV infection has not bee associated with fetal anomalies, premature delivery, low birth weight, or specific pregnancy-related abnormalities
- In developing areas have noted an increased incidence of preterm deliveries and low-birth-weight infants

Use of Antiretroviral Drugs in Pregnancy: Maternal Health & Reduce Transmission

- The goals of ART in pregnancy:
  - Optimize maternal health
  - Provide maximal suppression of the viral load
  - Prevent perinatal HIV transmission
  - Prevent horizontal HIV transmission to sexual partners
  - Avoid potential maternal or fetal toxicity

Use of Antiretroviral Drugs to Decrease Perinatal Transmission

- In February 1994: Administration of ZDV to the pregnant woman and her infant could reduce the risk for perinatal transmission by 67.5%
- Subsequent clinical trials and observational studies demonstrated that combination antiretroviral prophylaxis (initially dual- and then triple-combination therapy) given to the mother antenatally was associated with further declines in transmission to less than 2%
- At the moment: Combination drug regimens are considered the standard of care for both the treatment of HIV infection and prevention of perinatal HIV transmission

Use of Antiretroviral Drugs to Decrease Perinatal Transmission

- A longer three-part regimen (e.g., starting at or before 28 weeks' gestation) given antenatally, intrapartum, and postpartum is superior in preventing perinatal transmission to a shorter two-part antepartum/intrapartum (e.g., starting at 36 weeks' gestation) or intrapartum/postpartum regimen
- Current guidelines recommend that all pregnant women should be treated with combination suppressive ART as soon as possible

Potential Mechanisms of Antiretroviral Drugs to Reduce Perinatal Transmission

- Decreasing maternal viral load in the blood and genital secretions via antenatal drug administration, particularly in women with high viral loads
- Preexposure infant prophylaxis provided by administration of antiretroviral drugs that cross the placenta from the mother during labor, resulting in adequate systemic drug levels in the infant at a time of intensive exposure to maternal genital tract virus during passage through the birth canal
- Postexposure infant prophylaxis would protect against cell-free or cell-associated virus that might have obtained access to the fetal/infant systemic circulation

Recommended Guidelines on the Use of Antiretroviral Agents in HIV-Infected Adults and in Pregnancy:

- ART in pregnant women be the same as for nonpregnant women, unless clear fetal or maternal contraindications exist
- Antiretroviral prophylaxis to prevent perinatal HIV transmission should be provided to all pregnant HIV-infected women, regardless of CD4 count and HIV RNA copy number
- Pregnancy is not a reason to defer standard suppressive ART and outline unique considerations for combination therapy use

Management of Pregnant HIV-Infected Women

- **Antepartum Care:**
  - Assessment of HIV disease status*:
    - Evaluating past and current CD4 count
    - Current plasma HIV RNA copy number
    - Past and current ART
    - Previous antiretroviral drug use in pregnancy
    - Assessing the need for prophylaxis against opportunistic infections
    - Reviewing results of previous and current HIV antiretroviral drug resistance studies
    - Assessing supportive care needs
    - The usual antenatal assessments
  - Identifying any factors known to be associated with perinatal transmission:
    - History of STDs
    - Drug and alcohol use
    - Tobacco use
    - High-risk sexual activity

Management of Pregnant HIV-Infected Women

- **Antepartum Care:**
  - Complete physical examination
  - Choice of an antiretroviral regimen* based on:
    - Woman's health
    - Previous treatment
    - Known or suspected drug resistance
  - Risks of ART during pregnancy:
    - Information to date does not support major teratogenic effects of the majority of antiretroviral drugs
    - EFV should be avoided during the first trimester
    - Discontinuing antiretroviral medications may result in a rebound of viral load
    - Dual-combination therapy (i.e., ZDV/3TC) without the addition of a third drug (i.e., a protease inhibitor or an NNRTI) is not recommended because of the potential for inadequate viral suppression and rapid development of resistance, most commonly the M184V mutation

*

Management of Pregnant HIV-Infected Women

- **1)HIV-Infected Pregnant Women Who Have Never Received Antiretroviral Drugs:**
  - All HIV-infected pregnant women should receive potent combination ART regardless of CD4 count or plasma HIV RNA copy number
  - Two nucleoside reverse-transcriptase inhibitors (NRTIs) plus an NNRTI or protease inhibitor(PI)

Management of Pregnant HIV-Infected Women

- **NRTIs:**
  - Used as part of combination regimens; use of single or dual NRTIs alone is not recommended for treatment of HIV infections
  - Potential maternal and infant mitochondrial toxicity
  - Transplacental drug passage is an important mechanism of infant preexposure prophylaxis, thus, when selecting an antiretroviral regimen for pregnant women, at least one NRTI agent with high placental transfer should be included(ZDV, 3TC, emtricitabine [FTC], tenofovir [TDF], or abacavir [ABC]):
    - TDF/FTC
    - ZDV/3TC
    - ABC/3TC

Management of Pregnant HIV-Infected Women

- **NNRTIs:**
  - NNRTIs are recommended for use in combinations with two NRTI drugs
  - Hypersensitivity reactions, including hepatic toxicity, and rash more common in women; unclear whether increased in pregnancy
    - Nevirapine (NVP) for women with CD4 counts less than 250 cells/mm3
    - Women with CD4 counts greater than 250 cells/mm3 have an increased risk for developing symptomatic, often rash-associated, NVP-related hepatotoxicity, which can be severe, life threatening, and, in some cases, fatal within the first 18 weeks after initiation of therapy
    - Efavirenz (EFV) should be avoided in the first trimester

Management of Pregnant HIV-Infected Women

- **Protease Inhibitors (PIs):**
  - PIs are recommended for use in combination with two NRTI drugs
  - Hyperglycemia, new-onset or exacerbation of diabetes mellitus, and diabetic ketoacidosis reported with PI use; unclear whether pregnancy increases risk. Data are conflicting regarding risk for preterm delivery in women receiving Pis
    - Atazanavir (ATV) is one of the preferred PIs for use in combination regimens in pregnancy; should give with low-dose RTV once daily
    - Lopinavir/ritonavir (LPV/ RTV) is one of the preferred boosted PIs for use in combination regimens in pregnancy

Management of Pregnant HIV-Infected Women

- **2) HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Therapy**
  - EFV, the preferred NNRTI for non-pregnant adults, is not recommended for initiation in antiretroviral-naïve women in the first 8 weeks of pregnancy but may be continued in pregnant women who desire prenatal care in the first trimester who have achieved virologic suppression on the regimen
  - Hepatic toxicity is a concern in women with a CD4 count greater than 250 cells/mm3 at the time that they first initiate an NVP-based therapy, an increased risk for hepatic toxicity has not been seen in women who are receiving NVP-based therapy and have immune reconstitution with therapy

Management of Pregnant HIV-Infected Women

- **Stopping Antiretroviral Therapy during Pregnancy**
  - Discontinuation of ART during pregnancy may be indicated in:
    - Serious treatment-related toxicity
    - Pregnancy induced hyperemesis
    - Acute illnesses or planned surgeries that preclude oral intake
    - Lack of available medication
    - Patient request
  - If discontinuation of ART is indicated, all antiretroviral drugs should be stopped and reintroduced together
  - Drugs with long half-lives, such as NVP and EFV, may be detected for 21 days or longer after discontinuation resulting in functional monotherapy that can increase the risk for selection of NNRTI resistant mutations
  - To prevent this functional monotherapy, some experts recommend either:
    - (1) Stopping the NNRTI first and continuing the other antiretroviral drugs for a period of time (at least 7 days is recommended)
    - (2) Switching from an NNRTI to a protease inhibitor before interruption and continuing the protease inhibitor with the other antiretroviral drugs for a period of time before electively stopping the therapy

Management of Pregnant HIV-Infected Women

- **3) HIV-Infected Pregnant Women Who Have Previously Received Antiretroviral Treatment but Are Not Currently Receiving Medication:**
  - There is concern that some women with previous time-limited use of antiretroviral drugs during previous pregnancies may develop genotypic resistance to one or more components of the initial antiretroviral regimen
  - Careful monitoring of virologic response to the chosen antiretroviral regimen is important
  - Adjustments to therapy should be guided by repeat resistance testing

Management of Pregnant HIV-Infected Women

- **Monitoring of the Woman and Fetus during Pregnancy**
  - CD4 counts should be monitored in HIV-infected pregnant women at the initial visit and at least every 3 to 6 months during pregnancy, the CD4 percentage may be more stable than the absolute CD4 count during pregnancy
  - Viral loads should be monitored in HIV infected pregnant women at the initial visit, 2 to 6 weeks after initiating or changing ART, monthly until undetectable, and then at least every 3 months
  - Viral load should also be assessed at 34 to 36 weeks' gestation to inform decisions on the mode of delivery
  - Drug resistance testing
  - Monitoring for complications of ART:
    - NRTI: Hepatic enzymes and electrolytes monitored
    - NNRTI: An ultrasound scan in the first trimester
    - PIs: A glucose screening with a standard, 1-hour 50-g glucose loading test at 24 to 28 weeks of gestation

Management of Pregnant HIV-Infected Women

- **Intrapartum Antiretroviral Therapy/Prophylaxis**
  - Women who are receiving an antepartum combination antiretroviral regimen should continue this regimen on schedule as much as possible during labor and before scheduled cesarean delivery
    - Intravenous ZDV administration is recommended for pregnant women with HIV RNA greater than or equal to 400 copies/mL or unknown HIV RNA levels near delivery, regardless of antepartum regimen or mode of delivery
    - The 6-week neonatal component of the ZDV chemoprophylaxis regimen is recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV, preferably within 6 to 12 hours of birth

Management of Pregnant HIV-Infected Women

- **Intrapartum Antiretroviral Therapy/Prophylaxis**
  - 1)Women receiving fixed-dose combination regimens that include ZDV should have ZDV administered intravenously during labor while other antiretroviral components are continued orally
  - 2)For women who have received antepartum antiretroviral drugs but have suboptimal viral suppression near delivery (i.e., HIV RNA >1000 copies/mL), scheduled cesarean delivery at 38 weeks' gestation is recommended
  - 3)The addition of intrapartum/neonatal single-dose NVP is not recommended
    - Some experts would combine the intravenous intrapartum/6-week neonatal ZDV regimen with single-dose intrapartum/neonatal NVP
    - If single-dose NVP is given (alone or in combination with ZDV), consideration should be given to adding 3TC during labor and maternal ZDV/3TC for 7 days postpartum or longer, which may reduce development of NVP resistance in the woman

Management of Pregnant HIV-Infected Women

- **Intrapartum Antiretroviral Therapy/Prophylaxis**
  - 4)Women of unknown HIV status who present in labor should have rapid HIV antibody testing performed and intravenous ZDV initiated if the test is positive (without waiting for results of the confirmatory test) and infant ZDV therapy initiated. A confirmatory test should be done postpartum; if positive, 6 weeks of infant ZDV therapy is recommended, and if negative, the infant ZDV therapy can be stopped
  - 5)For HIV-infected women in labor who have not received antepartum antiretroviral drugs, intravenous administration of ZDV during labor and 6 weeks of infant ZDV therapy is recommended

- **THANKS FOR ATTENTION**