Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Panel’s Recommendations

- The management of prenatal care and general principles of antiretroviral therapy (ART) and HIV management do not differ between pregnant women with perinatally acquired HIV and those who acquired HIV infection postnatally. With effective ART and prenatal management, the risk of perinatal transmission does not appear to be increased in women who acquired HIV perinatally compared with those who acquired HIV infection postnatally (AII).
- Using the same guiding principles that are used for heavily ART-experienced adults, optimal ART regimens should be selected based on resistance testing, prior ART history, and pill burden (AII).
- Consultation with experts in HIV and pregnancy is recommended when the presence of extensive drug resistance warrants the use of antiretroviral drugs for which there is limited experience in pregnancy (AII).
- Pregnant women with perinatally acquired HIV warrant enhanced focus on adherence interventions during and after delivery (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

With the availability of potent antiretroviral therapy (ART), morbidity and mortality have significantly declined in individuals living with HIV, including those with perinatally acquired HIV. An increasing number of women with perinatally acquired HIV are now reaching childbearing age and becoming pregnant. A significant number of these pregnancies are unintended. The components of prenatal care and general principles of ART and HIV management do not differ between pregnant women with perinatally acquired HIV and those who acquired HIV infection in other ways (e.g., acquired through sexual contact or injection drug use). However, there are unique challenges in this population related to reproductive health care needs and the prevention of perinatal transmission. Adherence to ART is commonly a major challenge for women with perinatal HIV. In addition, because most of these women are still adolescents and young adults, they may be at higher risk of certain pregnancy complications such as preterm delivery, low birthweight, and preeclampsia.

As many as 30% to 70% of pregnant women with perinatal HIV have evidence of HIV drug resistance. This is due to extensive ART exposure prior to pregnancy, including exposure to suboptimal monotherapy or dual-therapy regimens as children. Optimal ART regimens should be selected on the basis of resistance testing, prior ART history, and the same guiding principles used for ART-experienced adults. Because of the potential for known or suspected complex drug-resistance mutation patterns in individuals who acquired HIV perinatally, clinicians may consider phenotypic resistance testing in these women during pregnancy when resistance testing is indicated. Consideration should be given to regimens that optimize dosing intervals and minimize pill burden. Consultation with experts in HIV and pregnancy is recommended. Regimens should be constructed using antiretroviral (ARV) drugs recommended for use in pregnancy whenever possible. However, in many cases, the presence of extensive drug resistance may warrant the use of ARV drugs for which there is limited experience in pregnancy; consultation with experts in HIV and pregnancy is recommended in such cases.

Women with perinatal HIV are more likely to have lower median CD4 T lymphocyte counts, detectable viral loads, and genotypic drug resistance (40% vs 12%) than women with non-perinatally acquired HIV. In a retrospective analysis of 37 pregnancies among women with perinatal HIV and 40 pregnancies among age-matched women with non-perinatally acquired HIV who delivered during the same time period, the viral load decline achieved during pregnancy in women with perinatal HIV was not sustained during postpartum follow-up in contrast to the age-matched comparison group. During 4 years of follow-up, there were 4 deaths.

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due to AIDS-related complications in women with perinatal HIV but none in the women with non-perinatally acquired HIV.\textsuperscript{12} Although genotypic mutations were more common in women with perinatal HIV, loss of viral suppression resulting in the progression of disease postpartum was more likely related to adherence difficulties, highlighting the need for special focus on adherence interventions after delivery.

Evidence from studies is conflicting as to whether women with perinatally acquired HIV have higher rates of preterm and small-for-gestational-age (SGA) infants when compared with women with non-perinatally acquired infection.\textsuperscript{13,14} Several studies have demonstrated no associations between perinatal route of maternal HIV infection and preterm birth, SGA, or low birth weight.\textsuperscript{8,11,13-15} Other studies have reported conflicting results:

- A case series reported high rates of preterm birth (31\%) among women with perinatally acquired HIV.\textsuperscript{9}
- Jao et al. reported a four-fold increased risk for SGA births among the women with perinatal infection compared to those with non-perinatally acquired infection.\textsuperscript{16}
- Munjal et al. reported earlier gestational age at delivery and lower average birthweights in infants born to women with perinatal compared to those with non-perinatally acquired infection.\textsuperscript{12}
- Jao et al. found that infants born to women with perinatally acquired HIV had lower mean length-for-age throughout the first year of life.\textsuperscript{7}

Several studies have suggested that pregnant women with perinatally acquired HIV are more likely to have a cesarean delivery most commonly indicated for prevention of HIV infection due to lack of viral load suppression.\textsuperscript{9,12} Cesarean delivery in these young women raises concerns for increased risk of adverse obstetric outcomes if repeated cesarean deliveries are required for future pregnancies. Reassuringly, despite prolonged HIV infection, receipt of multiple ART regimens, and increased likelihood of drug-resistant virus in women who acquired HIV perinatally, with appropriate prenatal management and ART that results in viral suppression, the risk of perinatal transmission does not appear to be increased in this population.\textsuperscript{8,9,11,12,17-19}

Psychosocial challenges may be magnified due to the presence of a lifelong chronic illness, high rates of depression,\textsuperscript{20} and frequently the loss of one or both parents. Attention to developmentally appropriate adherence counseling is critical. A systematic review and meta-analysis of 50 eligible studies on ART adherence in individuals living with HIV aged 12 years to 24 years, in which adequate adherence was defined as greater than 85\% by self-report or undetectable viral load, reported 62.3\% adherence overall among youth with HIV. Youth from U.S. studies had the lowest average rate of adherence at 53\%.\textsuperscript{21} In a 2014 study of 1,596 people with perinatal HIV living in New York City, only 61\% were virally suppressed. The authors attributed poor ART adherence to social, behavioral and developmental factors.\textsuperscript{23} A history of depression has also been associated with nonadherence to ART among pregnant women with perinatal HIV.\textsuperscript{23} Focused attention on diagnosis and treatment of depression in the preconception period may lead to more optimal medication adherence. Self-motivation and social support were key to medication adherence in a study of adolescents living with HIV in the United Kingdom.\textsuperscript{24}

Among adolescents with perinatal HIV, pregnancy may create additional complications in the transition from pediatric/adolescent HIV care to adult care due to the complexity of navigating an adult healthcare system with multiple providers. However, pregnancy may also be an opportune time for a young woman to transition to adult care. Studies have noted reduced rates of retention in care and viral suppression among pediatric and adolescent persons with HIV who are transitioning to adult health care.\textsuperscript{26} Continuing support for adherence to treatment is needed in this population. Coordination of care across multiple disciplines including HIV primary care, OB/GYN, and perinatal case management is advised. Integration of reproductive health counseling and pregnancy prevention including consistent condom use and developmentally appropriate skill building to support disclosure are all recommended.
References


