Prenatal Care, Antiretroviral Therapy, and HIV Management When HIV Was Perinatally Acquired

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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 perinatally acquired HIV (PHIV) or non-perinatally acquired HIV during pregnancy **(AII).** • PHIV is often associated with extensive ART experience, and multidrug antiretroviral (ARV) resistance may be a factor at the onset of pregnancy due to long-term HIV exposure and prior adherence difficulties. Consultation with experts in HIV and pregnancy is recommended when the presence of extensive drug resistance warrants the use of ARV drugs for which there is limited experience in pregnancy **(AIII).** • Managing PHIV during pregnancy necessitates enhanced focus on adherence interventions during pregnancy and after delivery **(AII).**
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 people with HIV, including those with perinatally acquired HIV (PHIV). Pregnancy with PHIV is becoming more frequent in the United States as childbearing age is reached. A significant number of these pregnancies are unplanned. [1-3] The components of prenatal care and general principles of ART and HIV management do not differ between pregnancies associated with PHIV and those with non–perinatally acquired HIV (NPHIV), in which HIV was acquired through other routes of transmission. However, the prevention of perinatal transmission in the context of PHIV can pose unique challenges related to lifelong HIV management and the use of antiretrovirals (ARVs) since birth. Adherence to ART is often a major challenge for people with PHIV.

Considering most people with PHIV have extensive ART experience, optimal ARV regimens should be selected using the same guiding principles as for ART-experienced adults. In particular, the ARV regimen should be selected on the basis of resistance testing, pill burden, and the patient's specific ART history and preferences. Because people who acquired HIV perinatally may be more likely to have developed complex drug-resistance mutation patterns, clinicians may consider performing phenotypic resistance testing, in addition to genotypic resistance testing, when resistance testing is indicated during pregnancy with PHIV. Regimens that can be given once daily and that minimize pill burden are preferred. Regimens should be constructed using ARV drugs that are recommended for use in pregnancy whenever possible (see Recommendations for the Use of Antiretroviral Drugs During Pregnancy: Overview and Table 7: Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive). 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.

People with PHIV experience lifelong HIV infection, have received multiple ARV regimens, and are more likely to harbor drug-resistant virus. As many as 30% to 70% of pregnant women with PHIV have evidence of HIV drug resistance.[4-7] Despite these factors, many studies have shown that the

risk of perinatal transmission does not appear to be increased in this population, as long as these women receive appropriate prenatal management and achieve viral suppression.[5,7-12] An analysis of data from SMARTT PHACS (Surveillance Monitoring for ART Toxicities Study—Pediatric HIV/AIDS Cohort Study) that included 2,123 births from 2007 to 2015, pregnant women with PHIV had a higher perinatal HIV transmission rate (1.1%; 95% confidence interval [CI], 0.3% to 4.3%) than pregnant women with NPHIV (0.4%; 95% CI, 0.2% to 1.0%); however, this higher rate was associated with a greater likelihood of detectable maternal viral load at delivery.[13] Historically, women with PHIV have been more likely to have detectable viral loads at delivery, lower CD4 T lymphocyte cell counts, and genotypic drug resistance than women with NPHIV; these factors can have implications during labor and delivery.[7,13-16] Several studies have suggested that pregnant women with PHIV are more likely to have a cesarean delivery to prevent HIV transmission; cesarean deliveries are most commonly indicated in these women due to a lack of viral load suppression.[4,10] Cesarean delivery in pregnancies with PHIV raises concerns for increased risk of adverse obstetric outcomes if repeated cesarean deliveries are required for future pregnancies.

Evidence is conflicting as to whether women with PHIV have higher rates of preterm birth and small-for-gestational-age (SGA) infants than women with NPHIV.[17,18] In one cohort, there was a fourfold increased risk for SGA births among women with PHIV, compared with those with NPHIV.[19] In another study, infants born to women with PHIV were born at an earlier gestational age and had lower average birth weights, compared with infants born to women with NPHIV.[10] In contrast, other studies have demonstrated no associations between maternal PHIV and preterm birth, SGA infants, or low birth weight.[18,20]

A retrospective cohort study reported poor rates of retention in care and low rates of viral suppression for up to 2 years postpartum among 22 pregnant women with PHIV.[21] In a retrospective analysis[10] of 37 pregnancies among women with PHIV and 40 pregnancies among age-matched women with NPHIV who delivered during the same time period, the viral load declines achieved during pregnancy in women with PHIV were not sustained during postpartum follow-up, in contrast to the age-matched comparison group of women with NPHIV. Another study found that during 4 years of follow-up postpartum, there were four deaths due to AIDS-related complications among women with PHIV but none among the women with NPHIV.[10] Although genotypic drug-resistance mutations were more common in women with PHIV, loss of viral suppression that resulted in postpartum disease progression was more likely to be related to adherence difficulties, highlighting the need for adherence interventions after delivery.

Psychosocial challenges related to lifelong HIV may be magnified by high rates of depression and, frequently, the loss of one or both parents.[22] Attention to developmentally appropriate adherence counseling is critical. A systematic review and meta-analysis of 50 eligible studies on ART adherence in young people with HIV who were aged 12 to 24 years reported 62.3% adherence overall. Youth from U.S. studies had the lowest average rate of adherence at 53%.[23] In a 2014 study of 1,596 people with PHIV who were living in New York City, only 61% were virally suppressed. The authors attributed poor ART adherence to social, behavioral, and developmental factors.[24] A history of depression also has been associated with nonadherence to ART among pregnant women with PHIV.[25,26] Attention to diagnosis and treatment of depression during the preconception period may lead to better medication adherence. Self-motivation and social support were key to achieving medication adherence in a study of adolescents with HIV in the United Kingdom.[27]

Rates of retention in care and viral suppression are lower among pediatric and adolescent patients with HIV who are transitioning to adult health care than in adults with HIV who are already in care.[28,29] Among adolescents with PHIV, pregnancy may create additional complications in the transition from pediatric and adolescent HIV care to adult care due to the complexity of navigating an adult health care system with multiple providers. However, pregnancy also may be an opportune time to transition to adult care. There is a need to identify, develop or adapt, and implement culturally

sensitive and women-centered interventions for improving HIV care continuum outcomes during pregnancy and postpartum.[30] Coordination of care across multiple disciplines—including HIV primary care, obstetric/gynecologic care, and perinatal case management—is advised.[31] Integration of reproductive health counseling and family planning services—including consistent counseling on condom use, sexually transmitted infection testing and prevention, optimal pregnancy spacing, and developmentally appropriate skill building to support disclosure—as indicated, is recommended.

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