Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Women may have an increased risk of HIV infection during pregnancy and breastfeeding. In a recent study of 2,751 HIV-serodiscordant couples in seven African countries, 686 pregnancies among HIV-negative women were identified and 82 incident HIV infections occurred. After adjusting for condom use, pre-exposure prophylaxis (PrEP) use, and HIV viral load, the probability of HIV acquisition per condomless sex act was higher in late pregnancy (adjusted relative risk [aRR] 2.82; *P* = 0.01) and the postpartum period (aRR 3.97; *P* = 0.01) as compared to that during the nonpregnant period. Women who are at risk for acquiring HIV during pregnancy and the postpartum period should consider using interventions that prevent HIV acquisition, such as PrEP.

Acute or recent HIV infection in pregnancy or during breastfeeding is associated with an increased risk of perinatal transmission of HIV and may represent a significant proportion of residual perinatal transmission in the United States. In a cohort analysis of HIV-exposed infants born in New York State from 2002 to 2006, maternal acquisition of HIV during pregnancy was associated with a higher risk of transmission (odds ratio...
Among 70 infants born with perinatal HIV infection in Florida during 2007 through 2014, 12 of their mothers (17%) had evidence of acute infection during pregnancy.\(^5\) In the United States, among 10,308 pregnant women with HIV who delivered live infants from 2005 to 2010 in 15 areas that conducted Enhanced Perinatal Surveillance, 124 women (1.2%) were identified as seroconverting during pregnancy. The rate of perinatal transmission was eight times higher among women who seroconverted during pregnancy (12.9%) than among those who seroconverted prior to pregnancy (1.6%) (\(P < 0.0001\)).\(^7\) Similarly, in the United Kingdom, of 108 new perinatal HIV infections that were identified between 2006 and 2013, 23 were associated with a concurrent maternal seroconversion.\(^8\) The high rate of transmission associated with acute infection is likely related to the combination of the high viral loads in plasma, breast milk, and the genital tract associated with acute infection\(^9\) and the fact that the diagnosis is easy to miss, which results in lost opportunities for implementing prevention interventions.

Health care providers should maintain a high level of suspicion of acute HIV infection in women who are pregnant or breastfeeding and have clinical signs and symptoms compatible with acute infection. Even when women do not report high-risk behaviors; it is still possible that their sexual partners are practicing high-risk behaviors without their knowledge. An estimated 40% to 90% of patients with acute HIV infection will experience symptoms of acute retroviral syndrome, which is characterized by fever, lymphadenopathy, pharyngitis, skin rash, myalgias/arthritis, and other symptoms.\(^10\)-\(^12\) Providers often do not recognize acute HIV infection because the symptoms are similar to those of other common illnesses, and individuals with the condition also can be asymptomatic.

When acute retroviral syndrome is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction with a routine HIV antibody screening test or an antigen/antibody immunoassay test. Updated guidance for HIV testing recommends initial testing for HIV with a Food and Drug Administration (FDA)-approved antigen/antibody combination (fourth-generation) immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. These tests are used to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection. More specific guidance on HIV testing can be found in the Acute and Recent (Early) HIV Infection section of the Adult and Adolescent Antiretroviral Guidelines, the Centers for Disease Control and Prevention (CDC) HIV testing algorithm, and the Maternal HIV Testing and Identification of Perinatal HIV Exposure section.

Recent HIV infection also can be detected by repeat HIV testing later in pregnancy in women whose initial HIV test earlier in pregnancy was negative.\(^13\) A report from the MIRAD study found that 6 of 54 women (11%) whose HIV was identified with rapid HIV testing during labor had acute or recent infection.\(^4\) Repeat HIV testing during the third trimester is recommended for pregnant women who are known to be at risk of HIV infection, who receive care in facilities with an HIV incidence of \(\geq 1\) case per 1,000 pregnant women per year, or who reside in jurisdictions with elevated HIV incidence (see Prenatal and Perinatal Human Immunodeficiency Virus Testing, Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings, the CDC HIV testing algorithm, and the Maternal HIV Testing and Identification of Perinatal HIV Exposure section).\(^15\) Despite this recommendation, a retrospective cohort study at a large metropolitan hospital in a high-prevalence jurisdiction reported that repeat prenatal HIV testing was performed in only 28.4% of women.\(^16\)

Acute or recent HIV infection during pregnancy and breastfeeding is associated with a high risk of perinatal transmission of HIV. Therefore, all pregnant women with acute or recent HIV infection should start antiretroviral therapy (ART) as soon as possible, with the goal of preventing perinatal transmission by optimal suppression of plasma HIV RNA below detectable levels. Baseline genotypic resistance testing should be performed to guide adjustment of an optimal ARV drug regimen. Data from the United States and Europe demonstrate that in 6% to 16% of patients, transmitted virus may be resistant to \(\geq 1\) ARV drug.\(^17,18\) If results of resistance testing are already available or the source virus’s resistance pattern is known, that information can be used to guide selection of the drug regimen.
A dolutegravir-based regimen that includes tenofovir disoproxil fumarate (TDF) and emtricitabine should be initiated in pregnant women (after the first trimester) and breastfeeding women with acute HIV infection, and breastfeeding should be discontinued (see Table 6. Dolutegravir should not be initiated during the first trimester (<14 weeks [≤13 6/7 weeks] gestational age by last menstrual period) due to concerns about a possible increased risk of neural tube defects. Although dolutegravir is not FDA-approved for use in the first trimester, some members of the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission would consider using dolutegravir at 12 weeks gestational age by last menstrual period on an individual patient basis. Clinicians should counsel patients who initiate a dolutegravir-containing regimen on the use of postpartum contraception. For additional information, see Recommendations for the Use of Antiretroviral Drugs During Pregnancy.

Dolutegravir should be considered for treatment of acute infection during pregnancy and breastfeeding because it has a higher barrier to resistance and can be administered with once-daily dosing. Raltegravir has a lower barrier to resistance than dolutegravir; thus, it is not recommended for use during acute infection, when viral loads are expected to be high. Alternatively, a regimen that includes a ritonavir-boosted protease inhibitor (PI) can be initiated for treatment of acute infection during pregnancy or breastfeeding.

Recent data suggest that the use of integrase strand transfer inhibitor (INSTI)-based regimens may be associated with shorter time to viral suppression. An observational study evaluated time to viral suppression among 86 nonpregnant adults with newly-diagnosed HIV infection: 36 participants (42%) had acute HIV infection, 27 (31%) had early HIV infection, and 23 (27%) had established HIV infection. ART was initiated within 30 days of diagnosis and the median time to documented viral suppression was 12 weeks. Time to viral suppression was significantly shorter in those receiving an INSTI-based versus a PI-based regimen (median time to viral suppression was 12 weeks and the interquartile range [IQR] was 4–24 weeks in those receiving INSTIs vs. a median time to viral suppression of 24 weeks and an IQR of 12–24 in those receiving PIs; P = 0.022; baseline viral loads did not differ between those two groups). Dolutegravir plus TDF and emtricitabine is considered a reasonable ARV regimen for treatment of acute infection in nonpregnant adults, but data are limited regarding transmission of INSTI-resistant HIV and efficacy of this regimen in treatment of early infection.

In cases where acute HIV infection is identified during the first trimester, a regimen that includes a ritonavir-boosted PI should be initiated. Use of a boosted PI-based regimen is recommended as an alternative regimen for women in their second and third trimester and women who receive an HIV diagnosis during breastfeeding. Resistance to PIs emerges slowly and clinically significant transmitted resistance to PIs is uncommon. The choice of PI should be based on recommendations for ARV drugs to use in pregnancy (see Table 6 and Table 10); these drugs include darunavir/ritonavir and atazanavir/ritonavir.

TDF plus emtricitabine is the preferred nucleoside reverse transcriptase inhibitor backbone for treatment of acute infection. Abacavir is not recommended for empiric treatment of acute infection unless the patient is known to be HLA-B*5701 negative.

When acute HIV infection is diagnosed during pregnancy, and particularly when it is documented in late pregnancy, cesarean delivery may be necessary when there is insufficient time to fully suppress a patient’s viral load. When acute HIV infection is diagnosed during breastfeeding, breastfeeding should be discontinued. In nursing mothers in whom seroconversion is suspected, breastfeeding should be interrupted, and it should not resume if infection is confirmed (see Guidance for Counseling and Managing Women Living with HIV in the United States Who Desire to Breastfeed). Women can continue to express and store breast milk while awaiting confirmation of infection status. Given the high risk of transmission to the infant with acute maternal infection, an infant should receive an ARV regimen appropriate for this elevated risk when acute HIV infection is diagnosed during pregnancy or breastfeeding. Consultation with a pediatric HIV specialist regarding appropriate infant management is strongly recommended (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). All women who receive a diagnosis of acute infection should be asked whether they know the HIV status of their partner. HIV testing of the sexual partners of all pregnant women who test HIV positive should be encouraged.
References


