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 serodifferent 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; \( P = 0.01 \)) than 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 during pregnancy or breastfeeding is associated with an increased risk of perinatal HIV transmission, and a significant proportion of perinatal transmission cases can be attributed to maternal acute infection. Among 10,308 pregnant women with HIV who delivered live infants from 2005 to 2010 in 15 areas in the United States that conducted Enhanced Perinatal Surveillance, 124 women (1.2%) were infected perinatally with HIV. Similar results have been reported from the United Kingdom, where 23 perinatal infections associated with concurrent maternal acute infection were identified between 2010 and 2013 in the United Kingdom. The high rate of transmission in people with acute infection is likely related to the high viral loads in plasma, breast milk, and the genital tract that are present during acute infection; in addition, acute HIV infection symptoms...
can be nonspecific, which results in missed opportunities to diagnose and implement interventions that can reduce the risk of perinatal transmission.

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 that are 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/arthralgias, and other symptoms.8-10 Providers often do not recognize acute HIV infection because the symptoms are similar to those of other common illnesses, and individuals with acute HIV infection may also be asymptomatic.

When acute retroviral syndrome is suspected during pregnancy or breastfeeding, a plasma HIV RNA test should be obtained in conjunction with an antigen/antibody immunoassay test. Updated guidance for HIV testing recommends using 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 for initial testing. 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.

Recent HIV infection also can be detected by repeat HIV testing later in pregnancy in women whose initial HIV test was negative.11 A report from the MIRAD study found that six of 54 women (11%) whose HIV was identified with rapid HIV testing during labor had acute or recent infection.12 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 ≥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 Maternal HIV Testing and Identification of Perinatal HIV Exposure).13 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.14

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 rapid suppression of plasma HIV RNA below detectable levels. Baseline genotypic resistance testing should be performed to guide adjustment of an optimal antiretroviral (ARV) drug regimen. Data from the United States and Europe demonstrate that in 6% to 16% of patients, transmitted virus may be resistant to ≥1 ARV drug.15,16 If results of resistance testing are already available or the source virus’s resistance pattern is known, that information can be used to guide the selection of the drug regimen.

A regimen that includes dolutegravir (DTG) plus tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) should be initiated in pregnant women and breastfeeding women with acute HIV infection (see Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, and Table 5). DTG exposure around the time of conception has been associated with a small but significant increase in the risk of infant neural tube defects (NTDs) in Botswana (0.3%). Although this risk was higher than the risk for NTDs in infants born to women who were receiving efavirenz (EFV; 0.05%) and women without HIV (0.08%), there are not enough data to determine the risk of NTDs with preconception use of all Preferred and Alternative regimens, including DTG, in the United States. Based on the available evidence, the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission recommends DTG as a Preferred drug for pregnant women, irrespective of trimester. When DTG use is continued after delivery,
clinicians should discuss reproductive desires as well as the risks and benefits of conceiving on DTG and contraceptive options with the patient. For additional information and recommendations on the use of DTG, see Recommendations for Use of Antiretroviral Drugs During Pregnancy and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

DTG is associated with higher rates of virologic suppression, faster rates of viral load decline, and a higher genetic barrier to drug resistance than other Preferred and Alternative agents. DTG plus TDF plus FTC is considered a reasonable ARV regimen for treatment of acute infection in nonpregnant adults, but data are limited regarding the transmission of integrase strand transfer inhibitor (INSTI)-resistant HIV and the efficacy of this regimen when treating early infection. Alternative regimens for treatment of acute infection during pregnancy and breastfeeding include raltegravir (RAL) plus TDF plus FTC or a regimen that includes a ritonavir-boosted protease inhibitor-based regimen (see Table 4 and Table 5). TDF plus FTC is the Preferred nucleoside reverse transcriptase inhibitor (NRTI) backbone for treatment of acute infection. Abacavir is not recommended for empiric treatment of acute infection unless the patient previously tested negative for HLA-B*5701; this will avoid delays in ART initiation while awaiting HLA-B*5701 test results.

Several studies have demonstrated that the use of INSTI-based regimens is associated with shorter time to viral suppression compared with other ARV regimens. 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 who received an INSTI-based regimen than in those who received a PI-based regimen. Median time to viral suppression was 12 weeks in those who received INSTIs (interquartile range [IQR] 4–24 weeks) and 24 weeks in those who received PIs (IQR 12–24 weeks; P = 0.022). The baseline viral loads did not differ between these two groups. In the ADVANCE study, 1,053 ART-naive individuals were randomized to receive DTG plus FTC plus TAF versus DTG plus FTC plus tenofovir alafenamide (TAF), or EFV plus FTC plus TDF. At 48 weeks, 84% of participants in the DTG plus FTC plus TAF group, 85% in the DTG plus FTC plus TDF group, and 79% in the EFV-based ART group had achieved HIV RNA <50 copies/mL. While both DTG-based regimens were noninferior to the EFV regimen, the time to viral suppression was substantially shorter among participants in the DTG arms.

While no data are available to inform the treatment of acute HIV during pregnancy, two recent studies in women who presented to care late in pregnancy demonstrated more rapid viral decline on INSTI-based regimens than on EFV-based ART. In the DolPHIN-2 study, 268 ART-naive pregnant women in Uganda and South Africa with a median gestational age of 31 weeks were randomized to receive either DTG plus two NRTIs or EFV plus two NRTIs. At delivery, women in the DTG arm were significantly more likely to have achieved HIV RNA <50 copies/mL than those in the EFV arm (73.8% vs. 42.6%; adjusted risk ratio 1.66; 95% confidence interval, 1.3–2.1; P < 0.0001). Similarly, IMPAACT 1081 randomized 408 ART-naive, late-presenting pregnant women in South America, Africa, Thailand, and the United States to receive RAL plus two NRTIs or EFV plus two NRTIs. Fifty percent of these women presented to care at 20 weeks to <28 weeks gestation and 50% presented at 28 weeks to <37 weeks gestation. Median time to achieve viral loads <200 copies/mL was 8 days for women who received RAL-based ART and 15 days for those who received EFV-based treatment. Viral load decline was greater in women who received RAL-based ART than in those who received EFV-based ART at Weeks 2, 4, and 6 after initiation.

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 with suspected seroconversion, breastfeeding should be interrupted, and it should not resume if infection is confirmed (see 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 that is appropriate for this elevated risk when acute HIV infection is diagnosed during pregnancy or breastfeeding (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection). Consulting a pediatric HIV specialist regarding appropriate infant management is strongly recommended. 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, and PrEP should be offered to partners who test HIV negative.

References


