Lack of Viral Suppression (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations

• Because maternal antenatal viral load correlates with risk of perinatal transmission of HIV, suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible **(AII)**.
• If an ultrasensitive HIV RNA assay indicates failure of viral suppression (after an adequate period of treatment):
  • Assess adherence and resistance (if HIV RNA level is high enough for resistance testing) **(AII)**.
  • Consult an HIV treatment expert and consider possible antiretroviral regimen modification **(AIII)**.
• Scheduled cesarean delivery is recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of 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*

Virologic suppression is defined as a confirmed HIV RNA level below the lower limits of detection of an ultrasensitive assay, and virologic failure is the inability to achieve or maintain an HIV RNA level <200 copies/mL.

Baseline HIV RNA levels have been shown to affect the time to response in both pregnant and non-pregnant individuals, with no difference in response between pregnant and non-pregnant women.[1,2] HIV RNA levels should be assessed 2 to 4 weeks after an antiretroviral (ARV) drug regimen is initiated or changed to provide an initial assessment of effectiveness.[3] Most patients with an adequate viral response at 24 weeks of treatment have had at least a 1 log copies/mL HIV RNA decrease within 1 to 4 weeks after starting therapy.[3] Suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible, because maternal antenatal HIV RNA level correlates with risk of perinatal transmission of HIV. The lack of virologic suppression by late pregnancy may indicate virologic failure but may also represent inadequate time on antiretroviral therapy (ART). In a retrospective multicenter cohort of 378 pregnant women, 77.2% achieved HIV RNA <50 copies/mL by delivery, with success of viral suppression varying by baseline HIV RNA level. With baseline <10,000 copies/mL, gestational age at initiation did not affect success up to 26.3 weeks. With baseline >10,000 copies/mL, however, delaying initiation past 20.4 weeks significantly reduced the ability to achieve maximal suppression at delivery.[1] Among 1,070 HIV-infected treatment-naive pregnant women participating in IMPAACT P1025, a prospective cohort study, initiation of ART at >32 weeks' gestation was also associated with a significantly higher risk of having viral load >400 copies/mL at delivery.[4] A recent report from the French Perinatal Cohort found no perinatal transmission among 2,651 infants born to women who were receiving ART before conception, continued ART throughout pregnancy and delivered with a plasma HIV-RNA <50 copies/mL (upper limits of confidence interval [CI] 0.1%). In the entire cohort of 8,075 mother/infant pairs followed from 2000 through 2011, HIV-RNA level and timing of ART initiation were independently associated with perinatal transmission in a logistic regression analysis.[5]

The response to ART may also be affected by the presence of acute HIV-1 infection. In a prospective study of serial measures of plasma HIV-RNA and CD4 T lymphocyte (CD4) counts after ART initiation (non-nucleoside reverse transcriptase inhibitor-based) in 25 women with acute HIV and 30 women with chronic HIV in Kenya, mean baseline HIV viral load was similar but the rate of viral decline following ART initiation was significantly slower among women with acute HIV than those with chronic infection (after adjustment for baseline CD4 count). Strategies to accelerate viral decline may be considered in this situation, in consultation with HIV treatment experts.[6]

A three-pronged approach is indicated for management of women on ART regimens who have suboptimal suppression of HIV RNA, taking into account time on treatment. The 3 steps should be:

- ARV drug resistance studies (if plasma HIV RNA is above the threshold for resistance testing, generally >500 or >1,000 copies/mL);
- Assessment of adherence, tolerability, incorrect dosing, or potential problems with absorption (e.g., nausea/vomiting, lack of attention to food requirements); and
- Consideration of ART regimen modification.

The role of therapeutic drug monitoring in reducing the risk of virologic failure is still undefined.[7-9]

Experts in the care of ARV-experienced adults should be consulted, particularly if a change in drug regimen is necessary due to resistance or adverse effects. In certain situations, regimen simplification may be considered to promote better adherence, as well. Hospitalization can be considered for directly observed drug administration, adherence education, and treatment of comorbidities such as nausea and vomiting.[10]

Among 662 pregnancies followed in Italy between 2001 and 2008, treatment modification during pregnancy was independently associated with an HIV-1 RNA level >400 copies/mL in late pregnancy (adjusted odds ratio, 1.66; 95% CI, 1.07–2.57; $P = 0.024$), highlighting the importance of using potent and well-tolerated regimens during pregnancy to maximize effectiveness and minimize the need to modify treatment.[11]

A recent systematic review and meta-analysis of adherence to ART during and after pregnancy in low-, middle-, and high-income countries (27% of studies were from the United States) found that a pooled estimate of 63.5% of pregnant women on ART had adequate (>80%) adherence to it.[12] Evaluation of and support for adherence during pregnancy is critical to achievement and maintenance of maximal viral suppression.

Because of the ability of raltegravir to rapidly suppress viral load (approximately 2 log copies/mL decrease by week 2 of therapy), the addition of raltegravir in late pregnancy has been suggested for women who have high viral loads and/or in whom multiple drug-resistant mutations have resulted in incomplete suppression of viremia.[13-16] However, the efficacy and safety of this approach have not been evaluated in clinical trials, and only anecdotal reports and case series are available.[17,18] In the setting of a failing regimen related to non-adherence and/or resistance, there are concerns that the addition of a single agent may further increase risk of resistance and potential loss of future effectiveness with raltegravir. There have been two recent reports of marked elevations in transaminase levels following introduction of a raltegravir-containing regimen in late pregnancy, with return to normal levels after raltegravir discontinuation.[17,19] At the current time, this approach cannot be routinely recommended.

Scheduled cesarean delivery is recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of delivery.[20,21]

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