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Considerations and Recommendations for Pregnancy and Postpartum Care for People Living With Human Immunodeficiency Virus

Matthew Givens, MD, Judy Levison, MD, MPH, and Lisa Rahangdale, MD, MPH

Considerable strides have been made in reducing the rate of perinatal human immunodeficiency virus (HIV) transmission within the United States and around the globe. Despite this progress, preventable perinatal HIV transmission continues to occur. Adherence to HIV screening and treatment recommendations preconception and during pregnancy can greatly reduce the risk of perinatal HIV transmission. Early and consistent usage of highly active antiretroviral therapy (ART) can greatly lower the HIV viral load, thus minimizing HIV transmission risk. Additional intrapartum interventions can further reduce the risk of HIV transmission. Although the current standard is to recommend abstinence from breastfeeding for individuals living with HIV in settings where there is safe access to breast milk alternatives (such as in the United States), there is guidance available on counseling and risk-reduction strategies for individuals on ART with an undetectable viral load who elect to breastfeed.

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Despite improved knowledge, medications, and access to care, human immunodeficiency virus (HIV) continues to cause significant morbidity and mortality worldwide. Women account for 42% of the estimated 38 million people worldwide who are living with HIV. Approximately 1.7 million people were newly diagnosed with HIV in 2019 with children accounting for 150,000 of those infections.[1] Children with HIV infection, especially in resource-limited settings, face a lifetime of health and social challenges.

From the Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; and the Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas.

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Perinatal human immunodeficiency virus transmission can be reduced by adhering to screening and treatment recommendations during pregnancy and postpartum.

Corresponding author: Lisa Rahangdale, MD, MPH, Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, Chapel Hill, NC; email: lisa_rahangdale@med.unc.edu.

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Perinatal HIV transmission is the leading cause of childhood HIV infection. Without adequate antiretroviral therapy (ART), a pregnant individual with HIV has an approximately 15–45% risk of transmitting the virus to their child.[2] This risk can be reduced to less than 1% with an appropriate ART regimen.[3–5] Access to treatment with ART was responsible for prevention of an estimated 1.4 million childhood HIV infections between 2010 and 2018.[1] The vast majority of this progress was attributable to improved access to antiretroviral medications and education campaigns in low-resource countries. Within the United States, perinatal HIV transmission accounts for less than 1% of new HIV diagnoses (an estimated 65 cases of approximately 5,000 individuals with HIV delivering newborns).[5,6] However, there is a large racial disparity with approximately 65% of cases of perinatal HIV diagnoses being among Black children.[6]

Transmission of HIV during pregnancy may occur during the antepartum, intrapartum, or postpartum periods. Although the exact timing and mechanism of perinatal HIV transmission are not known, among breastfeeding individuals not on ART it is thought that approximately 25–40% of transmission occurs during the antepartum period (in utero),

approximately 50% occurs at the time of labor and delivery, and the remainder of transmission events occur during breastfeeding.[2]

In-utero HIV transmission can occur through ascending infection from the lower genital tract or through placental microtransfusions arising from breakdown of the placental interface. Intrapartum transmission occurs through contact between the pregnant individual's blood or genital tract secretions and the fetal mucous membranes. During the postpartum period, HIV can be transmitted to the infant through breast milk. Regardless of timing and route of perinatal HIV transmission, once the virus is integrated into an infant's cells, rapid replication occurs leading to a lifelong HIV infection and, if not controlled with ART, subsequent development of acquired immunodeficiency syndrome (AIDS).

Strategies to reduce the risk of perinatal HIV transmission center around reducing exposure of a fetus or infant to the virus. This is primarily accomplished by reducing the pregnant indivdual's HIV viral load through prolonged and consistent use of a highly active ART regimen. The risk of HIV transmission during pregnancy is directly related to the pregnant individual's viral load throughout the pregnancy and at the time of delivery. Further reduction of exposure occurs through interventions during the intrapartum period and by routinely recommended abstinence from breastfeeding. This article will focus on specific recommendations for individuals living with HIV preconception, during pregnancy, and postpartum.

MANAGEMENT OF HIV DURING PREGNANCY

Prepregnancy Counseling

All people, regardless of HIV status, should be counseled regarding safe sex practices and offered HIV and other sexually transmitted infection (STI) screening. Such screening includes at least one-time HIV testing in everyone 13–64 years of age, as well as annual or more frequent HIV testing in high-risk individuals (people with a sexual partner living with HIV, people who use injection drugs or partners of people who use injection drugs, people who exchange sex for money or drugs, and people who themselves or whose sex partners have had more than one sex partner since their last HIV test).[7] Additionally, all people considering pregnancy should receive HIV testing as part of routine preconception care.

Medical care for individuals of childbearing age who are living with HIV should begin before pregnancy and include a discussion of reproductive goals. If desired, health care professionals should offer access to contraceptive methods to reduce the risk of unplanned pregnancy. Reducing viral load to an undetectable level requires prolonged exposure to antiretroviral medications. Initiation of ART in the preconception period (or as early in pregnancy as possible) optimizes the likelihood of total viral suppression at the time of delivery. Therefore, individuals living with HIV who are planning pregnancy should be counseled to begin ART and attain maximal viral suppression before conception. The effectiveness of early ART initiation was demonstrated in a study of 8,075 mother–infant pairs, with no cases of perinatal HIV transmission among the 2,651 parents who began ART before conception, continued during pregnancy, and had a viral load less than 50 copies/mL at the time of delivery.[8]

Human Immunodeficiency Virus Testing During Pregnancy

Identification of HIV infection is crucial to initiating treatment and optimizing both parental and infant health. As such, universal HIV testing using an opt-out testing strategy is recommended for all pregnant people. Testing for HIV should be completed as soon as possible during pregnancy and should be repeated in the third trimester for individuals who are at increased risk of acquiring HIV, including individuals who receive their care in facilities that have an HIV incidence of 1 or more cases per 1,000 pregnant individuals per year, individuals who live in areas with elevated HIV incidence, those who live in states requiring third-trimester screening, and individuals engaging in high-risk behaviors.[9]

Screening for HIV is best accomplished by a combination antigen–antibody immunoassay, also known as fourth-generation HIV testing, which detects HIV-1 antibodies, HIV-2 antibodies, and HIV-1 p24 antigen. This combination test is better able to detect acute HIV infection (within 2 weeks of infection) compared with prior generations of testing that were typically antibody-only tests, which can take months to result positive. An initial positive fourth-generation test result needs to be confirmed with a second test, specifically an HIV-1–HIV-2 antibody differentiation immunoassay. If the results of both tests are positive, the individual has HIV. If the first is positive and the second is negative, a nucleic acid test or viral load must be done. In cases in which the viral load is not detected, the screening test was a false-positive. If virus is present, HIV infection is confirmed and the individual likely has acute HIV[10] (Fig. 1).

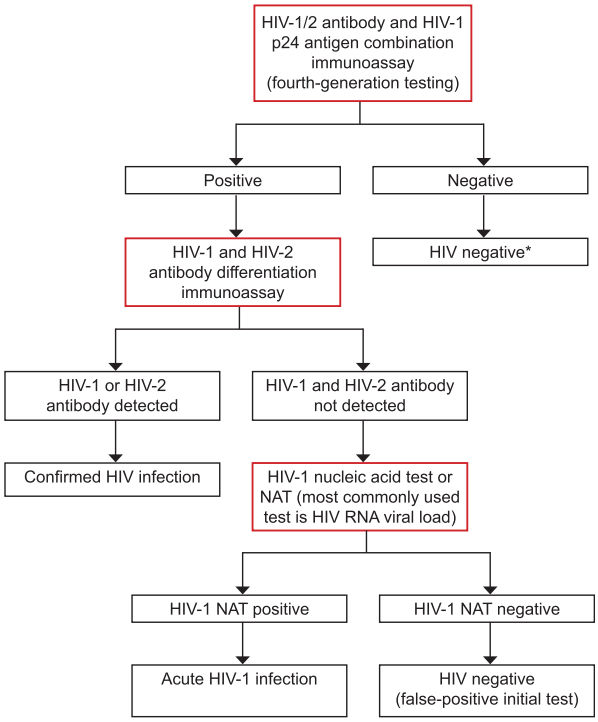

Fig. 1. Human immunodeficiency virus (HIV) testing algorithm.[10] *Fourth-generation testing can be positive 15–20 days after exposure.[42] *Red boxes* denote sequential tests to order. NAT, nucleic acid test. Modified from Centers for Disease Control and Prevention. 2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens. Accessed April 6, 2021. https://stacks.cdc.gov/view/cdc/50872.

Givens. Human Immunodeficiency Virus in Pregnancy and Postpartum. Obstet Gynecol 2021.

Initiation of Antiretroviral Medications

Antiretroviral therapy reduces HIV viral load and significantly reduces the risk of perinatal HIV transmission. Initiation of ART is recommended as soon as possible after HIV infection is diagnosed, whether that be in the preconception or antepartum period, and should be continued through the entire pregnancy and continued lifelong after delivery. Initial laboratory assessment of newly diagnosed HIV infection should include a CD4 count, plasma HIV RNA level, antiretroviral drug resistance genotype evaluation, complete blood cell count, renal and liver function testing, screening for hepatitis A, B, and C, HLA-B*5701 (to test for a genetic mutation that causes hypersensitivity to the antiretroviral abacavir), and screening for concomitant STIs (syphilis, *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Neisseria gonorrhea*). These laboratory studies can be obtained by the obstetric care professionals so that they are available to a consulting HIV specialist during the initial appointment.

There are many antiretroviral medications available. The choice of ART should include an assessment of the risks and benefits of each medication for both the parent and their fetus, an assessment of the person's past experiences with antiretroviral medications, their ability to swallow pills, and available information regarding the individual's drug resistance profile. In general, individuals who become pregnant while on a fully suppressive antiretroviral regimen should continue their current regimen. Selected antiretroviral agents are summarized in the Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States, which are updated frequently and available at www.hivinfo.nih.gov.[9] Antiretroviral drug-resistance genotype evaluation or assay should be performed before modifying ART regimens or in individuals whose HIV RNA levels are above the institutionally defined threshold for resistance testing (typically more than 500–1,000 copies/mL).

Fetal Monitoring

Although data regarding the risk of birth defects and the use of ART are limited, numerous studies have shown no increased incidence of birth defects among fetuses of individuals who are on ART compared with those who are not. Studies specifically looking at the risk of birth defects in individuals who are taking ART in the first trimester compared with those who are not have also found no difference.[11–13] The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal HIV Transmission notes the importance of thorough counseling and shared decision-making when deciding on an ART regimen.[9] Up to date specific information and counseling recommendations regarding specific ART medications are available within the Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States.[9]

Individuals living with HIV with or without ART use may be at increased risk of perinatal complications, including but not limited to preterm birth, low neonatal birth weight, stillbirth, and hypertensive disorders of pregnancy. Data regarding these outcomes are limited and no definitive causal link has been demonstrated. Health care professionals should be aware of the possibility of increased perinatal risk for individuals living with HIV; however, there are no agreed on additional monitoring recommendations. Most experts recommend that individuals who have been on an antiretroviral medication during

pregnancy have a second-trimester ultrasound evaluation of fetal anatomy, the same as would be recommended for individuals not living with HIV. Although no definitive recommendations for fetal growth surveillance have been made by professional organizations, some ART medications have been associated with low birth weight.[14] Monitoring fetal growth with fundal height monitoring or fetal growth ultrasonograms or both is reasonable.[9]

Monitoring Individuals Throughout Pregnancy

The HIV viral load, measured with a plasma HIV RNA level, should be monitored throughout pregnancy including at the initial prenatal visit, 2–4 weeks after initiating or changing the ART regimen, monthly if RNA levels are detectable, at least every 3 months during pregnancy, and at approximately 34–36 weeks of gestation. The CD4 T lymphocyte cell count should be assessed every 3–6 months among individuals who have been on ART less than 2 years, individuals with CD4 counts lower than 300 cells/mm^3, individuals with detectable viral loads, and in individuals who have inconsistent adherence to ART. Additional serum monitoring (CBC, renal, and liver function tests) should be based on the specific ART medications that the individual is taking. These recommendations are in addition to routine prenatal care, which is recommended for all pregnant people living with HIV.

Antenatal Procedures

In the past, HIV was considered a contraindication to amniocentesis. However, if an individual has an undetectable viral load on ART, the risk of transmission appears very low. It is, therefore, reasonable to perform an amniocentesis for appropriate obstetric indications in individuals with an undetectable viral load. Many experts recommend against performing a chorionic villus sampling or cordocentesis during pregnancy; although under specific circumstances, these procedures may also be reasonable after a discussion of the risks of HIV transmission and benefits of the procedure in a specific clinical scenario.

Hepatitis B or Hepatitis C Co-Infection

Infection with hepatitis B (HBV) or hepatitis C (HCV) is relatively more common among individuals living with HIV than those who are HIV negative. All pregnant individuals living with HIV should be screened for both HBV and HCV. People with HIV who screen negative for HBV (hepatitis B antigen, or HBsAg) and who lack immunity to HBV (negative hepatitis B surface antibody, or HBsAb) should receive the HBV vaccine series. Certain ART medications that are effective against both HBV and HIV, including lamivudine, emtricitabine, tenofovir disoproxil fumarate, and tenofovir alafenamide, can be used in combination regimens to reduce medication burden during pregnancy. Unfortunately, there are limited safety data regarding treatment of HCV during pregnancy so treatment is not recommended unless part of a research protocol.[9] Individuals should be counseled regarding their candidacy for treatment for HCV after delivery and those with HBV infection should be counseled regarding the benefits of lifelong treatment for HBV. Delivery recommendations regarding individuals with co-infections with HIV and HBV or HCV are discussed later.

Lack of Viral Suppression

Viral suppression to an undetectable level at the earliest possible time in pregnancy and at the time of delivery is paramount to prevent perinatal HIV transmission. Any person who has not attained full viral suppression should be evaluated for medication adherence and should have a viral resistance profile performed. Referral to an HIV infectious disease expert for regimen modification is also recommended. Integrase inhibitors such as raltegravir or dolutegravir have been shown to be associated with more rapid viral load reduction than other agents and may be considered in cases in which rapid viral load reduction is required.[15,16] Management during the intrapartum period for individuals who have not attained viral suppression by the time of delivery is discussed later.

Acute Human Immunodeficiency Virus Infection

Acute HIV infection typically presents as an asymptomatic or mild viral illness typified by the presence of a fever, fatigue, pharyngitis, rash, headache, myalgia, arthralgia, and lymphadenopathy. This constellation of symptoms can resemble and be confused with infectious mononucleosis, influenza, or another systemic viral illness. Evidence suggests that pregnant people may have an increased risk of acquiring HIV.[17,18] Further, acute HIV infection during pregnancy is associated with a higher risk of perinatal HIV transmission.[9,17,18] A high level of suspicion is required to identify those who may be presenting with acute HIV infection during pregnancy. Once acute HIV infection is identified during pregnancy, ART should be initiated as soon as possible.

Given the risks of HIV acquisition and transmission to fetus, prevention of HIV acquisition during pregnancy is important. Health care professionals may choose to counsel individuals about the following options: condom use, pre-exposure prophylaxis, and importance of ART use in known HIV-positive partners. Condom use prevents acquisition of HIV as well as other STIs. Pre-exposure prophylaxis should be discussed with people who might be at high risk of acquiring HIV. Pre-exposure prophylaxis is a combination ART (tenofovir disoproxil fumarate/emtricitabine) that is taken before a possible exposure to HIV for the purpose of preventing HIV. Individuals who are HIV-negative who are at high risk of acquiring HIV (eg, people with sexual partners living with HIV, sex workers, people using injection drugs or who have a sexual partner who uses injection drugs, people who have recently been diagnosed with an STI) should be offered pre-exposure prophylaxis.[9] In circumstances in which an individual's risk factor is a known partner with HIV (ie, sero-discordant couple), and if the partner is taking ART and HIV viral suppression has been sustained over time (eg, two recorded measurements of plasma viral loads that are below the limits of detection at least 3 months apart), condomless sexual intercourse is associated with effectively no risk of sexual HIV transmission.

INTRAPARTUM CARE

Rapid Intrapartum Human Immunodeficiency Virus Testing

Individuals who present in labor or who require delivery and whose HIV status is undocumented should undergo rapid HIV testing with an antigen–antibody combination immunoassay. Additionally, individuals at increased risk of HIV infection who tested negative for HIV in early pregnancy, but the testing was not repeated in the third trimester should be tested on admission to labor and delivery. If antigen–antibody combination testing is not immediately available, the most sensitive HIV testing modality should be performed. Twenty-four hour testing capability should be available at all facilities with maternity services.

If the initial HIV test result is positive, the person should be presumed to have HIV and follow-up testing should be performed to further clarify the person's HIV status. In these cases, intravenous (IV) zidovudine should be started immediately while awaiting confirmatory test results. In cases in which next level testing confirms a new HIV infection, the person is very unlikely to have an HIV RNA viral load or 1,000 copies/mL or less, and cesarean delivery for prevention of perinatal HIV transmission is recommended in a nonlaboring individual, as discussed below. If a person is in early labor, most clinicians would also opt for cesarean delivery. However, once in active labor, the efficacy of cesarean delivery for reducing perinatal HIV transmission is decreased. Clinicians have the option of contacting the Clinician Consultation Center's Perinatal HIV/AIDS hotline (888-448-8765), a 24/7 service offered by the University of California San Francisco's Clinician Consultation Center, for assistance in navigating complex perinatal HIV situations such as making the decision for vaginal delivery compared with cesarean delivery in individuals who are not optimally treated (https://nccc.ucsf.edu/clinician-consultation/perinatal-hiv-aids/).

Mode of Delivery

Among nonbreastfeeding individuals with HIV, the intrapartum period is the highest risk time for perinatal HIV transmission. The most effective way to reduce transmission risk is for an individual to have achieved an undetectable viral load with the use of ART by the time of delivery. Assessment of viral load between 34 and 36 weeks of gestation assists prenatal care professionals in determining the optimal mode of delivery. The incidence of perinatal HIV transmission through a vaginal delivery is exceedingly low in individuals with low viral HIV levels (defined as 1,000 copies/mL or less). Therefore, most organizations do not routinely recommend cesarean delivery for the primary purpose of preventing perinatal HIV transmission in individuals with an HIV viral load of 1,000 copies/mL or less. However, because there has been demonstrated HIV transmission even at very low HIV RNA levels, the decision regarding mode of delivery should be made using shared decision-making.

In contrast, prelabor cesarean delivery (typically at 38 weeks of gestation) significantly decreases the risk of perinatal HIV transmission in individuals with elevated viral loads (more than 1,000 copies/mL). A 1999 meta-analysis of 15 prospective cohort studies, performed before the routine use of combined ART, demonstrated a 50% reduction of perinatal HIV transmission with a scheduled cesarean delivery compared with other modes of delivery.[19] Among individuals presenting in labor or with ruptured membranes with elevated viral loads, the mode of delivery decision should take into account the most recent viral load, adherence to ART regimen, the duration of rupture of membranes, and the estimated remaining length of labor. Again, expert consultation for such

cases may be obtained through the Clinician Consultation Center's Perinatal HIV/AIDS hotline. If cesarean delivery is indicated for other obstetric indictions in a person without an elevated HIV viral load, delivery timing be per standard obstetric recommendations.

Perioperative and Intrapartum Antiretroviral Therapy

Regardless of mode of delivery, people should continue to receive their ART regimen as scheduled through the entire perioperative or intrapartum period. The most recent viral load before admission to labor and delivery is used to determine an individual's candidacy for additional perioperative or intrapartum ART with IV zidovudine (Table 1). Individuals undergoing scheduled cesarean delivery with a viral load greater than 1,000 copies/mL should receive IV zidovudine starting at least 3 hours before the scheduled delivery to ensure steady state plasma levels before delivery (2 mg/kg loading dose over 1 hour followed by 1 mg/kg/h until cord clamping). If delaying for 3 hours is not feasible due to rapid progression of labor,

Table 1. Labor and Delivery Intrapartum Management Recommendations

Intervention	Unlabored or laboring person Viral load less than 50 copies/mL (undetectable) Adherent to ART	Unlabored or laboring person Viral load 50 or greater but less than 1,000 Adherent to ART	Unlabored person with following clinical scenarios: Viral load 1,000 or greater Viral load unknown Individual did not receive ART Individual was nonadherent to ART	Person laboring or with ruptured membranes with following clinical scenarios: Viral load 1,000 or greater Viral load unknown Individual did not receive ART Individual was nonadherent to ART HIV diagnosis in labor
Mode of delivery	Based on obstetric indications		Cesarean delivery	Consider individualized management with expert consultation*
Intrapartum antiretroviral medications	Continue oral ART regimen intrapartum	Continue oral ART regimen intrapartum Consider intrapartum IV zidovudine	Continue oral ART regimen perioperative (if applicable) Perioperative IV zidovudine	Continue oral ART regimen intrapartum (if applicable) Intrapartum or perioperative IV zidovudine
Timing of delivery	Based on obstetric indications		38 wk of gestation or earlier for obstetric indications	Expert consultation if less than 34 wk of gestation
Induction of labor	Based on obstetric indications. Individuals with viral load less than 1,000 should not routinely be induced at 38 wk		NA, cesarean delivery recommended	NA
Artificial rupture of membranes	Based on obstetric indications	Avoid if possible	AN, cesarean delivery recommended	Avoid if possible
Fetal scalp electrode	Avoid if possible		NA, cesarean delivery recommended	Avoid if possible
Intrauterine pressure catheter	Use with caution for obstetric indications		NA, cesarean delivery recommended	Use with caution for obstetric indications

ART, antiretroviral therapy; HIV, human immunodeficiency virus; IV, intravenous; NA, not applicable.

Data from Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Transmission in the United States. Accessed March 15, 2021. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/overview.

* There is insufficient evidence that cesarean delivery after presentation in spontaneous labor or with ruptured membranes reduces the risk of perinatal transmission among individuals with an unknown viral load. Management may be individualized in coordination with an infectious disease expert or with consultation with the National Perinatal HIV/AIDS Clinical Consultation Center (1-888-448-8765).

it is recommended to administer at least a loading dose of IV zidovudine 2 mg/kg over 1 hour.

Among individuals who are adherent to their ART regimen and have a viral load of 50 copies/mL or less, intrapartum zidovudine has not be found to further reduce the small risk of perinatal HIV transmission (1% or lower risk) and is not recommended.[9,20] For individuals who are adherent to their ART regimen and have a viral load between 50 and 1,000 copies/mL, there are not enough data to recommend intrapartum IV zidovudine so the decision whether or not to administer is made on a case-by-case basis, and often based on institutional protocols. Although there is a 1–2% transmission risk with a viral load in this range (vs 1% or lower transmission risk in individuals with 50 copies/mL or less), studies looking at administration of IV zidovudine in this group show a trend toward but no definitive evidence of perinatal HIV transmission risk reduction.[20] Many experts continue to administer IV zidovudine to individuals in this group. For individuals with a viral load greater than 1,000 copies/mL, with poor adherence to an ART regimen, or with an unknown viral load, IV zidovudine is recommended surrounding the time of vaginal or cesarean delivery.[20]

Intrapartum Obstetrics Procedures

With few exceptions, intrapartum management for individuals living with HIV is the same as for a person not living with HIV. Before widespread use of ART, the duration of rupture of membranes was associated with increased risk of perinatal HIV transmission. However, with routine use of ART, data suggest that duration of rupture of membranes is no longer associated with increased risk of transmission.[21–23] In individuals with detectable viral loads, artificial rupture of membranes should be avoided until there is a clear obstetric indication. In all individuals with HIV regardless of viral load, the routine use of fetal scalp monitors and operative deliveries with forceps or vacuum extractor should be avoided unless there is a clear obstetric indication (Table 1).

POSTPARTUM CARE

Infant Feeding

Human immunodeficiency virus RNA and HIV-infected cells are secreted in colostrum and breast milk and can lead to perinatal HIV transmission.[24,25] Although ART reduces the risk of breastfeeding-associated HIV transmission to a neonate, it does not eliminate the risk. Studies performed in times or locations without availability of antiretroviral medications have shown that HIV transmission through breastfeeding in the absence of any intervention is approximately 9–16% over a 2-year period.[25,26] Although individuals who achieve total viral suppression (undetectable viral load) have essentially no risk of sexual transmission of HIV (Undetectable=Untransmissible, or U=U), the same principle has not been proven to apply to breastfeeding-associated HIV transmission.[27,28] A systematic review of six studies from resource-limited settings found a pooled estimate of postnatal HIV transmission rate among breastfed infants of individuals on ART of 1.08% at 6 months and 2.93% at 12 months.[29] The PROMISE (Promoting Maternal-Infant Survival Everywhere) trial has demonstrated a postnatal HIV transmission risk of 0.3% at 6 months and 0.6% at 12 months among breastfeeding individuals on ART.[30]

The reason undetectable does not necessarily mean untransmissible with regards to breastfeeding has not been completely elucidated. There is likely a role of cell-associated HIV DNA, which is not a target of ART agents. Even among virally suppressed individuals, cell-associated HIV DNA can be transmitted and reactivated to produce infectious HIV RNA thus leading to transmitted infection. The total exposure volume to breast milk over the course of 6 months is relatively high–an estimated 150 million immune cells transmitted over the course of 6 months.[24] These immune cells can harbor cell-associated HIV DNA and thus lead to transmission despite viral RNA suppression.[27] Additionally, there may be a role of inflammation from mastitis, abscess, or breast engorgement leading to additional cell-associated HIV activation, although this has not been demonstrated in people on ART. Finally, adherence to ART can significantly decrease in the postpartum period when individuals face postpartum depression, anxiety, unpredictable sleep patterns, focusing on the care of a newborn, and a lack of social support among many other challenges.[31,32] Therefore, because an undetectable viral load during breastfeeding does not always mean the virus is untransmittable, in high resource settings where there are safe and affordable alternatives to breast milk, numerous society and government-sponsored guidelines recommend avoidance of breastfeeding for individuals living with HIV regardless of ART adherence or viral load.[9,33–36]

In settings with fewer resources, where access to safe water and health care is limited, exclusive breastfeeding in combination with additional HIV transmission prevention strategies (use of parental ART and infant chemoprophylaxis) is recommended. This risk-reduction approach balances the risk of HIV

transmission with the higher risk of morbidity and mortality associated with infants acquiring diarrheal and other infectious diseases from unsafe water used in formula. The recommendation for exclusive breastfeeding is based on evidence of increased risk of transmission with mixed feeding (formula and breast milk) compared with exclusive breastfeeding, before the availability of antiretrovirals.[33] Theories include: 1) damage to infant gut mucosa from nonphysiologic formula may allow for easier penetration of HIV than when exclusive breast milk is introduced, and 2) engorgement and inflammation of the breast when not continuously breastfeeding may draw more HIV into the breast and breast milk. Whether exclusive breastfeeding remains as advantageous in the era of ART is not known.

Despite recommendations to abstain from breastfeeding, some individuals in resource-rich countries report a desire to or elect to breastfeed. Some people may experience social or cultural pressure to breastfeed or feel fearful that not breastfeeding may reveal their HIV status, or they may have a strong personal desire to breastfeed for the health benefits for them and their infants or to promote bonding. Other individuals may not have access to safe water or cannot afford feeding alternatives such as formula, donor breast milk, or an HIV-negative wet nurse. Finally, some individuals may have recently immigrated from a low-resource region where they were breastfeeding their infant per recommendations and may elect to continue.

The contrast between recommendations for high and low-resource settings as well as increasing evidence of low HIV transmission rates with appropriate antiretroviral interventions have caused patients and health care professionals to look at these recommendations critically. In a recent U.S.-based survey study of 93 health care practitioners, 75% had been asked by individuals living with HIV if they could breastfeed and 29% reported taking care of individuals who breastfed.[34] In response to increasing interest in breastfeeding among individuals living with HIV, many countries, including the United States, have updated their recommendations to acknowledge that the infant feeding decision for individuals living with HIV is complex and must take into account many factors.

There are a number of ways to reduce the risk of HIV transmission for individuals living with HIV who choose to breastfeed. Some of these perinatal HIV transmission risk-reduction strategies for people who elect to breastfeed are outlined in the U.S. Perinatal Guidelines.[9,35,36] The most critical measure is for a breastfeeding individual to maintain strict adherence to their ART regimen. Health care professionals should assess the HIV viral load approximately every 1–2 months to ensure ongoing viral suppression. If a person's viral load becomes detectable, they should be counseled to wean the infant from breastfeeding. Because mastitis can potentially increase the risk of HIV transmission, health care professionals should counsel individuals to be aware of symptoms and should promptly diagnose and treat mastitis. Box 1 provides an outline of risk-reducing management strategies for individuals who elect to breastfeed.

With increased knowledge and availability of antiretroviral medications, the risk of perinatal HIV transmission through breastfeeding has been significantly reduced. This in combination with increased focus on shared decision-making and patient autonomy has led many experts to call for a move away from the directive of "Do not breastfeed," and instead

Box 1. Management Strategies for Individuals Living with Human Immunodeficiency Virus Who Choose to Breastfeed

- Discuss the risks and benefits of breastfeeding as well as feeding alternatives such as formula, donor breast milk, or use of a lactational surrogate.
- Ensure the person receives an effective ART regimen. Specifically, address barriers to adherence and counsel on the importance of this regimen in reducing transmission.
- Counsel on the importance of exclusive breastfeeding rather than mixed feeding with formula and breast milk.
- Discuss the benefits of infant antiretroviral prophylaxis. Ensure the infant has a pediatrician who feels comfortable and supportive managing an infant breastfeeding from a parent with HIV.
- Monitor an individual's viral load every 1 to 2 mo during breastfeeding to ensure viral suppression. If the viral load becomes detectable, counsel regarding the increased risk of transmission and consider breastfeeding weaning.
- Educate the individual regarding the signs of mastitis or infant oral thrush, which may increase the risk of HIV transmission, to ensure prompt treatment.
- Test the infant for HIV acquisition during breastfeeding, typically every 3 mo during breastfeeding.

ART, antiretroviral therapy; HIV, human immunodeficiency virus.

Data from Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Transmission in the United States. Accessed March 15, 2021. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/overview

promote a risk-reduction model. This model assumes that well-counseled individuals who are fully aware of the risks and benefits of both options will choose the feeding method that will best balance these considerations. Health care professionals' role is to educate, support, and empower a person to make the best choice for them.

In addition to maintaining viral suppression in the breastfeeding parent, HIV prophylaxis should be considered for the infant. It is standard of care for all infants born to an individual living with HIV to receive 4–6 weeks of antiretroviral prophylaxis with zidovudine. The choice of agent and the length of therapy is dependent of the level of perinatal HIV risk (ie, whether or not the individual was adherent to their ART regimen and virally suppressed during pregnancy and at the time of delivery). For infants with low risk of HIV transmission because the individual was virally suppressed, 4 weeks of zidovudine is considered adequate prophylaxis. Infants who are at high risk of HIV transmission typically receive a combination ART regimen, usually zidovudine, lamivudine, and nevirapine, in doses consistent with full therapy.

In the setting of a breastfed HIV-exposed infant, there is insufficient evidence to demonstrate additional benefit with a longer duration of neonatal chemoprophylaxis in infants of a parent who has chosen to breastfeed and are adherent to an ART regimen. This was illustrated in the HPTN 046 trial, which showed no difference in rates of perinatal HIV transmission among infants who received an additional 6 months of nevirapine as long as the infant's breastfeeding parent was on an ART regimen.[37] Nonetheless, some experts advocate to continue infant antiretroviral prophylaxis throughout the duration of breastfeeding plus an additional 1–4 weeks.[38] With effective parental ART, postnatal HIV transmission can be reduced to 0.3% (95% CI 0.1–0.6).[30]

Follow-up Medical Care

Perinatal care professionals have a unique opportunity during the postpartum period to optimize a person's transition to long-term health care. Health professionals should ensure that the person has adequate access to comprehensive medical and supportive services including but not limited to primary care, HIV specialty care, gynecologic care, pediatric care, mental health services, substance use disorder treatment, and case management to assist with coordination of care and access to community resources. Comprehensive postpartum care including multiple points of contact in the weeks after delivery can optimize person's access to health care and allow adequate time for access to postpartum contraceptive care, as well as ensuring referrals are made to supportive services.[39]

During this transition to long-term care, health care professionals should ensure that the individual's ART regimen is continued. Lifelong ART optimizes a person's long-term health and prevents progression of HIV-associated disease.[40] Further, viral suppression through ART significantly reduces the risk to nearly no risk of transmission of HIV to a sexual partner.[41] Unfortunately, despite the benefits, ART adherence typically declines significantly in the postpartum period, likely from a combination of loss of access to health care and prescription medications, loss of intensive antepartum surveillance, or reduced motivation to reduce vertical HIV transmission.[32,42]

Choices of specific agents in the nonpregnant adult should be made in combination with an HIV specialist and should take into consideration the individual's future pregnancy goals. Specific attention should be paid about ways to reduce the complexity of an ART regimen by trying to schedule once daily and combination formulations. Pregnancy care professionals should ensure that the person has access to contraceptive options that will help the individual to achieve their reproductive goals. Health care professionals can also assess ways in which the risk of HIV transmission to HIV-negative sexual partners can be reduced. Specifically, health care professionals should discuss usage of pre-exposure prophylaxis by the partner and should emphasize the importance of maintaining consistent adherence to the ART regimen.

SUMMARY

Considerable strides have been made in the understanding, prevention, management, and treatment of HIV in the past 40 years. Access to antiretroviral medications for pregnant individuals has never been more widespread and affordable. The estimated number of children newly infected with HIV has decreased every year for the past 10 years. Despite this progress, preventable cases of perinatal HIV transmission still occur worldwide. Effective interventions such as early HIV detection, treatment with prolonged ART, appropriate delivery decisions and intrapartum management, and thorough postpartum counseling can reduce the risk of transmission from up to 45% to less than 1%. Universal application of these management standards as well as increased access to ART will help with the goal of eliminating perinatal HIV transmission globally.

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