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Committee on Obstetric Practice HIV Expert Work Group

The Society for Maternal-Fetal Medicine endorses this document. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Obstetric Practice in collaboration with committee member Neil S. Silverman, MD, and the HIV Expert Work Group.

Labor and Delivery Management of Women With Human Immunodeficiency Virus Infection

ABSTRACT: This Committee Opinion is being revised to provide updated guidance on the management of pregnant women during pregnancy and delivery to prevent mother-to-child transmission of the human immunodeficiency virus (HIV). Prevention of transmission of HIV from the woman to her fetus or newborn is a major goal in the care of pregnant women infected with HIV. Continuing research into mother-to-child transmission of HIV has suggested that a substantial number of cases of perinatal HIV transmission occur as the result of fetal exposure to the virus during labor and delivery. The precise mechanisms are not known. Established and ongoing research has shown that treatment of HIV-infected pregnant women with combined antiretroviral therapy can achieve a 1–2% or lower risk of mother-to-child transmission if maternal viral loads of 1,000 copies/mL or less can be sustained, independent of the route of delivery or duration of ruptured membranes before delivery. Vaginal delivery is appropriate for HIV-infected pregnant women who have been maintained on combined antiretroviral therapy and who have viral loads of 1,000 copies/mL or less at or near delivery. The risk of mother-to-child transmission in HIV-infected women with high viral loads can be reduced by performing cesarean deliveries before the onset of labor and before rupture of membranes (termed *scheduled cesarean delivery* in this document), in conjunction with the use of peripartum maternal antiretroviral therapy. Discussion of the option of scheduled cesarean delivery and its advantages in the situation of suboptimal viral suppression should begin as early as possible in pregnancy with every pregnant woman with HIV infection to give her an adequate opportunity to ask questions and consider her decision-making concerning the delivery plan. The patient's decision regarding her route of delivery should be respected after maternal and neonatal risks have been discussed.

Recommendations

The American College of Obstetricians and Gynecologists makes the following recommendations:

- Established and ongoing research has shown that treatment of human immunodeficiency virus (HIV)-infected pregnant women with combined antiretroviral therapy (cART) can achieve a 1–2% or lower risk of mother-to-child transmission if maternal viral loads of 1,000 copies/mL or less can be sustained, independent of the route of delivery or duration of ruptured membranes before delivery.
- Women should receive antiretroviral therapy during pregnancy according to currently accepted guidelines for adults. Plasma HIV ribonucleic acid (RNA) levels in pregnant women should be monitored at the initial prenatal visit, 2–4 weeks after initiating (or changing) cART drug regimens; monthly until RNA levels are undetectable; and then at least every 3 months during pregnancy.
- Pregnant women infected with HIV whose viral loads are more than 1,000 copies/mL at or near delivery, independent of antepartum antiretroviral therapy, or whose levels are unknown, should be counseled

regarding the potential benefit of and offered scheduled prelabor cesarean delivery at 38 0/7 weeks of gestation to reduce the risk of mother-to-child transmission. These patients also should receive intravenous zidovudine (ZDV), ideally 3 hours preoperatively as a 1-hour intravenous loading dose (2 mg/kg), followed by continuous infusion over 2 hours (1 mg/kg/hr) until delivery to achieve adequate levels of the drug in maternal and fetal blood.

- Regardless of maternal viral load results before delivery, planning for the care and management of all newborns delivered to HIV-infected women should be initiated with pediatric care providers experienced in initiating and monitoring the continuation of HIV prophylactic therapy for at-risk neonates and infants. Ideally this process should occur before delivery, but otherwise as soon as possible after birth.
- Some medications used to treat HIV may have significant interactions with medications used during labor and delivery, specifically uterotonics. Concomitant use of methergine or other ergotamines with protease inhibitors or cobicistat, or both, has been associated with exaggerated vasoconstrictive responses.
- The patient's autonomy in making the decision regarding route of delivery should be respected. A patient's informed decision to undergo vaginal delivery despite a viral load above the accepted cutoff should be honored. The converse holds true for an informed decision regarding cesarean delivery in the setting of a viral load of 1,000 copies/mL or less.
- Importantly, rapid screening during labor and delivery or during the immediate postpartum period using the opt-out approach should be done for women who were not tested earlier in pregnancy or whose HIV status is otherwise unknown. Results should be available 24 hours a day and within 1 hour.
- Duration of rupture of membranes before delivery is not an independent risk factor for maternal-child transmission in women who are otherwise appropriately virally suppressed and is not a consideration regarding route of delivery.

Introduction

This Committee Opinion is being revised to provide updated guidance on the management of pregnant women during pregnancy and delivery to prevent mother-to-child transmission of HIV. Prevention of transmission of HIV from a woman to her fetus or newborn is a major goal in the care of pregnant women infected with HIV. An important advance in this regard

was the mother with ZDV during pregnancy and labor, and of the neonate for the first 6 weeks after birth, could reduce the transmission rate from 25% to 8% (1).

Continuing research into mother-to-child transmission of HIV has suggested that a substantial number of cases occur as the result of fetal exposure to the virus during labor and delivery. The precise mechanisms are not known. Transmission could occur by transplacental maternal-fetal microtransfusion of blood contaminated with the virus during uterine contractions or by exposure to the virus in maternal cervicovaginal secretions and blood at delivery. Data also indicate that the risk of mother-to-child transmission is proportional to the concentration of virus in maternal plasma (ie, viral load). Earlier studies helped establish a threshold level for maternal viral load (1,000 copies/mL or less) below which the observed incidence of vertical transmission among 141 mother-infant pairs was no greater than 2% (2, 3). In a more recent report of the results of contemporary management of HIV-infected pregnant women, the combination of continuation or initiation of cART with maintenance of low or undetectable viral loads during the pregnancies, mother-to-child transmission rates of less than 1% were reported (4). Overall, established and ongoing research have shown that treatment of HIV-infected pregnant women with cART can achieve a 1–2% or lower risk of mother-to-child transmission if maternal viral loads of 1,000 copies/mL or less can be sustained, independent of the route of delivery or duration of ruptured membranes before delivery.

Management of Labor and Delivery of HIV-Infected Women

The risk of mother-to-child transmission in HIV-infected women with high viral loads can be reduced by performing cesarean deliveries before the onset of labor and before rupture of membranes (termed *scheduled cesarean delivery* in this document), in conjunction with the use of peripartum maternal antiretroviral therapy. Early studies of the relationship between the mode of delivery and the risk of vertical transmission yielded inconsistent results. Data from two prospective cohort studies, (5, 6) an international randomized trial, (7) and a meta-analysis of individual patient data from 15 prospective cohort studies, including more than 7,800 mother-child pairs, (8) indicated that there was a significant relationship between the mode of delivery and vertical transmission of HIV. This body of evidence, accumulated mostly before the use of cART and without any data regarding maternal viral load, indicated that scheduled cesarean delivery reduced the likelihood of vertical transmission of HIV compared with either unscheduled cesarean delivery or vaginal delivery. This finding held true whether or not the patient was receiving ZDV therapy, although those studies drew from a time when ZDV monotherapy was the standard of care in pregnancy.

In contemporary practice when treating pregnant women with cART and monitoring viral loads to assess response, there is no evidence that elective cesarean delivery offers any additional protection against mother-to-child transmission in pregnancies in women with undetectable or even low (50–999 copies/mL) maternal viral loads (4, 9). In women with a viral load of 1,000 copies/mL or less at term for whom a vaginal delivery is planned, elective delivery before 40 0/7 weeks estimated gestational age (EGA) has not been shown to lower risks of mother-to-child transmission (10). These women (like those who are not infected with HIV) can await spontaneous labor after 40 0/7 weeks EGA. Delivery timing and mode per current obstetric guidelines for HIV-negative pregnant women is appropriate for this group of women.

Women should receive antiretroviral therapy during pregnancy according to currently accepted guidelines for adults. Plasma HIV RNA levels in pregnant women should be monitored at the first prenatal visit; 2–4 weeks after initiating (or changing) cART drug regimens; monthly until RNA levels are undetectable; and then at least every 3 months during pregnancy. Human immunodeficiency virus RNA levels also should be assessed at approximately 34 0/7 to 36 0/7 weeks of gestation to inform decisions about mode of delivery and optimal treatment of the newborn (11). Pregnant women infected with HIV whose viral loads are more than 1,000 copies/mL at or near delivery, independent of antepartum antiretroviral therapy, or whose levels are unknown, should be counseled regarding the potential benefit of and offered scheduled pre-labor cesarean delivery at 38 0/7 weeks of gestation to reduce the risk of mother-to-child transmission. In this situation, scheduling cesarean delivery as a medically-indicated early term delivery at 38 0/7 weeks of gestation is intended to decrease the likelihood of onset of labor or rupture of membranes before delivery (11, 12). These patients also should receive intravenous ZDV, ideally 3 hours preoperatively as a 1-hour intravenous loading dose (2 mg/kg), followed by continuous infusion over 2 hours (1 mg/kg/hr) until delivery to achieve adequate levels of the drug in maternal and fetal blood (1). This recommendation is based on demonstration of significantly higher ratios of cord blood-to-maternal ZDV levels in women who received ZDV intravenously for 3–6 hours compared with less than 3 hours before delivery (13). If the patient has opted for vaginal delivery despite nonsuppressed viral load, then intravenous ZDV should be initiated at the onset of in-house labor monitoring and continue through labor until delivery along with other drugs in their current antiretroviral regimen (11).

Although intravenous ZDV is not required for women with HIV receiving cART with HIV RNA 1,000 copies/mL or less in late pregnancy, or near delivery, or both, with no concerns about adherence to or tolerance of their cART regimens, some experts have expressed concern that there are inadequate data to

determine whether administration of intrapartum intravenous ZDV to such women provides any additional protection against perinatal transmission. These experts have recommended intrapartum intravenous ZDV administration to women with RNA levels in this range, as the transmission risk is slightly higher (approximately 1–2%) when HIV RNA is in the range of 50–999 copies/mL compared to less than 50 copies/mL (1% or less) (4, 14, 15). However, regardless of viral load, in these circumstances the clinician may elect to use or not use intrapartum intravenous ZDV based on clinical judgment (11). Regardless of maternal viral load results before delivery, planning for the care and management of all newborns delivered to HIV-infected women should be initiated with pediatric care providers experienced in initiating and monitoring the continuation of prophylactic antiretroviral therapy for at-risk neonates and infants. Ideally this process should occur before delivery, but otherwise as soon as possible after birth.

Management of Human Immunodeficiency Virus-Infected Women With Prelabor Rupture of Membranes at Term

Questions have surrounded the optimal management of HIV-infected women with prelabor rupture of membranes (also referred to as premature rupture of membranes) (PROM) at term. Although earlier pre-cART studies demonstrated increasing rates of mother-to-child transmission related to duration of PROM before delivery, (16) this risk factor has more recently been shown to be significantly affected by maternal viral load at delivery. In two studies, one retrospective (17) and one prospective, (18) using a low-viral-load definition of 1,000 copies/mL or less, there were no cases of mother-to-child transmission among a total of 539 women who had low viral loads at the time of vaginal delivery. In the prospective cohort, (18) no mother-to-child transmission was identified after vaginal delivery with rupture of membranes duration up to 25 hours. In both studies, there was no difference reported in rates of mother-to-child transmission in virally-suppressed women when routes of delivery were compared. A larger, more recent study evaluated 2,116 term pregnancies in cART-treated women delivered from 2007 to 2012 in the United Kingdom and Ireland, using a cutoff of less than 50 copies/mL to define undetectable viral load. Only 23 women in the cohort had a viral load more than 1,000 copies/mL. Sixty-five percent of the women in the study had a planned vaginal delivery, 32% had an emergency cesarean for an indication other than HIV, and 3% had unplanned vaginal deliveries. For these women delivering at term with a viral load of less than 50 copies/mL, no difference in mother-to-child transmission rates was seen between women with a rupture of membranes (ROM) time less than 4 hrs and those with a ROM time of 4 hrs or more (0.12% versus 0.14%; OR 1.14, 95% CI 0.07–

18.27). There was also no mother-to-child transmission identified in the smaller subcohort of 163 preterm deliveries after ROM where maternal viral load was less than 50 copies/mL (19). These data support allowing vaginal delivery, even in the setting of prolonged rupture of membranes before delivery, if the woman has been on an effective cART regimen and has a viral load of 1,000 copies/mL or less at or near delivery.

In contrast, in pregnant women with viral loads more than 1,000 copies/mL or unknown viral loads who present at term in labor or with ruptured membranes, it is unclear whether urgent cesarean delivery offers the same mitigation of mother-to-child transmission risk as a scheduled cesarean delivery. Some studies have shown a similar risk of transmission for cesarean delivery performed for obstetric indications after labor and membrane rupture as for vaginal delivery. In one study, the HIV transmission rate was similar in women undergoing emergency cesarean delivery and those delivering vaginally (1.6% versus 1.9%, respectively) (20). A meta-analysis of pregnant women with HIV, most of whom were receiving no antiretroviral drugs or only ZDV, demonstrated a 2% increased transmission risk for every additional hour of ruptured membranes (16). However, it is not clear how soon after the onset of labor or the rupture of membranes the benefit of cesarean delivery is lost (21). Because it is not clear whether cesarean delivery after onset of labor reduces the risk of perinatal HIV transmission, management of women originally scheduled for cesarean delivery who present in labor should be individualized at the time of presentation. In these circumstances, consultation with an expert in perinatal HIV may be helpful. Because the delivery plan in the setting of labor must frequently be made quickly, telephone consultation with a 24-hour, 7-days-a-week hotline (eg, the National Perinatal HIV/AIDS Clinical Consultation Center [(888) 448-8765]) may be helpful in rapidly developing an individualized plan (11).

Other Considerations

Scheduled Delivery Versus Expectant Management

Recent data also suggest that for women with durably suppressed viral loads during pregnancy, delivery by 40 0/7 weeks EGA does not result in lower rates of mother-to-child transmission compared with delivery after 40 0/7 weeks, and as such, does not appear to be indicated. In an analysis of 2,250 newborns born to HIV-infected women with viral loads of 1,000 copies/mL or less, there was no significant difference in mother-to-child transmission for pregnancies delivered at before 40 0/7 weeks EGA compared with those delivered at or after 40 0/7 weeks EGA (0.3% versus 0.5%; rate ratio, 1.57; 95% CI 0.4–8.09; $P=.77$). There were no differences in maternal viral load or timing of mother-to-child transmission between the two EGA groups (10).

Maternal Morbidity

Maternal morbidity is greater with cesarean delivery than with vaginal delivery for HIV-infected women, as is true for women not infected with HIV (22–24). Increases in postpartum morbidity have been reported particularly among women infected with HIV who also have low CD4 cell counts (23).

Fetal Scalp Electrodes

Obstetric procedures that increase the risk of fetal exposure to maternal blood, such as invasive fetal monitoring, have been implicated in increasing vertical transmission rates by some but not all investigators, primarily in studies performed in the pre-cART-therapy era (2, 25, 26). Data are limited on use of fetal scalp electrodes in labor in women receiving suppressive antiretroviral therapy who have undetectable viral loads; therefore, routine use of fetal scalp electrodes for fetal monitoring generally should be avoided in the setting of maternal HIV infection, regardless of maternal viral suppression status. Regarding other intrapartum procedures, current guidelines suggest that operative vaginal delivery also should generally be avoided regardless of maternal viremia status because of a potential increased risk of transmission, unless there are clear obstetric indications (11).

Drug Interactions

Some medications used to treat HIV may have significant interactions with medications used during labor and delivery, specifically uterotonics. Women who are treated in the antepartum period and who have achieved viral suppression should continue their regimen during labor. Awareness of these potential interactions is important for their intrapartum health care providers. Specifically, methergine should not be co-administered with drugs that are potent CYP3A4 enzyme inhibitors, including protease inhibitors (PIs). Concomitant use of methergine or other ergotamines with PIs or cobicistat, or both, has been associated with exaggerated vasoconstrictive responses (27). When uterine atony results in excessive postpartum bleeding in women receiving PIs or cobicistat, methergine should be used only if alternative treatments such as prostaglandin F₂-alpha, misoprostol, or oxytocin are unavailable or are contraindicated. If no alternative medications are available and the need for pharmacologic treatment outweighs the risks, methergine should be used in as low a dose and for as short a period as possible. In contrast, additional uterotonic agents may be needed when other antiretroviral drugs that are CYP3A4 inducers (eg, nevirapine, efavirenz, and etravirine) are used because of the potential for decreased methergine levels and inadequate treatment effect (11).

Patient Autonomy

The patient's autonomy in making the decision regarding route of delivery should be respected. A patient's

informed decision to undergo vaginal delivery despite a viral load above the accepted cutoff should be honored. The converse holds true for an informed decision regarding cesarean delivery in the setting of a viral load of 1,000 copies/mL or less. Preoperative maternal health status affects the degree of risk of maternal morbidity associated with cesarean delivery. All women should be clearly informed of the risks associated with cesarean delivery. Ultimately, the decision to perform a cesarean delivery should be individualized. Although the American College of Obstetricians and Gynecologists (ACOG) generally recommends that scheduled cesarean deliveries not be performed before 39 0/7 weeks of gestation, ACOG has supported the role of early-term deliveries for maternal or fetal medical indications (12). Pregnancies in HIV-infected women with viral loads greater than 1,000 copies/mL at term should be viewed as such a medical indication, and delivery at 38 0/7 weeks of gestation is recommended to reduce the likelihood of onset of labor or rupture of membranes before delivery and, thereby, lower the risk of mother-to-child transmission. If the patient is on cART and the virus is suppressed (1,000 copies/mL or less), a scheduled cesarean delivery (eg, elective repeat) should be timed per standard obstetric guidelines. The best clinical estimates of gestational age should be used for planning a scheduled prelabor medically indicated cesarean delivery. Amniocentesis to determine fetal lung maturity is not indicated (12) and should be avoided.

Standard Universal Precautions

A skin-penetrating injury (eg, needlestick or scalpel laceration) is a risk to health care providers during all deliveries, whether vaginal or cesarean. Appropriate care and standard universal precautions against such injuries should always be taken and should not affect decision-making regarding route of delivery (28). If such an injury does occur despite precautions, immediate washing of the injury site should be followed by discussion and consideration of initiating postexposure antiviral prophylaxis.

Perinatal Testing

Human immunodeficiency virus testing is an important component of prenatal care and the reader is referred to ACOG Committee Opinion No. 752, *Prenatal and Perinatal Human Immunodeficiency Virus Testing: Expanded Recommendations* for additional guidance (29). Importantly, rapid screening during labor and delivery or during the immediate postpartum period using the opt-out approach should be done for women who were not tested earlier in pregnancy or whose HIV status is otherwise unknown. Results should be available 24 hours a day and within 1 hour (see For More Information for more details about perinatal management of HIV). Obstetrician-gynecologists and other obstetric care providers should

be aware of and comply with their states' legal requirements for perinatal screening.

Conclusion

In summary, vaginal delivery is appropriate for HIV-infected pregnant women who have been maintained on cART and who have viral loads of 1,000 copies/mL or less at or near delivery. These women can be managed in a manner similar to HIV-uninfected women. Duration of rupture of membranes before delivery is not an independent risk factor for maternal-child transmission in women who are otherwise appropriately virally suppressed and is not a consideration regarding route of delivery. For women who are untreated or suboptimally suppressed because of poor adherence, resistance to their cART regimens, or inadequate time on cART to attain suppression, with viral loads more than 1,000 copies/mL at term, a scheduled medically indicated early-term cesarean delivery at 38 0/7 weeks of gestation should be offered, in conjunction with peripartum maternal antiretroviral therapy (intravenous ZDV) administered 3-hours preoperatively. In these women, early-term cesarean delivery, ideally before the onset of labor and before rupture of membranes, reduces the risk of HIV transmission. As with all complex clinical decisions, the choice of delivery should be individualized. Discussion of the option of scheduled cesarean delivery and its advantages in the situation of suboptimal viral suppression should begin as early as possible in pregnancy with every pregnant woman with HIV infection to give her an adequate opportunity to ask questions and consider her decision-making concerning the delivery plan. The patient's decision regarding her route of delivery should be respected after maternal and neonatal risks have been discussed.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at www.acog.org/HIV.

These resources are for information purposes only and are not meant to be comprehensive. Referral to these resources does not imply ACOG's endorsement of the organization, the organization's website, or the content of the resource. The resources may change without notice.

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