Approximately one million people in the United States are living with Human Immunodeficiency Virus (HIV) and it is estimated as many as 20% of them are unaware of their infection.(CDC, 2012) Women of childbearing age make up the fastest growing population of HIV infected adults in the US. The most common route of HIV infection in children occurs through mother-to-child transmission (MTCT) during pregnancy, labor and delivery, or breastfeeding. HIV diagnosis before or during pregnancy can reduce perinatal transmission to < 1% if appropriate medical treatment is provided and breastfeeding is avoided. (CDC, 2012)

Preconception counseling and care of HIV infected women includes discussions regarding childbearing intentions, contraceptive methods, safe sex practices, HIV status, and antiretroviral therapy (ART). Preconception counseling provides an opportunity to decrease unintentional pregnancies, decrease transmission rates to uninfected partners, provide ART to improve health, and decrease MTCT with antiretroviral (ARV) drugs. (AIDSinfo, 2012)

Screening

In 1999, the Institute of Medicine, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists recommended that "the United States should adopt a national policy of universal HIV testing, with patient notification, as a routine component of prenatal care". (ACOG, 1999, reaffirmed 2014, 2007, 2014) Alabama law requires written consent of the individual being tested for HIV infection either by antibody tests or other methods (Code of Ala. 1975, §22-11A-51 and -
52.)Information on HIV testing can be included in a general consent for care form if the patient is provided an opportunity to opt out. A separate consent for HIV testing is not recommended but can be used if the provider prefers. If the patient does opt out of HIV testing, a note should be made in the medical record. HIV test results must be available to the patient along with information on the meaning of the results, methods of HIV transmission, ways to avoid becoming infected, or, if positive for HIV, on ways to avoid infecting others. Fact sheets on HIV and pregnancy can be found at http://aidsinfo.nih.gov/education-materials/fact-sheets. Intrapartum screening can be done for high-risk women using a rapid HIV test.

Management

Given the near-constant evolution in therapeutic recommendations and the complexities in caring for these women, obstetricians should seek consultation from clinicians with expertise in HIV disease when caring for a pregnant woman with HIV. Coordination of care services should include prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services as needed, and public assistance programs to ensure adherence with ARV drug regimens.

A list of AIDS service organizations available to assist in the care of HIV pregnant women in Alabama can be found on the Alabama Department of Public Health website http://adph.org/aids/Default.asp?id=6128. The listed AIDS organizations provide a variety of assistance including medical management of the HIV treatment and social services to assist with patient needs. Services include but are not limited to: management of HIV treatments; provision of avenues for patient to receive medications (such as mailing them to patients in rural areas); help with transportation to and from appointments (including OB appts); adherence education; and close tracking of patients.

Antepartum

Initial assessment includes determination of disease status and recommendations regarding the initiation of ARV drugs or modification of current ART. The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on perinatal HIV care. All HIV positive women should receive a combination ARV drug regimen antepartum to prevent MTCT. (AIDSinfo, 2012) The risks and benefits of ARV drugs should be discussed with the patient. Due to the possibility of transmitted virus with drug resistance, current guidelines recommend that women with HIV RNA levels >500 to 1,000 copies/mL have ARV drug-resistance studies performed before initiating or modifying ARV drug regimens. When HIV is diagnosed in the third trimester, a combination ART regimen should be initiated without waiting for the results of resistance testing although resistance testing should still be ordered. Adherence to ARV regimens should be monitored and emphasized.

Management

- Review prior HIV-related illness and past CD4 T-lymphocyte (CD4-cell) counts and plasma HIV viral loads.
- Obtain current CD4-cell count; repeat each trimester or more often as needed.

- Obtain current plasma HIV RNA copy number; repeat each trimester or more often as needed.
- Additional labs for women commencing ART: CBC with diff & platelets and liver function tests.
- All HIV positive pregnant women should have a test for exposure to tuberculosis using either PPD testing or an interferon-gamma release assay (e.g. QuantiFERON).
    - Women with a positive result on either test should receive a standard workup for tuberculosis including chest x-ray and symptom evaluation.
    - Women with CD4-cell counts <200 have a greater risk of anergy. Therefore, women who undergo PPD testing, do not need additional workup if negative, unless there is a high likelihood of exposure to tuberculosis. Consultation with an infectious disease specialist should be sought for these patients.
- Risk of fetal HIV inoculation posed by invasive procedures used for prenatal diagnosis (amniocentesis) should be weighed against the benefits of the procedure on an individual basis.
- CD4-cell counts < 200/µL should prompt initiation of the following prophylactic therapy:
    - *Pneumocystis carinii* pneumonia: Bactrim DS 1 tab p.o. every day.
- CD4-cell counts <50/µL should prompt initiation of these additional prophylactic therapies:
    - *Mycobacterium avium-intracellulare* complex: Azithromycin 1200mg p.o. every week.
    - For women with severe or recurrent vaginal/esophageal candidiasis: Diflucan 150mg p.o. every week.
- Antiretroviral therapy: All HIV infected women should receive a potent combination antiretroviral (ARV) regimen to reduce the risk of transmission.

Vaccinations

Regardless of CD4-cell count, all HIV infected pregnant women should receive:

1) The inactivated influenza vaccine, unless a specific contraindication exists.
2) The pneumococcal vaccine, unless vaccinated within the last 5 years.
3) The Hepatitis B vaccine series, unless they have been previously vaccinated or have serologic evidence of past infection/exposure (positive IgG to core Antigen).

Antiretroviral Drugs during Pregnancy and Delivery

In pregnancy, a combination ARV regimen with at least three agents is recommended. The goal is complete suppression of viral RNA in the plasma to reduce the risk of perinatal transmission of HIV.

Determining the timing of initiation of the ARV regimen, during first trimester versus delay until 12 weeks, is dependent upon CD4-cell counts, HIV RNA levels, and maternal conditions such as nausea and vomiting. Delaying initiation of ARVs until after the first trimester can be considered in women with high CD4-cell counts and low HIV RNA levels, but earlier initiation is more effective in reducing perinatal transmission of HIV. Benefits of first trimester ARV use must be weighed against potential fetal effects of first-trimester exposure. Initiation of efavirenz (pregnancy class D) or other potentially teratogenic drugs should be avoided in the first trimester.

ARV-naïve women: Women should be started on a combination regimen including two Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI) and either one Protease Inhibitor (PI) or one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI). The preferred NRTI drugs for ARV therapy include those with good placental passage such as: zidovudine (ZDV), lamivudine, emtricitabine, tenofovir, and adacavir. The preferred ARV agents in the protease inhibitor class are atazanavir/ritonavir or lopinavir/ritonavir. Dosing of protease inhibitors may need to be increased during the second and third trimesters. Nevirapine is the preferred NNRTI and it can be considered in ARV-naïve pregnant women with CD4 counts ≤250 cells/mm^3, and for continued use in ARV-experienced women already receiving a nevirapine regimen. Since nevriapine can increase the risk of severe hepatic toxicity in women with CD4-cell counts >250 cells/mm^3, it should be avoided in these women.

Based on results of ACTG-076, intrapartum ZDV should be administered with a loading dose of 2 mg/kg over 1 hr followed by a continuous infusion at 1mg/kg/hr until delivery. More recent data suggest that the infusion may not provide additional preventive benefit for women with HIV RNA <400 copies/mL and can be eliminated. However, given the extensive data on the safety of intrapartum ZDV and the potential risk associated with failing to administer this agent to women who might benefit, we advocate the general policy of administering both the loading dose and the continuous intrapartum infusion of ZDV to all HIV positive women. Ideally, ZDV should be initiated at least 3 hours prior to delivery, however even if it appears that the patient may deliver within 3 hours, the ZDV should still be initiated as soon as possible. ARV agents are continued orally regardless of mode of delivery. If oral ZDV is part of the antepartum regimen, the oral ZDV component of her regimen should be stopped while she receives continuous infusion of ZDV during labor. Scheduled cesarean delivery at 38 weeks is recommended for women with HIV RNA ≥1,000 copies/mL. Women with HIV RNA <1,000 copies/mL can be delivered vaginally. The duration of membrane rupture should not be a sole determining factor in choosing the mode of delivery.

HIV infected women on ART who become pregnant: Women on ARV drug treatment prior to pregnancy should continue these medications during the first trimester of pregnancy. If their ARV drug treatment includes efavirenz or other potentially teratogenic drugs, these drugs should be discontinued during the first trimester. HIV positive patients should continue their combined ARV regimen as long as at is tolerated and effective in suppressing viremia. ARV drug-resistance testing should be done on women on therapy with detectable viremia >500-1,000 copies/mL to determine if any modification of the regimen is needed. These women should continue the ART regimen during the intrapartum and postpartum periods. Follow guidelines above for intrapartum ZDV, both loading dose and continuous infusion.

HIV infected women who are ARV experienced but not currently receiving ARV drugs: It is important to review ARV drug history and test for HIV ARV drug resistance before reinitiating ARV prophylaxis or therapy. These results should be considered in regimen selection for antepartum treatment. Follow guidelines above for intrapartum ZDV, both loading dose and continuous infusion.

HIV infected women who have received no ARV before labor: Follow guidelines above for intrapartum ZDV, both loading dose and continuous infusion. Consultation should be sought with infectious disease experts to evaluate need for initiation of maternal therapy postpartum.

Mode of Delivery(ACOG, 2000)

- Scheduled cesarean delivery at 38 weeks is recommended for women with HIV RNA ≥1,000 copies/mL.
- Women with HIV RNA <1,000 copies/mL can be delivered vaginally. It is reasonable to await spontaneous onset of labor, but the patient should be instructed to present to Labor and Delivery at the first sings of labor to ensure that there is adequate time to initiate the ZDV infusion prior to delivery.
- Intrapartum ZDV, both loading dose and continuous infusion should be administered while other ARV agents are continued orally regardless of mode of delivery. If oral ZDV is part of the antepartum regimen, the oral ZDV component of her regimen should be stopped while she receives continuous infusion of ZDV during labor.
- ZDV continuous infusion: 2 mg/kg IV over 1 hour followed by continuous infusion of 1 mg/kg/hour until delivery. Ideally, ZDV should be started at least 3 hours prior to delivery.

Rapid HIV Testing

Due to the potential for intrapartum chemoprophylaxis to reduce maternal to child transmission of HIV, ACOG (ACOG, 2014) as well as a number of other organizations have advocated rapid HIV testing on admission to Labor and Delivery for select patients. Patients for whom this testing should be considered include:

- No prior documented negative HIV serology during this pregnancy
- High risk for HIV acquisition during the current pregnancy (e.g. IV drug use, other STDs acquired during pregnancy)

Patients should be counseled regarding the potential for false positive results and the need for further evaluation and follow-up testing in the event of a positive result. If a positive result is noted, immediate initiation of antiretroviral prophylaxis, using the ZDV regimen described above, is recommended without waiting for the results of the confirmatory test.

Postpartum

- Breastfeeding should be discouraged as vertical transmission can occur (cumulative additional risk ~15%).
- Mothers and infants should be referred to clinicians with HIV-specific expertise for long-term care. A list of AIDS service organizations available to provide care to HIV positive women in Alabama can be found at on the Alabama Department of Public Health website http://adph.org/aids/Default.asp?id=6128.
- Provide counseling on contraception options and the importance of condom use.

Quality Indicators/Benchmarks

- Universal HIV screening-all patients
- Co-management with HIV specialty provider

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