

Guideline on invasive obstetric procedures in the HIV-infected pregnant woman

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Antenatal invasive obstetric procedures in HIV-infected pregnant women are associated with a risk of mother-to-child HIV transmission. There are limited published data on the subject. The general consensus is that any HIV-infected pregnant woman who needs to undergo an invasive procedure should have combination antiretroviral therapy initiated before the procedure, regardless of the CD4+ cell count. The recommendations in this guideline, developed to assist clinicians in counselling and managing HIV-infected pregnant women in need of an invasive procedure, are based on small observational studies and local experience.

1. Introduction

Antenatal invasive obstetric procedures, which may be diagnostic or therapeutic, are performed at different stages of pregnancy for various indications. The commonest indication for an invasive procedure during pregnancy is for fetal karyotyping when a chromosomal abnormality or a genetic defect is suspected, either from the couple's history or from ultrasound assessment of the fetus. Other less common but equally important indications may be diagnostic (fetoscopy, fetal tissue sampling, estimation of fetal haemoglobin) or therapeutic (aspiration of various fetal cavities, fetal blood transfusion and embryo reductions).

In a high HIV prevalence setting like South Africa, where the estimated prevalence in antenatal clinic attendees was 30.2% in 2010, a significant proportion of pregnant women in need of invasive procedures will be HIV infected.¹ Clinicians need to be aware of the risk of mother-to-child transmission (MTCT) of HIV associated with invasive procedures, and also be aware of strategies available to minimise the risk.

This information, together with the procedure-related risks of invasive testing, should be given to clients during the counselling session. Written informed consent relating to the procedure and the risk of MTCT should be obtained before the procedure.

This guideline was developed to assist clinicians in counselling and managing HIV-infected pregnant women in need of invasive procedures. It is targeted at clinicians working in both the private and public sectors. For more detailed information on indications, techniques and risks associated with antenatal invasive procedures, the reader is referred to guidelines published elsewhere.²

2. Timing of invasive procedures in pregnancy

Below is a list of commonly performed antenatal invasive obstetric procedures and the gestational ages at which each procedure can or should be performed:

- amniocentesis: from 16 weeks
- chorionic villus sampling: from 11 to 14 weeks
- cordocentesis: from 20 weeks
- fetoscopy: usually in the 2nd and 3rd trimesters
- fetal tissue sampling (biopsies of organs, muscle, etc.): usually in the 2nd and 3rd trimesters
- aspiration of various fetal cavities, shunt insertion: any gestational age – usually from 16 weeks
- embryo reductions: from 11 weeks.

3. Risk of MTCT with antenatal invasive procedures

There is limited literature on invasive obstetric procedures in the context of maternal HIV infection. Few studies have been published on the topic, most with a small number of participants. Important risk factors for MTCT such as maternal HIV viral load and CD4+ cell count are not always controlled for, and it may be difficult to infer causality in the reported cases of transmission after an invasive procedure. Without any maternal antiretroviral therapy initiated prior to an invasive procedure, the risk of MTCT is high, with rates of over 30% reported in some studies.^{3,4} One study showed a fourfold increase in the risk of MTCT with third-trimester amniocentesis without any maternal antiretroviral cover.³ With the use of combination antiretroviral therapy prior to antenatal invasive procedures, the risk of MTCT is reportedly similar to that in an HIV-infected pregnant woman who has not had an invasive procedure.⁵⁻⁷

Despite the decrease in HIV transmission with antiretroviral cover, procedures such as chorionic villus sampling and cordocentesis should still be avoided in the HIV-infected woman as the risk of transmission to the fetus may be considerably higher.

Guidelines on the techniques of performing invasive procedures should be adhered to, and where possible the transplacental route should be avoided owing to the higher risk of transmission.⁸

4. Recommendations on antiretroviral prophylaxis prior to invasive procedures

There is now general consensus in the literature that any HIV-infected pregnant woman who needs to undergo an invasive obstetric procedure should have combination antiretroviral therapy initiated before the procedure, regardless of her CD4+ cell count.^{8,9} Ideally, antiretroviral therapy should be initiated at least 4 - 6 weeks before the procedure to achieve a significant level of maternal HIV viral suppression.¹⁰ If the gestational age precludes waiting for the period of 4 - 6 weeks, the clinician can still go ahead with the procedure as continuation of combination antiretroviral therapy after the procedure provides post-exposure prophylaxis.

Studies and surveillance data on MTCT suggest a strong correlation between maternal HIV viral load at delivery and transmission to the fetus, with undetectable viral loads being associated with the lowest risk of transmission.^{11,12} There are no data available to demonstrate a viral load threshold below which HIV transmission is unlikely to occur following an antenatal invasive procedure. Results from general MTCT studies cannot be extrapolated to cases with invasive procedures. However, both the Royal College of Obstetricians and Gynaecologists and the British HIV Association recommend an undetectable maternal viral load at the time of the invasive procedure.^{8,9} If resources allow and there is sufficient time to wait prior to the invasive procedure, maternal viral load should be determined as part of the pre-procedure counselling.

HIV-infected women with an indication for an invasive procedure may present already on antiretroviral treatment (ART), initiated either before or after conception. They may also present on zidovudine (AZT) monotherapy initiated during pregnancy or on no antiretroviral therapy. All these scenarios will be considered, and recommendations on antiretroviral prophylaxis made.

4.1 ART initiated pre-conception (Table I)

If a pregnant woman presents at a gestational age of less than 14 weeks, and is on an efavirenz (EFV)-containing regimen, EFV should be switched to either nevirapine (NVP) or lopinavir/ritonavir (LPV/r). In the public sector, NVP is the first choice unless contraindicated.

There is no need to switch drugs if a pregnant woman is on an EFV-containing regimen and presents at a gestational age of more than 14 weeks, or is on a NVP- or a LPV/r-containing regimen.

4.2 ART initiated post-conception

The rules above on ART initiated before conception also apply in pregnant women initiated on ART during pregnancy.

4.3 On no ART

Women not on ART can be classified by their CD4+ cell count level, and managed accordingly:

- CD4+ cell count ≤ 350 cells/ μ l
- CD4+ cell count > 350 cells/ μ l.

4.3.1 CD4+ cell count ≤ 350 cells/ μ l, or WHO stage 3 or 4

- Lifelong ART needs to be initiated as soon as possible. For the public sector, the choice of regimen is according to the South African National PMTCT guidelines (Table II).¹³

4.3.2 CD4+ cell count > 350 cells/ μ l, and WHO stage 1 or 2

- The pregnant woman needs to be initiated on combination ART before the invasive procedure. If AZT monotherapy has already been initiated, it must be stopped and combination therapy started.

Table I. Pre-conception ART regimen containing efavirenz (EFV)

Presentation before 14 weeks' gestation	Presentation after 14 weeks' gestation
Switch from EFV to: <ul style="list-style-type: none"> • NVP 200 mg 12-hourly OR • LPV/r 400/100 mg 12-hourly 	Continue EFV 600 mg daily

Table II. Antenatal ART regimens for PMTCT, based on CD4+ cell count

CD4 ≤ 350 cells/ μ l, or WHO stage 3 or 4 <i>Lifelong ART initiation</i>	CD4 > 350 cells/ μ l, and WHO stage 1 or 2 <i>Prophylactic ART for invasive procedures</i>
Combination of: TDF 300 mg daily or AZT 300 mg 12-hourly 3TC 150 mg 12-hourly or FTC 200 mg daily NVP 200 mg daily for 2 weeks then 200 mg 12-hourly	Combination of: TDF 300 mg daily or AZT 300 mg 12-hourly 3TC 150 mg 12-hourly or FTC 200 mg daily EFV 600 mg daily or LPV/r 400/100 mg 12-hourly
<small>ART = antiretroviral therapy; AZT = zidovudine; EFV = efavirenz; FTC = emtricitabine; 3TC = lamivudine; LPV/r = lopinavir/ritonavir; NVP = nevirapine; TDF = tenofovir; WHO = World Health Organization.</small>	

- Given the higher risk of hepatotoxicity at this CD4+ cell count, our recommendation is to use either an EFV- or an LPV/r-containing regimen with a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone. The NRTI backbone can be a combination of tenofovir (TDF) and lamivudine (3TC), or emtricitabine (FTC), or AZT and 3TC (Table II).

In all cases, combination ART should be continued until after delivery, and in cases where the mother elects to breastfeed, combination therapy must be continued until at least 1 week after breastfeeding cessation.

When stopping antiretrovirals, non-nucleoside reverse transcriptase inhibitors (NNRTIs) need to be stopped a week prior to stopping NRTIs. This is done because NNRTIs have a longer half-life, and their earlier discontinuation confers a lower risk of NNRTI resistance.¹⁴

This guideline on invasive obstetric procedures in the HIV-infected pregnant woman is meant to be a guide for clinicians, to be used in counselling the woman/couple, and also in managing the woman who is eligible for an invasive procedure. Expert advice should be sought wherever necessary.

As there are limited data on invasive obstetric procedures in HIV-infected pregnant women, our recommendations are based on small observational studies and local experience. There is a need for more research on the topic to better inform practice. There is a particular need for information on the optimal duration of antiretroviral therapy and maternal viral load prior to the invasive procedure.

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