

## CLINICAL PRACTICE

## Recommendations for amniocentesis in HIV-positive women

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There is limited literature on the known risk of HIV transmission during amniocentesis. Before the introduction of highly active antiretroviral therapy (HAART), amniocentesis was avoided owing to the increased risk of HIV transmission. Recent literature suggests that it is safe to perform amniocentesis in women on HAART with undetectable viral loads. In South Africa (SA), many women access antenatal care late in pregnancy and there is often insufficient time to attain undetectable viral loads within a pre-viability period. Guidelines and recommendations for invasive testing in HIV-positive women in the SA setting are lacking. This article provides recommendations to healthcare practitioners who are faced with an HIV-positive patient requiring amniocentesis.

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Aneuploidy is a major cause of perinatal death and childhood handicap.<sup>[1]</sup> Improved methods of screening for aneuploidy such as the nuchal translucency (NT) scan, first- and second-trimester serum biochemistry and assessment of fetal anatomy and markers by ultrasound at 18 - 22 weeks' gestation have replaced maternal age, which is known to be a poor method of screening. With improved screening methods, there is a need for diagnostic tests such as a chorionic villous sample and amniocentesis to confirm or exclude aneuploidy. These invasive tests are associated with a risk of miscarriage, and should therefore only be carried out in high-risk pregnancies.

### HIV and birth defects

The situation is complicated further if a woman at high risk for aneuploidy is also HIV-positive. Knowledge of the risks of HIV transmission to the fetus from invasive procedures is important to ensure adequate counselling and management.

More than half of the estimated 33 million people in South Africa (SA) living with HIV/AIDS are women, and most are of childbearing age.<sup>[2]</sup> The SA Department of Health study estimates that in 2011, 29.5% of pregnant women were HIV-positive. KwaZulu-Natal recorded the highest HIV prevalence of 37.4%, while the Northern Cape recorded the lowest at 17%.<sup>[3]</sup> The use of highly active antiretroviral therapy (HAART) has led to a significant reduction in morbidity and mortality from HIV infection and a decline in mother-to-child transmission (MTCT).

Globally, birth defects occur in approximately 2 - 3% of live births, although minor anomalies are more frequent.<sup>[4]</sup> The birth prevalence of serious defects is lower in industrialised countries than in developing countries. An HIV-positive woman is not at increased risk of having a child with a birth defect compared with the average population, even if she is on antiretroviral therapy (ART).<sup>[5,6]</sup>

### HIV and amniocentesis

There is limited literature on the known risk of HIV transmission during amniocentesis. Before HAART, invasive procedures such as amniocentesis were avoided owing to the increased risk of MTCT.<sup>[7-12]</sup> Recent literature suggests that it is safe to perform amniocentesis in women on HAART with suppressed viral loads (preferably undetectable) and when transplacental passage of the needle is avoided.<sup>[7,10-15]</sup>

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HIV counselling and testing at the booking antenatal visit is routine, and many patients will only discover their HIV status during the pregnancy. Unfortunately, in SA many women initiate antenatal care late in pregnancy – in a recent study of over 27 000 pregnancies in the Peninsula Maternity and Neonatal Service in the Western Cape, 62% of women booked after 20 weeks<sup>[16]</sup> – thus missing the opportunity for first-trimester screening. All women, regardless of whether they have had first-trimester screening, will ideally be offered a fetal abnormality scan between 18 and 22 weeks if resources are available. If a fetal abnormality is detected and amniocentesis is offered, there is often insufficient time to attain an undetectable viral load within the pre-viability period (i.e. before the generally accepted cut-off period of 24 weeks).

### Groote Schuur Hospital (GSH) experience

At GSH, Cape Town, we undertook a survey of a case series of 27 HIV-positive women who attended our genetics clinic over a 3-year period and accepted amniocentesis on the basis of screening tests that showed them to be at high risk. A total of 642 amniocenteses were undertaken over the period. Four per cent of these were in HIV-positive women, a small proportion because many HIV-positive patients declined amniocentesis after counselling and learning of the possible HIV transmission risk. The duration of HAART prior to amniocentesis, outcomes and postnatal care were recorded. In this group of 27 women, there were 6 pregnancy losses, 1 early neonatal death, 3 chromosomal abnormalities and 10 structural abnormalities. Although there were no cases of vertical HIV transmission in the 21 liveborns, the number of patients was small and the duration of ART prior to amniocentesis varied widely from no treatment in 3 patients to more than 3 years of HAART in 4. Eighteen out of 21 patients had at least 10 days of HAART.

### Discussion

All women should be able to opt for prenatal screening and diagnosis, and for amniocentesis if required, regardless of their

HIV status. It is a challenge to counsel patients about the risk of abnormality in their unborn child. In addition to this challenge, the risk of miscarriage and possible risk of HIV transmission associated with amniocentesis needs to be discussed in women who test positive for HIV.

We know that the overall risk of HIV transmission when amniocentesis is performed in early pregnancy is very low, and the addition of HAART reduces this risk significantly. It is reasonable to deduce that the longer the patient has been on HAART prior to amniocentesis, the lower the chance of HIV transmission. However, it is unclear what the minimum duration of treatment should be, and very large numbers of patients would be required to deduce the potential transmission rate with any reliability. While it is recognised that one of the biggest limitations in all studies is the absence of a control group, it would be unethical to do randomised controlled trials in this setting.

As clinicians, we have a responsibility to the mother to offer care that is standardised and does not discriminate in the presence of HIV infection. However, we also have a responsibility to the fetus and should not be exposing that fetus to an unnecessary risk of HIV transmission.

As with any diagnostic test, there should be a strong indication to do invasive testing, and this should only be offered when the risk of an abnormality is high. The risk of miscarriage and possible HIV transmission in HIV-positive women undergoing amniocentesis needs to be weighed against the benefits of a prenatal diagnosis, all of which needs to be communicated clearly to the patient so that she can make an informed decision. For some patients, having a child with a disability is not an option, and the benefit of a prenatal diagnosis outweighs the risks associated with amniocentesis. Conversely, amniocentesis should probably be avoided in patients who would not accept termination of pregnancy if the karyotype is abnormal.

### Recommendations for management

If an HIV-positive patient accepts amniocentesis after counselling and consideration of the risks, HAART should be initiated and the procedure delayed until the viral load is undetectable. If there is not enough time to attain an undetectable viral load, it is reasonable for the patient to be on HAART for as long as possible prior to amniocentesis, as long as she understands the possible risks. The nature of the fetal abnormality may influence the decision to proceed with amniocentesis even when the viral load is not suppressed. If the abnormality is severe and will be associated with significant morbidity, exposing the fetus to a very low risk of HIV transmission will be outweighed by the benefit of a prenatal diagnosis.

Although not available in the state sector, and to many private patients because of the cost, it is worth noting that there is the option of having a non-invasive prenatal screening test (e.g. the Harmony test, which analyses cell-free DNA in the maternal blood and will identify 99% of fetuses with trisomy 21, 97% of fetuses with trisomy 18 and 92% of fetuses with trisomy 13).<sup>[17]</sup> This highly effective screening test does not carry the risk of miscarriage and HIV transmission. However, it does not identify other chromosomal abnormalities, and the high cost makes it inaccessible to many patients.

### Summary

- There must be a strong indication to offer invasive testing. More effective screening methods such as an NT scan and a detailed fetal ultrasound scan looking for markers and defects must replace maternal age, which we know to be a poor method of screening.
- All women who have been offered and accept invasive testing must have an HIV test as part of their routine work-up.
- It is probably safe to perform amniocentesis in HIV-positive women on HAART, as long as their viral load is low (preferably undetectable) and transplacental passage of the needle is avoided.
- It may not be possible to wait for the viral load to become undetectable, and in carefully selected cases amniocentesis may be performed when the viral load is not suppressed.
- The risks of the amniocentesis must always be weighed against the benefit of a prenatal diagnosis.
- Amniocentesis should not be performed on HIV-positive women who are not on HAART.
- Careful consideration should be given to the patient who would not terminate the pregnancy if the karyotype is abnormal. In this case, invasive testing should preferably be avoided.
- Third-trimester amniocentesis, chorionic villous sampling and cordocentesis are not recommended in HIV-positive women.
- Consider a non-invasive – though costly – prenatal screening test.

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