CLINICAL GUIDELINE

DIAGNOSIS OF PERINATAL HIV-1 INFECTION IN SOUTH AFRICA

Recommendations for best practice under ideal and resource-constrained conditions

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1. INTRODUCTION

These guidelines for best practice under both ideal and resource-constrained conditions are intended to provide guidance for health care professionals on the laboratory diagnosis of HIV-1-infected and non-infected infants and young children. Resources, circumstances and decisions will differ across the wide range of clinical settings in South Africa. These guidelines have therefore been formulated recognising the following needs:

- Diagnosis of HIV infection in infants and young children born to mothers of unknown HIV serostatus or changing HIV serostatus in the perinatal or breast-feeding period
- Management of HIV-infected or HIV-exposed infants and children with regard to implementation of prophylaxis for opportunistic infections
- Early identification of HIV infected infants critical for clinical management and initiation of antiretroviral therapy
- Decisions regarding the continuation or cessation of breast-feeding practices and the possible implementation of alternative feeding practices
- Early diagnosis of HIV infection in infants considered for adoption
- Revised and updated guidelines as new data on laboratory techniques and the management of HIV infection are acquired.[1-3]

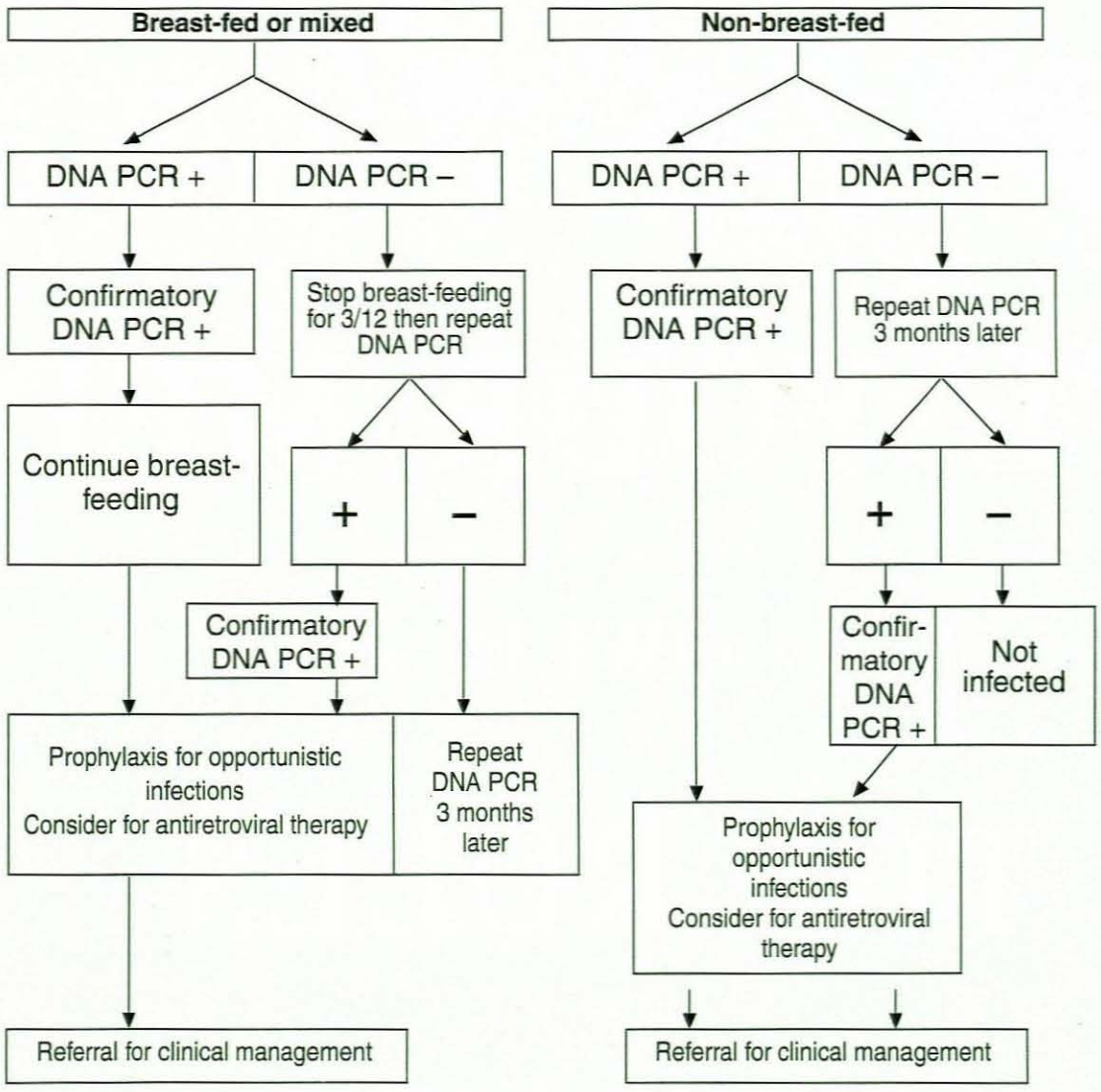
Rates of HIV infection among pregnant women are still increasing and the perinatal transmission of HIV in South Africa remains a pertinent and critical issue.[1] (Refer to the guidelines on preventing mother-to-child transmission of HIV-1 in South Africa, *Southern African Journal of HIV Medicine*, Issue 4, May 2001.) The diagnosis of HIV infection among infants should begin with identifying HIV infection in women before and during every pregnancy and this awareness should also identify the HIV-infected infant.[1,4] Nonetheless, perinatal HIV diagnosis presents challenges such as:

- Difficult, early and rapid diagnosis in exposed infants because of the persistence of transplacental passage of maternal immunoglobulin G (IgG) HIV antibodies
- Timing of HIV transmission from mother to child that affects the sensitivity and specificity of available HIV diagnostic assays
- The risk of the infant being exposed to HIV throughout the duration of breast-feeding
- The use and role of quantitative and qualitative HIV virological assays
- The use and role of the immune complex-dissociated (ICD) p24 antigen detection assay for diagnosis and prognosis
- The global existence of multiple clades or subtypes of HIV and the impact on assay detection.[1,5-10]

Clinical acumen should prevail in interpreting HIV test results, for example HIV infection can be ruled out in children 18 months of age or older who have negative HIV serology, a history of no breast-feeding or breast-feeding that ceased at least 3 months previously, no clinical symptoms of HIV disease and no hypo- or hypergammaglobulinaemia.[2] In turn, all women should be encouraged to undergo voluntary counselling and testing (VCT).[1]

2. DEFINITION OF AN HIV-UNINFECTED INFANT/CHILD

When HIV-exposed infants and young children have been identified, health care professionals still need to determine whether they are indeed HIV-infected or not. Such information is critical for the implementation of adequate medical care that must address monitoring of T-cell subsets, the viral load and institution of warranted prophylactic therapies.[11] An HIV-uninfected infant/child can



- In resource-poor settings:
  (a) serial ELISA antibody assays may be done at 3-monthly intervals from 6 months of age
  (b) serum p24 antigen assays (with ICD) may be useful in symptomatic subjects.
- Two +ve DNA PCRs are diagnostic of HIV infection.
- An HIV RNA quantitative assay may be used as the second confirmatory test.

Diagnosis of perinatally acquired HIV infection.

be defined as an infant/child who has undergone two negative HIV serological or virological tests; such children can be classified into two distinct age categories:

- For children older than 12 months of age, provided breast-feeding has ceased 3 months previously, two negative HIV serological tests based on the enzyme-linked immunosorbent assay (ELISA) method would indicate non-infection (if under 15 months of age, ELISA tests should be at least a month apart).
- For infants younger than 12 months yet older than 6 weeks of age, provided breast-feeding has ceased 3 months previously, two negative HIV DNA polymerase chain reaction (PCR) test results would indicate non-infection.

3. DEFINITION OF AN HIV-INFECTED INFANT/CHILD AND RECOMMENDATIONS ON THE USE OF HIV TESTS

HIV diagnostic techniques are difficult in infants and young children as a result of the persistence of maternal antibodies up to 18 months of age.[12,13] The HIV DNA PCR detecting the DNA proviral form of the integrated virus into the genome of peripheral blood cells, is considered the test of choice for the diagnosis of perinatally acquired HIV infection.[12] The PCR is a diagnostic qualitative reaction compared with the RNA quantitative reaction (viral load) which is applied in the prognostic staging or clinical monitoring of patients.[9] The HIV DNA PCR is a rapid and accurate method for identification of HIV infection in infants and young children less than 18 months of age and two tests performed on separate samples are 98.5% accurate in identifying infection status after 28 days of age.[12] However, PCR amplifications can be prone to carry over contamination and testing should take place strictly according to the manufacturer's instructions and only in areas dedicated for PCR work. HIV DNA PCR methods are commercially available and reliable when standardised and performed in laboratories following good laboratory practices. These tests have been accurate for all known HIV-1 subtypes but ongoing molecular surveillance is necessary should novel subtypes emerge. Two HIV DNA PCR tests should be performed on infants between 6 weeks and 12 months of age. If the HIV DNA PCR is positive, breast-feeding should continue where applicable and the infant should receive prophylaxis for opportunistic infections, such as *Pneumocystis carinii* pneumonia (PCP).

Reports have indicated that the HIV RNA quantitative detection assays were more sensitive for early detection of HIV infection in infants born to HIV-infected women than the HIV DNA PCR assay. Nonetheless, a quantitative assay should not be used as a diagnostic tool and its clinical applications are clearly related to prognosis and further management of the patient.[14] In infants with a positive HIV DNA PCR result, the quantitative RNA assay may confirm HIV infection and provide additional data relevant to prognosis and as a baseline before antiretroviral therapy.[15]

Measurement of HIV p24 antigen in blood is not sensitive enough to be used for early diagnosis of HIV infection in infants and young children, even if immune complex-dissociated methods are used for sample preparation.[12,13] However, repeatedly positive HIV p24 antigen tests could be diagnostic of HIV infection and may be utilised in a resource-constrained setting, but use of a single positive result as a sole diagnostic test must be discouraged. The Western blot assay and the CD4 count should not be used for diagnostic purposes. The CD4 count as a diagnostic tool remains unreliable until local reference ranges for infants and young children have been studied and established.

4. RECOMMENDATIONS FOR SPECIAL CIRCUMSTANCES

HIV TESTING FOR ABANDONED INFANTS AND INFANTS FOR ADOPTION

There is an urgent need to diagnose early HIV infection in abandoned infants, especially those considered for adoption. Often the experience has been that HIV-positive infants remain at the institutions for extended periods before a final diagnosis of infection or non-infection is made. In turn, if these children are already older than 1 year it is more difficult to find foster or permanent homes for them. It is therefore recommended that these guidelines on diagnosis of perinatal HIV infection in South Africa be applied in these circumstances.

HIV TESTING FOR SEXUALLY ABUSED INFANTS AND YOUNG CHILDREN

The management of sexually abused infants and young children is another area of controversy and uncertainty; however, it is recommended that these guidelines be applied in these circumstances.[16]

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