

therapeutic outcome in the co-infected population. In a small subset of individuals, however, the development of anti-IFNAb could be responsible for virological failure.

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Utilizing nucleic acid amplification to identify acute HIV infection

Truong *et al.* [1] noted an 8% increase in acute infection detection when nucleic acid amplification testing is incorporated into standard HIV testing. Following a high-risk cohort in South Africa, we have similarly noted the benefits of nucleic acid amplification testing for the identification of acute HIV infection before seroconversion.

It is important to identify patients with acute HIV infection as a potentially useful opportunity to implement interventions that may reduce HIV transmission in the light of data that suggest that the probability of transmission may be increased by up to 10-fold during the acute phase of infection [2–5]. The identification of acute HIV infection is also important for research on HIV diagnostics, vaccines, microbicides and the early initiation of antiretroviral therapy [5].

Current routine HIV antibody tests and clinical criteria are not effective in distinguishing between acute and established HIV infection. Frequent HIV testing of high-risk individuals is one strategy to identify those with recent HIV infection, but this is impractical and costly [6]. Laboratory techniques such as the standardized algorithm for recent HIV seroconversion [sensitive/less sensitive ‘detuned’ enzyme-linked immunosorbent assay (ELISA) or the BED assay] have been utilized to identify recent HIV infections [7]. These tests have questionable accuracy, however, and they only indicate whether an individual seroconverted within the past few hundred days, and cannot therefore distinguish between recent and acute HIV infection. Strategies using the p24 antigen ELISA have been used to identify acute HIV infection before seroconversion in some settings, e.g. blood banks.

An approach using a pooling algorithm with nucleic acid amplification (polymerase chain reaction; PCR) has recently been proposed to identify acute HIV infection in those testing negative with standard HIV antibody testing, thereby detecting individuals with acute infection who are viraemic but antibody negative [8,9]. This approach has the advantage of an earlier diagnosis of acute HIV infection than with the p24 antigen assay.

To assess the potential utility of this PCR method in a resource-constrained setting, we followed a cohort of 245 HIV-negative high-risk sex workers established as part of the CAPRISA 002 Acute Infection Study, which is a prospective observational cohort study being conducted at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in Durban, South Africa. Acute HIV infection was determined according to the testing algorithm in Fig. 1, i.e. a positive RNA PCR at a study visit that follows a previous monthly visit at which the individual was found to have a negative HIV-RNA PCR. HIV-RNA PCR was performed using the Cobas AmpliScreen Multiprep HIV-1 test version 1.5 and the Cobas AmpliPrep/Cobas AmpliCor HIV-1 Monitor Test, version 1.5 (Roche Diagnostics, Branchburg, New Jersey, USA). The first step in the testing algorithm is testing with two rapid HIV tests: the Determine HIV-1 test (Abbott Diagnostics, Johannesburg, South Africa) and the Capillus HIV-1/HIV-2 test (Trinity Biotech, USA). Patients with at least one negative rapid HIV test are then tested by RNA PCR. RNA-PCR-positive samples are then tested by an ELISA using Enzygnost anti-HIV-1/2 plus (Dade Behring, Deerfield, Illinois, USA) to confirm the absence of anti-HIV antibodies.

Of the 23 acute HIV infections identified using this algorithm, 14 were identified through two concordant positive results on rapid HIV tests, three were negative on both the HIV rapid tests but were found to be ELISA positive, and six were rapid HIV test and ELISA negative.

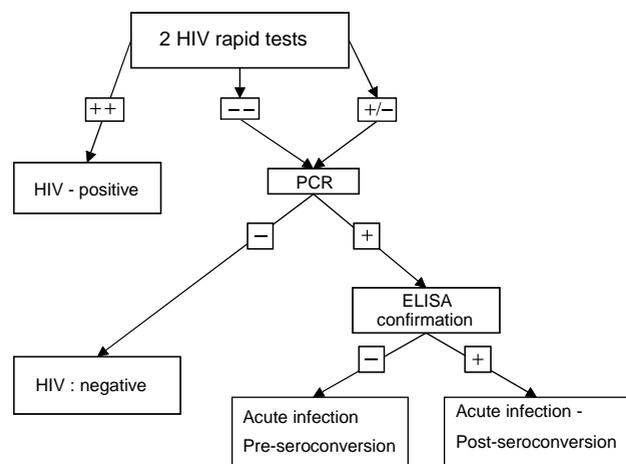


Fig. 1. HIV testing algorithm. ELISA, Enzyme-linked immunosorbent assay; PCR, polymerase chain reaction.

All 23 were RNA-PCR positive and were confirmed at later timepoints to be HIV seropositive by ELISA. The RNA-PCR cutoff used for positivity was greater than 1000 copies, and no false RNA positives were identified. There were 14 instances of discordant rapid HIV test results, and all were found to be HIV-RNA-PCR negative.

As the pre-antibody window period during which there is viral replication and detectable virus in the blood is short, monthly testing with two rapid HIV tests was able to detect 60.8% of patients (14/23) with acute HIV infection. If ELISA testing is added to the testing strategy, in addition to the rapid HIV tests (without PCR), then the detection of acute HIV infection increases from 14 to 17 of the 23 (73.9%) cases as a result of the false-negative rapid tests at low levels of anti-HIV antibodies. Incorporating RNA-PCR testing after two rapid HIV tests into the HIV testing strategy in this cohort increased the detection of acute HIV infections by 39.1%.

The incorporation of nucleic acid amplification testing into standard HIV antibody testing, either by ELISA or rapid HIV tests, is a potentially useful strategy for screening for acute HIV infection in populations at high risk of HIV acquisition. RNA PCR improves the detection of acute HIV infection substantially in high-risk cohorts, and could potentially have wider public health applications in a generalized population level epidemic with high HIV incidence rates, such as the HIV epidemic in South Africa.

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