Journal of Clinical Virology 61 (2014) 132–137

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Pooled nucleic acid testing increases the diagnostic yield of acute HIV infections in a high-risk population compared to 3rd and 4th generation HIV enzyme immunoassays

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ARTICLE INFO

Article history:
Received 8 May 2014
Received in revised form 20 June 2014
Accepted 24 June 2014

Keywords:
Acute HIV
Pooled nucleic acid testing
4th generation EIA
HIV diagnostics

ABSTRACT

Objectives: We compared a 3rd generation (gen) and two 4th gen HIV enzyme immunoassays (EIA) to pooled nucleic acid testing (PNAT) for the identification of pre- and early seroconversion acute HIV infection (AHI).
Study Design: 9550 specimens from males >18 year from clinics attended by men who have sex with men were tested by Siemens ADVIA Centaur® HIV 1/O/2 (3rd gen) and HIV Combo (4th gen), as well as by Abbott ARCHITECT® HIV Ag/Ab Combo (4th gen). Third gen non-reactive specimens were also tested by Roche COBAS® Ampliprep/COBAS® TaqMan HIV-1 Test v.2 in pools of 24 samples. Sensitivity and specificity of the three EIAs for AHI detection were compared.
Results: 7348 persons contributed 9435 specimens and had no evidence of HIV infection, 79 (94 specimens) had established HIV infection, 6 (9 specimens) had pre-seroconversion AHI and 9 (12 specimens) had early seroconversion AHI. Pre-seroconversion AHI cases were not detected by 3rd gen EIA, whereas 2/6 (33.3%) were detected by Siemens 4th gen, 4/6 (66.7%) by Abbott 4th gen and 6/6 (100%) by PNAT. All three EIAs and PNAT detected all individuals with early seroconversion AHI. Overall sensitivity/specificity for the EIAs relative to WB or NAT resolved infection status was 93.6%/99.9% for Siemens 3rd gen, 95.7%/99.7% for Siemens 4th gen and 97.9%/99.2% for Abbott 4th gen.
Conclusions: While both 4th gen EIAs demonstrated improved sensitivity for AHI compared to 3rd gen EIA, PNAT identified more AHI cases than either 4th gen assay. PNAT is likely to remain a useful strategy to identify AHI in high-risk populations.

1. Background and objectives

Individuals with acute HIV infection (AHI) have high viral loads and have been reported to account for up to 50% of forward HIV transmissions [1–3], making early diagnosis a public health priority to reduce HIV transmission and to facilitate early engagement of individuals into care. Currently available 3rd generation (gen) HIV enzyme immunoassays (EIA) can detect HIV infection in those with early stage HIV seroconversion [4], but these assays fail to identify AHI when viral loads are typically very high and antibodies have not reached sufficient levels to be detectable [5,6]. HIV nucleic acid tests (NAT), or p24 antigen assays (either stand-alone assays or when incorporated into 4th gen EIAs), can assist with detection of pre-seroconversion HIV infections, with the former exhibiting greater sensitivity and a shorter window period between infection and detection of HIV antibodies [7].

HIV confirmatory algorithms have changed very little since their introduction in the 1980s. While HIV screening EIAs have become more sensitive over time and display shorter window periods, the HIV western blot (WB) has not evolved in tandem with the WB assay having a longer window period than current 3rd and 4th gen EIAs [7]. Consequently, algorithms using WB usually cannot confirm HIV infection during the acute phase [8]. In 2010,

Abbreviations: EIA, enzyme immunoassay; NAT, nucleic acid test; PNAT, pooled nucleic acid test; gen, generation; AHI, acute HIV infection; WB, western blot.

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http://dx.doi.org/10.1016/j.jcv.2014.06.024

the U.S. Centers for Disease Control and Prevention (CDC) proposed a new HIV testing algorithm, both to improve identification of AHI and to discriminate HIV-1 from HIV-2 infections. The proposed algorithm recommends screening with a sensitive 4th gen EIA and replaces the WB with a supplemental HIV-1/HIV-2 differential antibody assay to confirm the presence of HIV-1 and/or HIV-2 antibodies [9]. Specimens with a reactive primary EIA and a non-reactive or indeterminate differential assay are then tested for HIV nucleic acid to identify AHI prior to detection of HIV antibodies. A number of recent studies have demonstrated the utility of the proposed algorithm for confirming HIV infection and improving the detection of AHI [10–12].

Studies have shown that the use of pooled NAT (PNAT) for specimens with a non-reactive antibody screen test increases the diagnostic yield of AHI [5], especially in high-risk populations [13–16]. We previously showed that the use of PNAT among males at high risk of HIV infection with a non-reactive 3rd gen EIA led to increased detection of AHI [6]. However, HIV screening algorithms are now switching to preferential use of 4th gen EIAs, and the relative contribution of PNAT with respect to 4th gen EIAs is less well understood. In this study, we compare the performance of PNAT to a 3rd gen and two 4th gen HIV EIAs for the identification of AHI.

2. Study design

2.1. Study population

Six clinics in Vancouver, British Columbia with historically high HIV detection rates among men who have sex with men were included in the study [6]. All HIV test requests received from these clinics between September 2012 and September 2013 for male, transgendered and sex unspecified individuals >18 year were included. Specimens were excluded from analysis if there was insufficient volume of serum for all tests.

2.2. Laboratory methods

All serum specimens were screened by a 3rd gen (Siemens ADVIA Centaur® HIV-1/O/2; Siemens, Mississauga, Ontario,

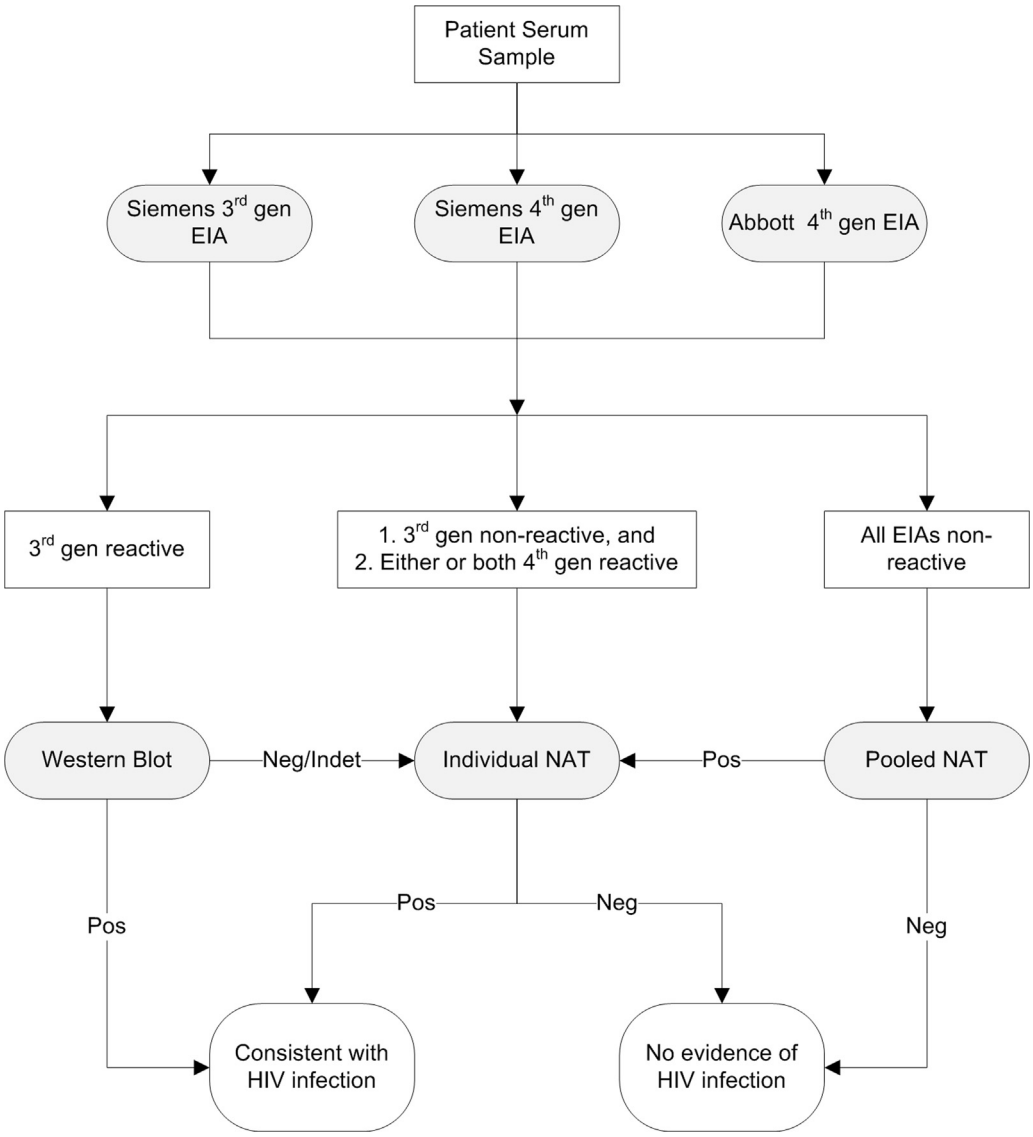

Fig. 1. HIV testing algorithm.
Abbreviations: gen: generation; EIA: enzyme immunoassay; NAT: nucleic acid test; neg: negative; indet: indeterminate; pos: positive.