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Performance of a parallel diagnostic algorithm for HIV diagnosis in low risk pediatric and obstetric patient populations

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ABSTRACT

Background: Little is known about the clinical performance of the 2010 APHL/CDC Western-blot independent HIV testing algorithm in low risk pediatric and obstetric patients.
Objective: To evaluate the performance of an alternate Western-blot independent algorithm and the individual algorithm components in diagnosing HIV infections in low risk pediatric and obstetric patients.
Study design: 6242 specimens from pediatric and obstetric patients were tested by the Bio-Rad Multispot HIV-1/HIV-2 (MS) and VITROS Anti HIV 1+2 (VITROS) assays. 913 specimens were also tested by the ARCHITECT HIV Ag/Ab Combo assay (ARCHITECT). Discordant specimens were tested by the APTIMA HIV-1 RNA qualitative assay (RNA Qual).
Results: Twenty-eight specimens tested positive for HIV-1 by both MS and VITROS, 4 of these 28 specimens were also tested by and positive by ARCHITECT; all 28 positives identified by the algorithm were positive by viral load analysis. MS identified 164 preliminary positives, which were not confirmed as true positives, representing a specificity of 97.4%. This specificity varied between patient populations (96.1% in the pediatric population and 99.1% in the obstetric population). The specificities of VITROS and ARCHITECT were 99.2% and 99.4% for pediatric patients; 99.7% and 99.8% for obstetric patients, respectively.
Conclusion: Our results highlight suboptimal specificity of MS in pediatric patients, and a lower specificity in both pediatric and obstetric patients relative to either VITROS or ARCHITECT. Additionally, parallel testing with both a third and fourth generation EIA in a low risk patient population provides a potential alternative to Western-blot dependent algorithms for confirmation.

1. Background

Rapid and accurate diagnosis of Human Immunodeficiency Virus (HIV) infection is critical for patient management, reduction of mortality and prevention of forward transmission [1]. For the past two decades the diagnosis of HIV infection has been based on a testing algorithm that included an initial screen using an enzyme immunoassay (EIA) followed by confirmatory testing with either a Western blot (WB), or an indirect immunofluorescence assay (IFA) [2–6]. Although results of this algorithmic approach are highly specific, the ability of WB to detect only IgG antibodies can result in failure to diagnose acute and early HIV infection, resulting in delays in appropriate prompt retroviral therapy and leading to an increased risk of onward HIV transmission, thereby sustaining the HIV epidemic [7–10]. Additionally, the frequent indeterminate results from the HIV-1 WB and the inability to differentiate HIV-1 from HIV-2 infections results in delays in confirmation, and may result in delays in the appropriate initiation of therapy for a significant number of patients [11,12]. Furthermore, supplementary confirmatory tests are not only complex and time consuming, but also expensive and subject to shortages [12–15].

Significant improvements in HIV diagnostics, including the development of newer assays with improved sensitivity and specificity led to the 2010 proposal of an alternative diagnostic algorithm by the Centers for Disease Control (CDC, Atlanta, GA)

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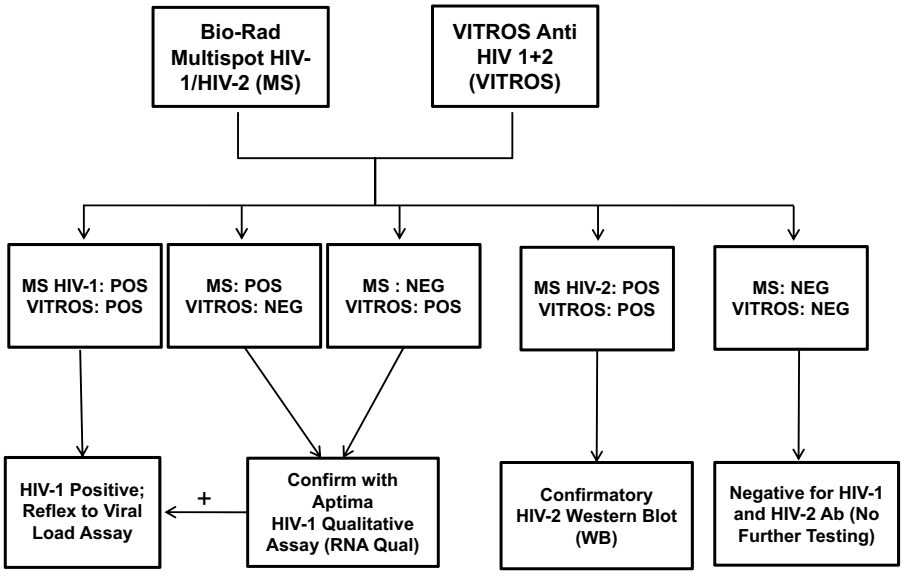

Fig. 1. HIV diagnostic algorithm at Texas Children's Hospital.

and Association of Public Health Laboratories (APHL, Silver Spring, MD) in the United States [8,16–18]. The proposed algorithm starts with a sensitive 4th generation HIV screening test that detects both HIV-1 p24 antigen and HIV-1 and HIV-2 antibodies, followed by confirmation of reactive specimens with a supplemental antibody immunoassay that differentiates HIV-1 from HIV-2 rather than the traditional WB assay. This proposed strategy was designed to facilitate accurate diagnosis of HIV-1 infections with minimal number of tests, to improve continuity of care, and also to differentiate between HIV-1 and HIV-2 infections.

Texas Children's Hospital (TCH) serves two distinct patient populations both of whom are typically low risk for HIV infection. In the absence of a 4th generation platform at TCH, and to best address the unique needs of the pediatric and obstetric populations served by the hospital, TCH instituted a modified algorithm that incorporated aspects of the proposed CDC/APHL diagnostic algorithm. The TCH HIV diagnostic algorithm (as shown in Fig. 1) tests both a rapid immunoassay (Multispot HIV-1/HIV-2 rapid test (MS); Bio-Rad Laboratories, Redmond, WA) and a third-generation enzyme immunoassay (EIA) (VITROS Anti HIV 1+2 assay (VITROS);Ortho-Clinical Diagnostics, Rochester, NY) in parallel; concurrent positive results are considered confirmed HIV infection. The Aptima HIV-1 RNA qualitative assay (RNA Qual) (Aptima; Hologic-Gen-Probe, Inc., San Diego, CA) is used as the confirmatory test in cases of discrepancies between the two initial screens. Upon acquisition of the Abbott ARCHITECT platform, all specimens received were also tested by the ARCHITECT HIV Ag/Ab Combo assay (ARCHITECT) (Architect; Abbott Diagnostics, Abbott Park, IL), in addition to the clinical diagnostic algorithm. Parallel testing by MS and the VITROS reduced the time to result thus supporting the needs of the labor and delivery populations at TCH. Although multiple studies have evaluated the performance of alternative WB independent diagnostic strategies, and the newly recommended CDC/APHL algorithm for the rapid diagnosis of HIV infections in adults in high risk populations [11,19–24], none of these studies have focused on either pediatric or obstetric patients, two relatively low risk populations in which varying degrees of differences in immune response have been reported compared to the average adult population [25–31]. Additionally, only a limited number of studies have evaluated the performance of the individual components of this algorithm in these low risk patient populations [32].

2. Objectives

The objectives of this analysis were: to determine the clinical utility of the modified TCH HIV diagnostic algorithm in diagnosing HIV infection in the pediatric and obstetric patient populations, and to evaluate the diagnostic performance of the individual components of the algorithm in the same pediatric and obstetric populations. The sensitivity, specificity and positive and negative predictive value of each individual assay was determined.

3. Study design

All pediatric patients (>18 months to <18 years) and all women seen at TCH for obstetric care who were tested for HIV infection using the HIV diagnostic algorithm were included in this study. Demographic information including the age, gender and the HIV infection status of each patient was obtained from the electronic medical records. The Institutional Review Board at Baylor College of Medicine approved this study.

From March 2012 to December 2013, a total of 6242 clinical samples consisting of whole blood or serum specimens were submitted for standard HIV diagnostic testing to the TCH laboratories. Additionally, from May 2013 to October 2013, pending sufficient quantity and quality, 913 specimens were also tested in parallel using the ARCHITECT. The diagnostic algorithm used at TCH is depicted in Fig. 1. All specimens were tested in parallel by MS and VITROS. Patients with negative results by both MS and VITROS were reported as negative for antibodies to HIV-1 and HIV-2. When both the screening tests were positive, the patient was reported positive for HIV-1 or HIV-2 infection followed by testing with the HIV-1 viral load assay (COBAS-AmpliPrep/COBAS TaqMan HIV-1 test version 2.0; Roche Molecular Laboratories, Branchburg, NJ) or a HIV-2 WB performed at an external, CAP-accredited referral laboratory [ARUP Laboratories, Salt lake City, UT] respectively. Specimens with discordant results were subjected to the RNA Qual assay. If the specimen tested positive by the RNA Qual assay, it was considered confirmatory evidence of HIV-1 infection and viral load testing was performed. Those that were discrepant by the screening tests and were neither confirmed as positive nor negative with the confirmatory tests were considered indeterminate.

All commercial assays were performed and interpreted using the assay protocols described in the package inserts [33–36]. MS