Background

- Accurate estimates of HIV incidence are critical for surveillance and prevention efforts in high-risk populations.1
- In order to have an accurate measurement of HIV incidence in a target population, assays must produce a False Recent Ratio (FRR) < 20%. 2
- Currently, the United States Centers for Disease Control (CDC) test for HIV in populations across the world using the Limiting Antigenic Avidity Assay (LAg Avidity) in conjunction with quantitative viral load. 4
- However, the LAg Avidity assay can be affected by individual and population-level factors like differences in HIV subtype and delayed antibody maturation that can alter the assay performance. 5,6
- Limited information exists on the performance of cross-sectional incidence assays on samples from Central Africa which contain the broadest subtype diversity and the highest rates of recombination. 7
- This study evaluated the misclassification rate of a population of HIV-infected individuals located in Cameroon using the LAg Avidity assay and viral loads.

Methods

- Plasma samples were obtained from participants from the Medical Diagnostic Center (MDC) cohort in the capital Yaounde located in Cameroon. Samples were known to be HIV-infected for more than one year and were taken prior to antiretroviral therapy initiation.
- All the samples were tested by the LAg Avidity assay (Sedia Biosciences Corporation, Portland, OR) and the Johns Hopkins modified (JHU) BioRad Avidity assay (Bio-Rad Laboratories, Redmond, WA).
- The proportion of samples infected greater than one year being misclassified as recent were examined using predetermined cut off values, specifically LAg Avidity assay (<1.5 ODn) or viral loads (VL) >1000 HIV RNA copies/ml.
- Misclassified samples were also examined with a JHU Avidity assay (Bio-Rad Laboratories, Redmond, WA).
- Evaluation of results included:
  - Misclassification of chronic infections as ‘recent’ was examined at the sample-level and subject-level. These analyses were first conducted among individuals who were known to be infected for at least 1 year (T=1). A separate analysis was conducted for individuals who were known to be infected for at least 2 years (T=2).
  - For subject-level analyses, if an individual contributed discordant results (one sample was false-recent whereas the second sample was not false-recent), then that individual contributed a count of 0.5.
  - An overall subject-level false recent ratio (FRR) and 95% confidence interval (CI) was calculated using a binomial exact test.
- Statistical Analyses were performed using Stata 14 and the “incatools” package in R.8

Results

- We like thank the MDC cohort staff and study participants and all other laboratory staff for their assistance. This work was supported by the National Institute of Allergy and Infectious Diseases.

Study Population

- A total of 375 subjects from 133 individuals were tested by LAg Avidity assay with 91 individuals providing one time point and 42 individuals providing two time points. Most of the individuals were female 78.9% and the median age of individuals was 34 years. Among individuals with known subtype, the predominant subtype was of recombinant form CRF02_AG at 60.3% (36/60).

Main Findings

- Overall, the FRR for the LAg Avidity (>1.5 OD-n) + VL (>1000 HIV RNA copies/ml) algorithm was 5.3% (2.1%-10.5%) for individuals known to be infected ≥1 year and 3.9% (0.8%-11.0%) for individuals known to be infected ≥2 years.
- All of the 8 samples that were misclassified by the primary LAg Avidity + VL algorithm had a JHU BioRad Avidity Index above 0.40. Therefore, the FRR algorithm was reduced to 0% for individuals known to be infected at least 1 or 2 years.

Summary and Conclusions

- The LAg Avidity assay (>1.5 OD and viral load testing (>1000 HIV RNA copies/ml) algorithm yielded a FRR >2% in this sample population, suggesting this algorithm may not be sufficient for incidence estimation in this setting.
- The performance of LAg avidity assays and viral loads for HIV incidence estimation in Cameroon and other central African countries with diverse subtypes should continue to be further investigated.

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References