Human Immunodeficiency Virus (HIV) diagnostic limbo: a retrospective review of discordant HIV test results in a large, academic healthcare system over a 10-year period to guide clinicians in distinguishing false positive versus acute HIV infection

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RESULTS: Acute HIV vs. False Positive

Table 1: Univariate analysis of factors in discordant patients (N=488)

<table>
<thead>
<tr>
<th>Category</th>
<th>False Positive</th>
<th>Acute HIV</th>
<th>p-value</th>
<th>Unresolved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>322 (78.9%)</td>
<td>86 (21.1%)</td>
<td>408 (83.6%)</td>
<td>80 (16.4%)</td>
<td>488</td>
</tr>
</tbody>
</table>

Setting

- Hospital: 135 (64.9%), 73 (35.1%), 208 (81.1%) <0.001< 48 (18.8%) 256
- Clinic: 187 (93.5%), 13 (6.5%), 200 (66.2%) 32 (13.5%) 232

Sex

- Male: 125 (66.1%), 64 (33.9%), 189 (82.9%) <0.001< 39 (17.1%) 228
- Female: 197 (96%), 23 (10%), 219 (64.3%) 41 (15.5%) 260

Age

- 18-24: 51 (70.6%), 17 (25.0%), 68 (82.9%) <0.001< 14 (17.1%) 82
- 25-34: 34 (72.5%), 12 (27.5%), 103 (81.0%) 24 (19.0%) 126
- 35-44: 66 (78.6%), 18 (21.4%), 84 (84.0%) 16 (16.0%) 100
- 45-54: 58 (78.4%), 16 (21.6%), 74 (88.1%) 10 (11.9%) 84
- 55-64: 49 (97.9%), 7 (2.1%), 56 (81.3%) 13 (18.8%) 69
- 65+: 24 (100%), 0 (0%), 24 (88.9%) 3 (11.1%) 27

Race

- Asian: 1 (100%), 0 (0%), 19 (90.5%) <0.001< 2 (5.5%) 21
- Black: 102 (70.3%), 43 (29.7%), 145 (81.0%) 34 (19.0%) 179
- White: 105 (96.0%), 5 (4.0%), 110 (90.2%) 11 (9.8%) 126
- Hispanic: 176 (81.9%), 39 (18.1%), 215 (88.1%) 29 (11.9%) 244
- Native American: 2 (100%), 0 (0%), 2 (100%) 0 2

Comorbidities

- Pregnancy: 33 (91.7%), 3 (8.3%), 36 (83.3%) 0.494 <7.663< 43
- SLE: 2 (100%), 0 (0%), 2 (100%) 0 2
- RA: 4 (80%), 1 (20%), 5 (100%) 0 5
- RPR 1:4: 5 (23.8%), 16 (76.2%), 21 (92.3%) <0.001< 2 (7.7%) 23
- HIV: 1 (100%), 0 (0%), 1 (100%) 0 1

RESULTS: Time to Resolution

Table 2: Median time to testing associated with acute HIV vs. false positive

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Setting</td>
<td>6.35 (3.21-12.57)</td>
</tr>
<tr>
<td>Age &lt;= 55</td>
<td>4.54 (1.75-11.78)</td>
</tr>
<tr>
<td>Black race</td>
<td>2.38 (1.33-4.26)</td>
</tr>
<tr>
<td>RPR 1:4</td>
<td>10.4 (4.9-22.9)</td>
</tr>
<tr>
<td>Male sex</td>
<td>3.46 (1.9-6.29)</td>
</tr>
</tbody>
</table>

- Of 7,077 positive 4th generation HIV-2 ELISA tests, 488 (13%) unique discordant cases were identified with a prior positive NAT were identified.
- Hospital setting, age <= 55, black race, RPR 1:4, and male sex were identified as significantly associated with increased rates of acute HIV and included in our multivariable model, shown in table 2.

METHODS

- From 2014 to 2018, positive 4th generation HIV-1/2 ELISA tests were retrospectively analyzed across centers in the Harris Health system in Houston, Texas.
- Discordant was defined as having a positive 4th generation HIV-1/2 immunocass with negative or indeterminate 4th generation HIV-1/2 antibody confirmation testing.
- Time to resolution (TR) was defined as the time in days between the results from the antibody confirmation test and the NAT.
- Results were analyzed (Fisher’s exact test or Chi square plus logistic regression) by year, setting (clinic/hospital), sex, age, race and comorbid conditions (pregnancy, rheumatoid arthritis, lupus, hepatitis B and syphilis [rapid plasma reagin, or RPR1:4]) for associations with acute HIV versus false positivity.
- Differences in TR for the above variables were analyzed using a log-rank test.

DISCUSSION

- Several clinical factors correlated with a higher rate of acute HIV, likely reflecting the impact of disease prevalence on the positive predictive value of any diagnostic test.
- Clinicians may consider these factors when counseling their patients during the limbo period.

LIMITATIONS AND FUTURE DIRECTIONS

- Signs and symptoms associated with acute HIV were not examined.
- Negative ELISA tests were not included; specificity and positive predictive value cannot be determined.
- Future studies are planned to identify factors associated with unresolved cases or delayed NAT, with the goal of improving TTR across Harris Health centers.

REFERENCES