Performance of point-of-care birth HIV testing in primary health care clinics: an observational cohort study

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Background

- Laboratory capacity for early infant diagnosis of HIV has expanded, but health systems struggle with long test turnaround times associated with centralized testing.
- Only 51% of infants born to women living with HIV received a virological test within the first two months of life (2015).
- High rates of loss to follow-up before initiation of ART remains a public health problem and contributes to HIV-related infant mortality.
- WHO recently prequalified two point-of-care technologies for early infant diagnosis.
WHO recommends adding NAT at Birth to the EID strategy

Box 1 Adding NAT at birth to the existing EID strategy

As EID programmes are further scaled up, every effort should be made to improve uptake of NAT at 4–6 weeks, strengthen retention along the testing-to-treatment cascade, ensure confirmation of NAT positive results with a second sample and ensure that infants who test negative by NAT are retained in care until a final diagnosis is made.

To add NAT at birth, effective linkage to maternal HIV screening at the time of delivery should be ensured and the following steps taken:

- collection of data on performance and feasibility of birth testing during implementation;
- improvement of uptake and retention in the testing-to-treatment cascade;
- active tracking of infants with negative NAT at birth to ensure that they return at six weeks for retesting and cotrimoxazole initiation, and
- retesting of infants who test positive at birth with collection of a second specimen as soon as possible. ART should be started immediately after the first positive test and can be stopped if the second specimen tests negative.

Objectives

**General objective:**
The overall aim of this study was to evaluate the performance and benefit of POC EID testing of HIV-exposed newborns at birth in maternities.

**Specific objectives:**
- Specific Objective 1: Determine the sensitivity, specificity and predictive values of POC EID at birth compared with laboratory-based EID testing at birth.
- Specific Objective 2: Determine the proportion of HIV infected infants diagnosed by testing at birth and four to six weeks compared by testing only at four to six weeks.
Methods-General

- Study Design: prospective observation study
- Study sites were 7 maternity wards and respective PMTC clinics.
- Conventional: Roche CAP/CTM 96 HIV-1 Qualitative Test v2 (Roche Molecular Diagnostics, Branchburg NJ, USA).
- POC: Alere q HIV-1/2 Detect system (Alere Inc, Waltham, Massachusetts, USA)
- Both POC and SOC EID were performed by nurses at maternity wards using whole blood collected from infants < 24 hours of age.
- A total of 2,350 infants were enrolled in the study from November 2014 to July 2016.
Methods - Study Design

Maternity Wards: <24 h

Follow-up

Child At Risk Consultation: >4-6 weeks

- Infomed Consent/Inclusion
- Demographic data collection
- Sample collection and testing on POC

Active tracing and reminders

- Demographic Table
- Sample collection and testing on PÔC
Methods- Eligibility Criteria

• Inclusion Criteria:
  • HIV-exposed infants born of HIV-positive pregnant women over 18 years of age, regardless of their PMTCT history.
  • Less than 24 hours of age.
  • Whose mothers or guardians provide informed consent.

• Exclusion Criteria:
  • Older than 24 hours of age when being tested at birth.
  • Serious medical conditions, like hemophilia, idiopathic thrombocytopenic purpura and hemolytic disease of the newborn which would make testing harmful for the infant, or disrupt the accuracy of normal laboratory analysis and its interpretation.
  • Mothers given a delivery by Cesarean or with any delivery complications.
Results (1)-Flow Diagram at birth

Figure 1. Flow diagram of study participants at birth.

POC results invalid correspond to reported testing errors.
No laboratory EID result correspond to dried blood spot specimens that were rejected from testing or results not reported.
Results (2) - Patient characteristics

### Birth laboratory Test

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Total</td>
<td>2350</td>
<td>100.0%</td>
<td>2051</td>
<td>87.3%</td>
<td>37</td>
<td>1.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1185</td>
<td>50.4%</td>
<td>1024</td>
<td>86.4%</td>
<td>24</td>
<td>2.0%</td>
</tr>
<tr>
<td>Male</td>
<td>1141</td>
<td>48.6%</td>
<td>1005</td>
<td>88.1%</td>
<td>12</td>
<td>1.1%</td>
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<tr>
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<td>24</td>
<td>1.0%</td>
<td>22</td>
<td>91.7%</td>
<td>1</td>
<td>4.2%</td>
</tr>
<tr>
<td>Mother regimen</td>
<td>None</td>
<td>13</td>
<td>0.6%</td>
<td>10</td>
<td>76.9%</td>
<td>2</td>
</tr>
<tr>
<td>Option A</td>
<td>11</td>
<td>0.5%</td>
<td>10</td>
<td>90.9%</td>
<td>1</td>
<td>9.1%</td>
</tr>
<tr>
<td>ART</td>
<td>1981</td>
<td>84.3%</td>
<td>1733</td>
<td>87.5%</td>
<td>29</td>
<td>1.5%</td>
</tr>
<tr>
<td>Data not available</td>
<td>345</td>
<td>14.7%</td>
<td>298</td>
<td>86.4%</td>
<td>5</td>
<td>1.4%</td>
</tr>
<tr>
<td>Infants breast feeding</td>
<td>No</td>
<td>41</td>
<td>1.7%</td>
<td>26</td>
<td>63.4%</td>
<td>2</td>
</tr>
<tr>
<td>Yes</td>
<td>1174</td>
<td>50.0%</td>
<td>974</td>
<td>83.0%</td>
<td>41</td>
<td>3.5%</td>
</tr>
<tr>
<td>Data not available</td>
<td>1135</td>
<td>48.3%</td>
<td>501</td>
<td>44.1%</td>
<td>16</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

Option A=WHO recommended prophylaxis which includes: ante-partum AZT starting as early as 14 weeks gestation; intra-partum single-dose NVP and first dose of AZT/3TC at onset of labour; post-partum daily AZT/3TC for 7 days. NVP=Nevirapine. AZT=Zidovudine. ART=antiretroviral therapy. Invalid=Results not available or DBS sample rejected due to poor quality
### Resultados (3)- Performance of Alere a at Birth

**Table 1**: Results of at birth point-of-care testing with the Alere q HIV-1/2 Detect system vs reference birth laboratory testing using the Roche CAP/CTM Qualitative HIV-1 assay.

<table>
<thead>
<tr>
<th>Laboratory Early Infant Diagnosis</th>
<th>Point-of-Care Early Infant Diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>33</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>Invalid</td>
<td>Invalid</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>Total</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

**Sensitivity (95% CI)**: 100% (89.4-100)
**Specificity (95% CI)**: 100% (99.8-100)
**Positive Predictive Value (95% CI)**: 100% (89.4-100)
**Negative Predictive Value (95% CI)**: 100% (99.8-100)

**Table 2**: Performance of Alere q at birth
Results (4)- Flow Diagram at birth vs routine EID test at 4-6 weeks

Around 50% were already positive at Birth (29/61)

Increase of 16.4% of patient yield if birth testing is added (71 vs 61)

Figure 2. Flow diagram of study participants at birth and at routine EID testing time point

Lost to follow up = patients tested at birth but who did not attend routine early infant diagnosis time point.
POC = point-of-care test. EID = early infant diagnosis. Lab = laboratory test.
Results (5) - Patients with discordant test results between birth and after four weeks.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mother Prophylaxis</th>
<th>Infant Prophylaxis</th>
<th>Infant Breastfeeding</th>
<th>POC</th>
<th>Lab</th>
<th>Age (Days)</th>
<th>POC</th>
<th>Lab</th>
<th>Age (Days)</th>
<th>POC</th>
<th>Lab</th>
<th>Age (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>ART NVP</td>
<td>Yes</td>
<td>Pos</td>
<td>Pos</td>
<td>1</td>
<td>Neg</td>
<td>DBS</td>
<td>Rejected</td>
<td>31</td>
<td>Pos</td>
<td>Pos</td>
<td>142</td>
</tr>
<tr>
<td>Patient 2</td>
<td>ART NVP</td>
<td>No</td>
<td>Pos</td>
<td>Pos</td>
<td>1</td>
<td>Not Processed</td>
<td>Neg</td>
<td>51</td>
<td>Pos</td>
<td>Pos</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>Patient 3</td>
<td>ART NVP</td>
<td>Yes</td>
<td>Pos</td>
<td>Inv</td>
<td>1</td>
<td>Neg</td>
<td>DBS</td>
<td>Rejected</td>
<td>32</td>
<td>Not Processed</td>
<td>Neg</td>
<td>127</td>
</tr>
<tr>
<td>Patient 4</td>
<td>None NVP</td>
<td>Yes</td>
<td>Pos</td>
<td>Inv</td>
<td>1</td>
<td>Neg</td>
<td>DBS</td>
<td>Rejected</td>
<td>29</td>
<td>Neg</td>
<td>Neg</td>
<td>63</td>
</tr>
</tbody>
</table>

POC=Point-of-Care test. LAB=laboratory test ART=antiretroviral therapy. NVP=Nevirapine. Pos=Positive. Neg=Negative. Inv=Invalid.
Conclusions

- In conclusion, we have demonstrated that POC HIV EID at birth is feasible and accurate when conducted by nurses in primary health care clinics in low-resource settings, and may be an important tool to expand access to birth testing.

- We also highlighted that birth testing in combination with routine 4-6 weeks screening may increase access to EID.

- However, implementing POC EID at birth will need confirmatory testing of positives and supportive health systems to ensure reliable testing and retention of infants after birth.

- Nevertheless, POC testing may improve opportunities for newborns to access ART especially in decentralised and task-shifted low-resource settings.
Acknowledgments

- Study participants and their families
- Staff at all study sites and laboratories

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  - UNITAID
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