Point-of-Care CD4 Testing in Low & Middle Income Countries: Current and Future perspectives

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Introduction

- HIV epidemics
- HIV diagnosis & HIV continuum of care
  - Availability
  - Cost
  - Accessibility
- HIV point-of-care (POC) Tests
  - HIV antibody
  - Early Infant Diagnosis (EID)
  - CD4
  - Viral load

Why CD4 Point-of-care Test

- Treatment eligibility assessment
- Treatment monitoring
- Patient benefit
  - Increased accessibility
  - Same day result
  - One stop services of testing, counseling and initiation of therapy => Reduce loss-to-follow up
- Service provider benefit:
  - Decentralizing HIV related testing to clinic level =>
  - No need for specialized laboratories and highly skilled laboratory staff

Research question

- Implementation of POC CD4 tests in resource-constrained settings (LMICs)?
  - In-field diagnostic performance
  - Acceptability
  - Feasibility
  - Impact on continuum of care

Systematic review

- In-field studies/evaluation of POC CD4 technologies in LMICs (Jan 2005 – Jan 2015)
Result – Study characteristics

- Three out of six reportedly available POC CD4 tests have published data from field studies in LMICs: Pima™ CD4, PoinCare NOW™, MyT4™ CD4
- Pima: ~ 90% (24/27) of included studies
- Test operators: non-lab technician
- Quality of studies: “moderate” to “strong”

Result – Acceptability & Feasibility

- No studies have assessment of acceptability/feasibility in field settings as primary objective
- High acceptance: 90-100%
- Service provider perspectives:
  - “Efficient in resources used” “user friendly” “easy to use by non-lab person” “responded well to patient need” (Galiwango, R.M., et al., 2014; van Rooyen, H., et al., 2013; Manabe, Y. C., et al., 2012; Thakar, M., et al., 2012)
- Patient perspectives:
  - Having POC CD4 test on site “We now receive our result there and then” (Mtapuri-Zinyowera, S., et al., 2013)

Result – Impact on continuum of care

- Increased access to CD4 testing (ART eligibility assessment)
  - Clinical setting: 90% vs 67% RR: 2.4, p<0.001
  - Home based care & treatment: 96% vs 52%
- Reduced loss to follow-up by 50%
  - HIV confirmation and ART eligibility assessment
  - No/little effect between ART eligibility assessment and ART initiation

Result – Diagnostic performance

- Across studies...
  - Strong performance: sensitivity: 80-100%; specificity: 79-99% (CD4 threshold of 350 cells/µl)
  - Differences in test performance: Venous vs Capillary blood
  - Failure rate: 5% - 23%

Result – Meta analysis

- Pima™ CD4: 11 studies (2 studies report both capillary & venous sample results)
- Multi-level bivariate random-effect modeling
- Covariate for blood sample type (venous/capillary)
- Adjusted standard error for multiple sets of diagnostic data taken from single studies
- Diagnostic statistics & sensitivity analysis on effect of outlier bias

Meta analysis
Capillary vs. Venous...

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>No of point estimates</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled estimate (Meta-analysis)</td>
<td>13</td>
<td>0.92 (0.89-0.94)</td>
<td>0.87 (0.83-0.88)</td>
</tr>
<tr>
<td>Capillary</td>
<td>6</td>
<td>0.89 (0.83-0.93)</td>
<td>0.87 (0.82-0.89)</td>
</tr>
<tr>
<td>Venous</td>
<td>7</td>
<td>0.84 (0.79-0.89)</td>
<td>0.86 (0.82-0.89)</td>
</tr>
</tbody>
</table>

Wald χ² (3) = 4.77, p = 0.09

Key findings

- Acceptable diagnostic accuracy
- Increased accessibility & improved retention
- High acceptance
- Feasible in primary health & community settings

Issues & Questions

- Data scarcity...
- Differences in performance by blood types?
- Failure rate: technology failure vs. test operator error? Venous vs. capillary?
- Influencing factors?
  - Training for test operators & supervisors: Impact of blood sampling on test performance
  - External Quality Assurance
  - Staff workload/incentive
  - POC test throughput vs. patient volume
  - Service delivery organization: POC testing at ART-initiation site
Future of CD4 testing?

- Early initiation of ART: New evidences from START & TEMPRANO
- WHO guidelines on ART: ART initiation independence of CD4 count?
- Health system capacity
- Feasibility and sustainability of ART programs
- Financial & resource constraints in LMICs
- “90-90-90” Goal: priority given to PIUHA CD4 less than 350 cells/µl

References

- Mtapuri- Zinyowera, S., et al., PIMA Point of Care CD4+ Cell Count Machines in Remote MNCH Settings: Lessons learned from Seven Districts in Zimbabwe’s 3000 (3K) Project, 2013. 16(6): p. 31-66
- van Rooyen, H., et al., High HIV testing uptake and linkage to care in a novel program of home-based HIV counseling and testing with traditional leaders in KwaZulu-Natal, South Africa. AIDS Access (Auckl), 2013. 04(01): p. 45-49

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