Evaluation of Maternal and Infant HIV Point-of-Care Diagnostics at Birth in Tanzania

Abstract Presentation Number 788

Issa Sabi[1], Hellen Mahiga[1], Jimson Mgaya[1], Otto Geisenberger[2,3], John France[4], Michael Hoelscher[2,3], Arne Kroidl[2,3]

[1]NIMR-Mbeya Medical Research Centre (MMRC), Mbeya, Tanzania; [2]Department of Infectious Diseases and Tropical Medicine, Medical Center of the University of Munich (LMU), Germany; [3]German Center for Infection Research (DZIF), partner site Munich, Germany; [4]Division of Gynaecology and Obstetrics, Mbeya Referral Hospital, Mbeya, Tanzania

Background

HIV Early Infant Diagnostic (EID) in HIV-exposed infants is routinely performed at week 4-6 after delivery by qualitative HIV-DNA analysis from Dry Blood Spots (DBS). However, this procedure faces several challenges:

- Requirement of specialized laboratory infrastructure and trained personnel
- Complicated linkage procedures including (i) DBS-samples are send to the lab; (ii) turn-round time of sample processing; (iii) results are send back to the clinics; (iv) results need to be disseminated to the mothers; (v) HIV-infected infants will then be referred to HIV-clinics for ART initiation

Based on these procedures timely and life-saving infant ART is delayed, and by 2015 only 42% of infants received HIV EID and 56% of children living with HIV were accessing ART in Tanzania.

Novel Point-of-Care (PoC) technologies provide the opportunity to have qualitative or quantitative HIV nuclear acid testing (NAT) performed by non-laboratory personnel at the health centres and receive test results within 1 hour. PoC-EID testing affiliated with immediate initiation of very early infant ART initiation has the potential to:

- Reduce infant mortality & morbidity
- Preserve immune functions
- Reduce viral reservoirs
- Lead to sustained viral remission or even cure

PoC maternal viral load screening has the potential to:

- Immediately identify high-risk for mother-to-child transmission and initiated enhanced antiretroviral infant prophylaxis.
- To identify HIV-infected mothers with potential virological treatment failure and subsequently switch of the ART regimen for her own health as well as to reduce the risk for mother-to-child transmission during breastfeeding.

The Baby Study addressed the lack of operational experience and data on test accuracy for the implementation of HIV PoC testing as a requirement for neonatal test & treat procedures.

Methods

The Baby Study was a prospective diagnostic cohort study with the **objectives** to: :

1. Investigate the operational specificity, sensitivity and predictive values of the **qualitative Cepheid Xpert HIV-1 Qual PoC test** to identify vertical HIV newborn transmission at different time points
2. Evaluate the **quantitative Cepheid Xpert HIV-1 Quant** test for viral load monitoring in HIV-infected mothers at delivery
3. Assess vertical transmission rates and risk factors associated with mother-to-child transmission

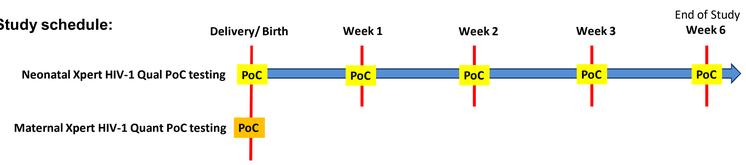
HIV-1 PoC test:

- Infant **Xpert HIV-1 Qual PoC** test from whole blood at obstetric clinics performed by nurses/midwives (turn-around time ~90 minutes)
- Maternal **Xpert HIV-1 Quant PoC** from plasma performed at centralized laboratory

Confirmatory HIV diagnostics: - DBS HIV-DNA (Roche COBAS TaqMan)
- Plasma HIV-RNA viral load (Roche COBAS TaqMan) in mothers at delivery and PoC positive infants

Study population: 600 HIV-infected mothers & exposed neonates from Mbeya, Tanzania

Study schedule:



Results

Table 1: Demographic, obstetric and HIV characteristics of mothers giving birth to 614 infants (included 8 twin pairs)

Variable	N=614
Age, median (range)	29 (18-44)
Mode of delivery	
– Vaginal, at hospital	498 (81.1%)
– Vaginal, at home	25 (4.1%)
– Caesarean section	89 (14.5%)
Not on ART at delivery	51 (8.3%)
CD4 count categories	
– <200 cells/µL	97 (15.8%)
– 200 to 350 cells/µL	156 (25.4%)
– >350 cells/µL	353 (57.5%)
Plasma HIV-RNA* >1000 copies/mL	133 (21.7%)
Plasma HIV-RNA* >1000 copies/mL in women on ART (N=561)	89 (15.9%)

** Measure by Roche TaqMan*

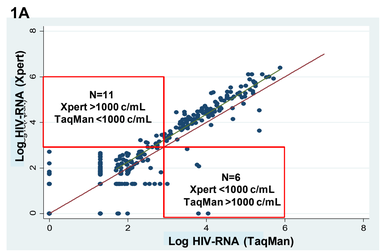
Table 2: Vertical HIV transmission in HIV exposed neonates until 6 weeks post-partum

Neonatal HIV Status	N=614
Not HIV-infected neonates	597 (97.2%)
HIV-infected neonates	15 (2.5%)
– At birth	11 (73%)
– Week 1 post-partum	1 (7%)
– Week 2 post-partum	1 (7%)
– Week 3 post-partum	2 (13%)
– Week 6 post-partum	0
No valid HIV result at birth & early termination	2 (0.3)

→ The majority on HIV infected neonates had evidence for intra-uterine HIV transmission

Figure 1: Maternal HIV-RNA at delivery. Comparison of plasma HIV-RNA (Roche TaqMan) versus PoC plasma HIV-RNA (Cepheid HIV-1 Xpert Quant) in matched pairs from N=574 HIV-infected mothers. **Figure 1A** shows the correlation between the TaqMan and Xpert Quant HIV-RNA. In the red boxes clinical relevant discrepancies between both test are indicated based on the decision to switch ART regimen (WHO-definition of virological failure >1000 c/mL). **Figure 1B** demonstrates results by Bland Altman Analysis (only quantifiable HIV-RNA results included). Overall, a good agreement between quantitative tests were seen, the HIV-1 Xpert Quant provided general slightly higher HIV-RNA results than the TaqMan (mean difference 0.3 log, 95% higher limit 1.2 log and lower limit -0.5 log).

1A



1B

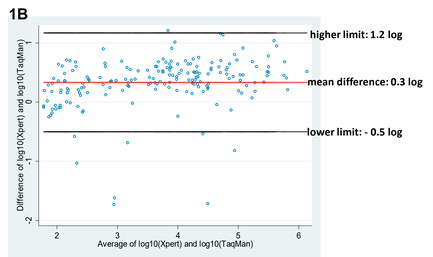


Table 3: Maternal risk-factors associated with vertical HIV transmission (n=infected infants/N=mothers with factor)

Maternal risk factor	n/N (%)	RR (95% CI)	p-value
Not on ART at delivery	4/51 (7.8%)	4.0 (1.3-12.1)	**0.014**
VL >1000 copies/mL	14/133 (10.5%)	50.4 (6.7-380.1)	**<0.001**
On ART at delivery but VL >1000 copies/mL	10/89 (11.2%)	53.7 (7.0-414.0)	**<0.001**
CD4 count <200 cells/µL	9/97 (9.3%)	7.8 (2.8-21.5)	**<0.001**

Non-adjusted Poisson regression, RR=risk factor

Outcome neonatal HIV PoC testing

All Xpert Qual PoC results:

- correctly identified neonatal HIV infection (**no false negative test result**)
  - → Confirmed by positive DBS qualitative HIV-DNA and/or plasma VL at the time of test positivity
- correctly identified HIV negativity (**no false positive test result**)
  - → Confirmed by negative DBS qualitative HIV-DNA at Week 6

Table 4: Infant HIV-PoC testing at birth by infants born

HIV-PoC testing at birth	N=614
Time between birth and testing, median (range)	16 hours (0.5-58)
Test performed:	
<12 hours after birth	233 (39.3%)
12 to 24 hours after birth	222 (37.4%)
24 to 48 hours after birth	129 (21.8%)
>48 hours after birth	9 (1.5%)

Table 5: Infant HIV-PoC test performance by study visits

HIV-PoC test performance	N=2736
Valid test result	2673 (97.7%)
Time between sample collection and result communication to the mother of valid test results, median (range)	110 minutes (94 minutes – 7 days)
No valid test result or error message	63 (2.3%)
PoC test problem reported by nurse	183 (6.7%)
Due to power cut	106 (57.9%)
Error/invalid result	61 (33.3%)
Problem with computer or analyser	4 (2.2%)
Clotted blood	2 (1.1%)
No reason indicated	10 (5.5%)
Repeated PoC testing	132 (4.8%)
PoC testing performed at other site (sample transferred)	210 (7.7%)

Conclusions 1

1. Most vertical HIV transmissions occur intra-uterine as indicated by neonatal HIV diagnosis at birth. Neonatal HIV-1 PoC screening at birth should in general be recommended in high PMTCT coverage areas.
2. The Cepheid HIV-1 Xpert Qual PoC test demonstrated a 100% sensitivity & specificity to detect neonatal HIV infection.
3. HIV-PoC testing was very well perceived by nurses and midwives in terms of operational feasibility and handling. However, HIV-PoC test related problems were reported in 6.7% of visits mainly due to early analysis interruption because of power cuts. This resulted into repeated testing in 4.8%, sample transfers to other obstetric sites for analysis in 7.7% and invalid test results in 2.3%.
4. HIV-PoC testing provided rapid test results communication to mothers in median less then 2 hours which enables potential immediate infant ART initiation in HIV-PoC positive infants.

Conclusions 2

1. The greatest risk for vertical transmission is high maternal viral load at delivery irrespectively of maternal ART. Virological treatment failure was seen in ~16% of mothers on ART.
2. A good test agreement was seen between maternal Xpert HIV-1 viral load and TaqMan analysis.
3. Maternal PoC HIV-RNA monitoring is suitable to detect high risk situations for mother-to-child transmission and therefore can trigger enhanced neonatal prophylactic regimens and identify mothers with potential virological treatment failure.

Funded by DZIF Deutsches Zentrum für Infektionsforschung **&** Cepheid. A better way.