High proportion of false-positive HIV results with point-of-care birth testing in Botswana

959

Authors: **Gbolahan Ajibola**[1], Nyaladzi Maphorisa[1], Aischa Niesar[2], Terence Mohammed[1], Maureen Sakoi-Mosetlhi[1], Oganne Batlang[1], Sikhulile Moyo[1,3], Molly Pretorius Holme[3], Kathleen Powis[1,3,4], Shahin Lockman[1,2,3], Joseph Makhema[1], Mathias Lichterfeld[2], Roger Shapiro[1,3]

Affiliations: Botswana Harvard Health Institute Partnership[1], Gaborone, Botswana, Brigham and Women's Hospital[2], Harvard T.H. Chan School of Public Health[3], Massachusetts General Hospital[4]

BACKGROUND

Infant outcomes can be markedly improved by starting ART from the first week of life, but this requires the ability to make prompt and accurate diagnosis of HIV in children as close to birth as possible.

Point-of-care testing (POCT) offers a low-cost alternative for HIV diagnosis at birth and can be added to current 6-week testing for highest-risk infants.

As countries in Sub-Saharan Africa move toward the rollout of POCT, the risk for false positive testing, and pathways to make accurate HIV diagnoses, need to be understood.

METHODS

- The Moso Study identified newborns at high risk of HIV acquisition at 35 delivery facilities in Botswana.
- High-risk status was defined primarily (but not exclusively) as limited maternal ART duration in pregnancy.
- HIV testing was performed using the Cepheid Xpert® HIV-1 qualitative POCT platform, with Roche CAP/CTM HIV-1 qualitative confirmation for those testing positive.
- Further testing with HIV-1 RNA quantification and droplet digital polymerase chain reaction (ddPCR) was conducted for discordant results.
- Subsequent 6-week HIV test results for infants with negative birth POCT were abstracted from national electronic laboratory/medical records.

The Xpert® POCT platform offers affordable and easily implementable birth testing for HIV, but false positive testing may occur. All positive testing must be confirmed by either HIV-1 RNA testing, HIV-1 DNA testing, or both.

RESULTS

- From July 2022–August 2023, 1479 high-risk newborns were tested for HIV with POCT at a median of 21 hours of life (range 0, 158 hours).
- Thirty-one newborns (2%) had initial positive results, but only 11 (39%) were confirmed positive by Roche CAP/CTM testing, for an overall *in utero* transmission rate of 0.7% in high-risk neonates.
- The 20 (1.4%) false positives were further evaluated by HIV-1 RNA testing (all undetectable < 40 copies/mL).
- ddPCR testing was performed on 18 (90%) false positive samples with no target detected in any sample.
- Follow-up testing of false positives to date has remained negative.
- Of the 20 initial false positive samples, 18 (90%) were tested on 1 of the 6 Xpert® machines; this machine was removed from service and is under evaluation, without an identifiable cause for the false positive results.
- Excluding all 453 samples tested on this machine yields an overall false positivity rate of 0.2% (2/1026) for the 5 other machines.
- The median cycle threshold (CT) value for false positive results on the Xpert® platform was 39.2 (range 34.5, 43.9) compared with a median of 32.9 (range 24.2, 41.0) for true positives, indicating some overlap between groups (Figure 1).

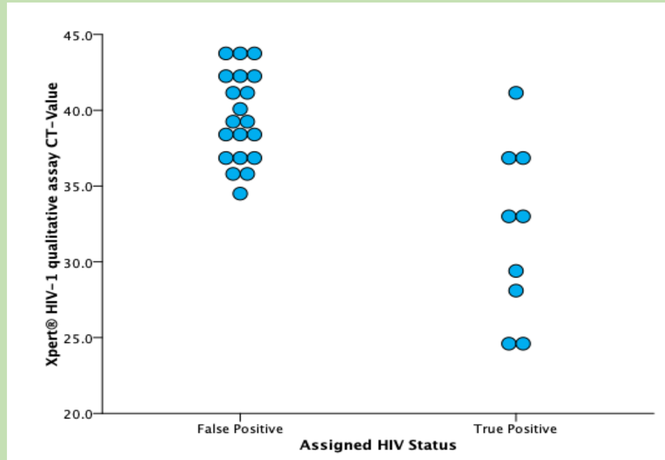

Figure 1: Cycle threshold values at birth using Cepheid Xpert® HIV-1 qualitative assay

CONCLUSIONS

The Xpert® POCT platform offers affordable and easily implementable birth testing for HIV, but false positive testing may occur. High CT values provide an initial indication of a possible false positive result, but all positive testing must be confirmed by either HIV-1 RNA testing, HIV-1 DNA testing, or both.

Acknowledgements

Support for this work was provided by the Eunice Kennedy Shriver National Institute of Child Health & Human Development, **We thank the** co-authors, the study team; Tshepho Theodorah Frank, Obonwe Pule, Otwel Elias, Seretlogelwa Moseki, Gorata Kenyaditswe, Leungo Veronica Olaotse, Tsholofelo Rebatenne, Kaone Pearl Molefi, Mercy Mupahua, Atlasaone Morongwana, Johannes Gabaitse, Tsitsi Shamiso Moyo, Modiegi Diseko, Judith Mabuta, Shally Morgan, Tumalano Sekoto, Ngozana Seonyaneng. Special thanks to the management and technical staff of Cepheid South Africa.

Author Contact Information
Gbolahan Ajibola (Botswana Harvard Health Research Institute) email; gajibola@bhp.org.bw