ASSESSMENT OF ROCHE COBAS®6800/8800 SYSTEM FOR HIV PCR INDETERMINATE RESULTS ON EARLY INFANT DIAGNOSIS

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BACKGROUND

Early infant diagnosis (EID) of HIV in South Africa is standardized to the COBAS® AmpliPrep/COBAS® TaqMan (CAP/CTM) HIV-1 Qualitative Test. Cycle threshold (Ct) <33.0 is the most accurate value for differentiating clearly positive from irreproducible cases, but HIV-and antiretroviral exposed infants may give indeterminate or negative results. HIV PCR indeterminate results are defined as Cycle threshold [Ct]>33 with any relative fluorescent intensity [RFI] value or Ct≤33 and RFI <5. Roche diagnostics introduced the cobas®6800/8800 System and the current study compared indeterminate results because of impact in retention and linkage to care.

METHODS/DESIGN

The study comprised of 642 DBS samples; (i.e. 235 HIV PCR positive, 193 HIV PCR negative and 214 HIV PCR indeterminate), previously tested with the COBAS®AmpliPrep (CAP)/COBAS®TaqMan® (CTM) HIV-1 Qualitative Test (CAP/CTM) (Roche Molecular Systems, Pleasanton, CA) platform with 97% confidence. The results were compared for both systems. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria (Approval number: 266/2018, 406/2019), and the National Health Laboratory Service

RESULTS

Overall Results:

Of the CAP/CTM HIV PCR negative samples, 99.5% (192/193) remained HIV PCR negative on the Roche cobas® 6800/8800 System, while one sample tested HIV PCR positive with a Ct value of 39 (Figure 1).

HIV PCR Indeterminate:

A total of 37.4% (80/214) CAP/CTM HIV PCR indeterminate samples tested HIV PCR positive with the Roche cobas® 6800/8800 System, with 22.5% (18/80) having a Ct value >38. The remaining 62.6% (134/214) tested HIV PCR negative with the Roche cobas® 6800/8800 System (Figure 2).

Figure 1: Comparison of the HIV PCR results outcome on the Roche cobas® 6800/8800 System compared to the CAP/CTM (N = 642)

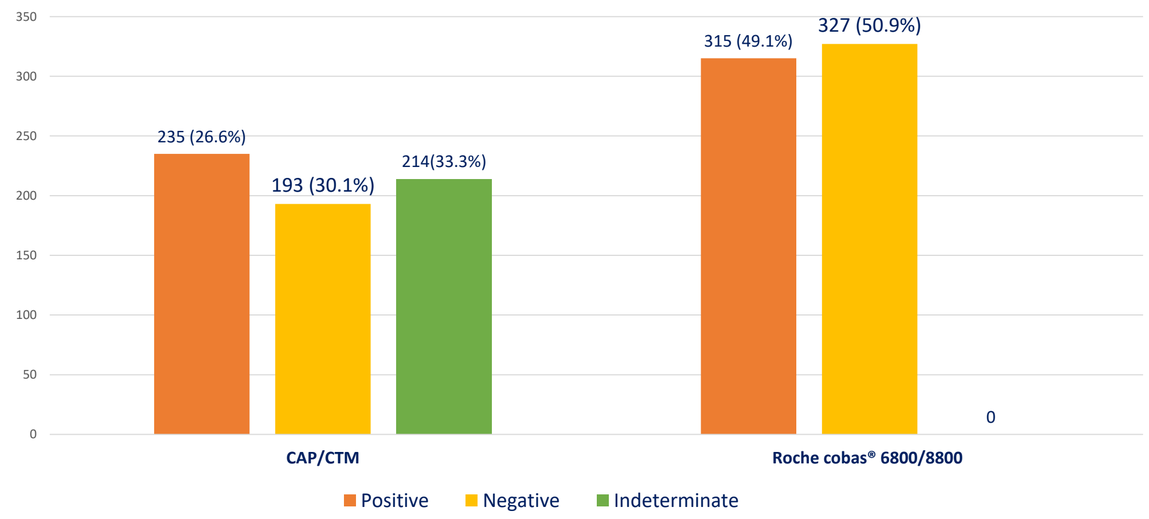

Figure 2: Overall Roche cobas® 6800/8800 System results from CAP/CTM indeterminate samples (N = 214)

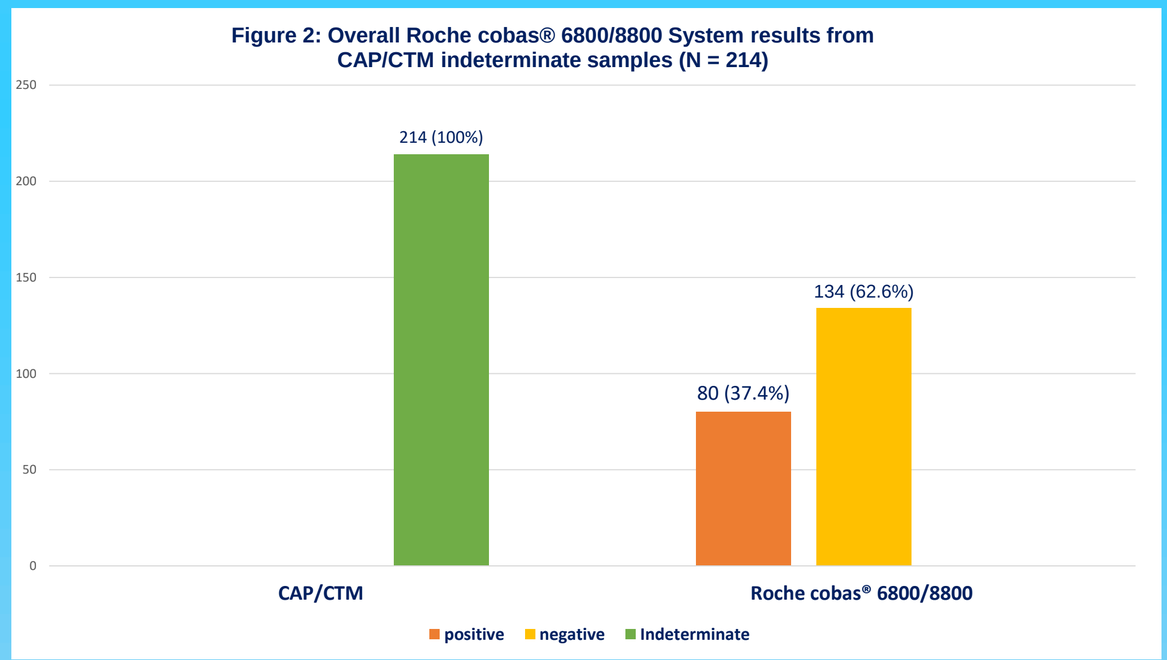

Figure 3: Comparison between the Roche cobas® 6800/8800 System and confirmation testing results (N= 30)

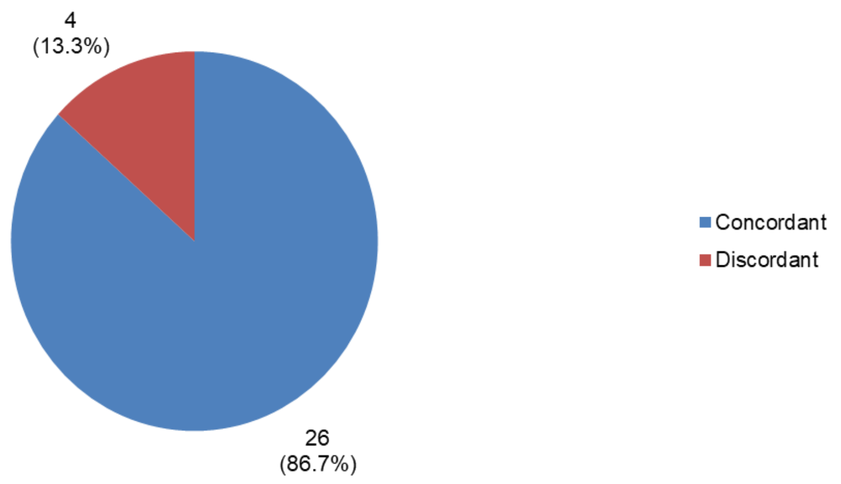

Figure 3: Only 14% (30/214) HIV PCR indeterminate samples had confirmatory CAP/CTM PCR results from the NHLS laboratory information system. Half of these samples (50.0%) were also confirmed as HIV PCR negative as Roche cobas® 6800/8800 System, while 36.7% HIV PCR positive on Roche cobas® 6800/8800 System were confirmed as such. Only 13% had discorded results.

DISCUSSION

When a sample result is HIV PCR indeterminate, a repeat HIV PCR and viral load is done according to South African SA PMTCT guidelines, 2019. The Roche cobas®6800/8800 System had a sensitivity of 90.8% and a specificity of 96.3% when HIV PCR indeterminate results were included. However, the sensitivity and specificity were much higher (99.6% and 99.5% respectively) when HIV PCR indeterminate results were excluded, thus emphasising the challenges arising from HIV PCR indeterminate results. Most importantly, the HIV PCR indeterminate results decrease the ability of an EID assay to detect true HIV PCR positive and true HIV PCR negative cases. Some infants receive an indeterminate result when only the RFI failed the criteria, thus these infants need to return for follow-up testing. This creates the possibility of loss to follow-up. The cobas®6800/8800 System relies solely on Ct values, thus has the potential to reduce HIV PCR indeterminate results and prevent loss to follow-up.

Conclusion

The performance of the cobas®6800/8800 was comparable to the CAP/CTM; with more conclusive results, and thus potentially lowering the amount of infants lost to follow-up