The performance of virological testing for early infant diagnosis of HIV: a systematic review

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Background and objectives

Scale up of more effective PMTCT interventions requires review of the existing testing algorithms to optimize infant testing in the context of wider exposure to ARVs as a result of maternal ART and infant prophylaxis. Knowledge of the performance of virological assays at different time points and in the context of ARV exposure is critical for such revision. This systematic review informed the revision of the World Health Organization (WHO) infant testing algorithm by assessing diagnostic accuracy for virological testing at birth and at 6 weeks in the context of ARV exposure.

Methods

The search strategy aimed to consider studies published from 2009 (date of the most recent WHO guidelines on infant testing) and included the following search terms: WHO-HIV-1, WHO-2, MAMING, PCR, whole blood, plasma, DBS, newborns, infants, children. PubMed, Embase, Cochrane, Clinical Trials, and LACE5 as well as conference proceedings from CROI, CIGA, AAS and the International Workshops on HIV Pediatrics were consulted. Studies were included if investigating performance of virological assays against a standard comparator, in infants exposed to ARV and exposed to maternal ART in pre-natal prophylaxis.

Two independent reviewers conducted the screening and a third reviewer was consulted to resolve discrepancies. Relevance of incoming information was sought by contacting authors. Summary estimates for performance were calculated. In order to assess the risk of bias the GRADE 2 tool was used and the overall assessment of the quality of evidence was performed using the GRADE approach.

Results

A total of 2393 records were screened with final selection of 5 manuscripts. Three studies were included to assess the accuracy of virological testing at birth and three for the context of ARV exposure. The point estimates and 95% CI were compared and specificity was 97.6% (96.8, 98.1); 98.1% (97.5, 98.3); 99.9% (99.7, 99.9) respectively. The risk of bias was judged to low and the quality of the evidence, by using the GRADE approach, was considered to be of high quality due to the generalisability and small sample sizes.

The studies were identified to assess PCR performance at birth compared to 6 weeks of age. The calculated pooled sensitivity and specificity were 98.1% (93.30, 99.80) and 100.00 (99.10, 100.00) respectively. The risk of bias in these studies was judged to be low due to the generalizability and a small sample size.

A total of 2203 records were screened with final selection of 5 manuscripts. Three studies were included to assess the accuracy of virological testing at birth and at 6 weeks in the context of ARV exposure. The point estimates and 95% CI were compared and the sensitivity and specificity were 99.4% (98.27, 100) and 99.63% (99.11, 100) respectively. The risk of bias was judged to be low due to the generalizability and a small sample size.

Conclusion

Our systematic review shows that there is currently no evidence to suggest that virological assays on DBS have poor performance when infants are exposed to ARVs. However only few subjects in the studies and the risk of bias was assessed to be low. Further research to assess accuracy of PCR at different time-points and in the context of more effective PMTCT interventions is urgently needed.

References


