RESEARCH PAPER

Challenges in the Early Diagnosis of HIV Infection in Infants: Experience from Tamil Nadu, India

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Objective: To analyze critical steps in the testing algorithm of the National Early Infant Diagnosis (EID) program in India. **Methods:** A retrospective analysis of data on cases enrolled in the EID program during 2010-2012 from Tamil Nadu was undertaken. **Results:** 2745 dried blood spots were tested; 9% of these tested positive. Median age of infants at the time of testing was 4 months. Second specimen for confirmation was received from 67% of cases with a turn-around time of 10-270 days. **Conclusions:** Even with high levels of uptake into the program, huge delays and loss-to-follow-up observed between the first and second sampling, suggests need for revision of the current testing algorithm.

Keywords: *Care, Children, Implementation, Management, Program.*

In infants who acquire HIV infection, disease progression occurs rapidly and often leads to death [1]. Current guidelines recommend prompt initiation of antiretroviral therapy in HIV-infected children aged <24 months [2], for which timely and accurate diagnosis of infection is a priority. National guidelines recommend testing of all infants exposed to HIV initially at 4-6 weeks of age, and thereafter at 6 and 12 months until final confirmation at 18 months [3,4]. However, testing children for HIV is complicated because of passively transferred maternal HIV-antibodies; molecular testing represents the gold standard for diagnosis in children <18 months [5].

Under NACP III, NACO implemented the Early Infant Diagnosis (EID) project in India in 2010. The EID cascade involves a number of events including offer and acceptance of EID testing, accurate specimen collection, transport to centralized testing laboratory, processing of specimens and relay of results. Substantial implementation barriers exist that can lead to loss-of-outcomes at each step in the cascade. A periodic review of the EID program is essential to assess its performance in the country and to identify areas that need strengthening to maximize the benefits of the program. We herein analyze critical steps in the diagnosis of infection in the EID cascade that need further strengthening.

METHODS

A retrospective data analysis was performed on all cases enrolled in the EID program in the state of Tamil Nadu during March 2010-March 2012. Written informed consent was obtained from the parent/guardian before each testing and confidentiality was maintained throughout the time period. The study was approved by the Institutional Ethical Committee.

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Specimens in the form of dried blood spots collected at the Integrated collection and testing centres (ICTCs) were received through courier at the testing laboratory at the National Institute for Research in Tuberculosis, Chennai. Samples were tested for HIV-1 DNA using the Manual Roche Amplicor HIV-1 DNAv1.5 kit. A positive or indeterminate test result was confirmed by a second test on a fresh whole blood specimen transported in cold chain. Children confirmed to be HIV-infected were traced and referred for management to the nearest ART Centre. Data collected in this process were de-identified and analyzed based on specimens collected and sent for testing, age of infants at the time of testing, number of samples tested, test results, and turn-around-time for confirmatory result.

RESULTS

A total of 2753 samples were received from 123 centers across Tamil Nadu. Eight specimens were invalid and had to be rejected. Of the 2745 specimens tested, 246 (8.96%) were positive for HIV-1. The median age at the time of sampling was 4 months. Only 13% of the positive

WHAT THIS STUDY ADDS?

- The study highlight the areas in the existing diagnostic algorithm for HIV-exposed infants that require programmatic attention and strengthening to ensure early diagnosis of infection and timely initiation of treatment.

babies were tested within 6 weeks of birth; 29% had their first test by 4 months, 52% by 6 months and 85% by 12 months.

Second specimen for confirmatory test was received for only 164 (67%) of these 246 babies. For cases where both specimens were received, the turn-around time for final confirmatory result ranged from 10-270 days (median: 46 days). The median age of babies at the time of sampling for second specimen was 7 months. Of the 164 specimens tested, 151 were positive and 8 samples turned out to be negative; 5 samples gave indeterminate results and required a re-sampling of the infants.

DISCUSSION

Timely and accurate determination of infection in exposed infants is critical and highly beneficial [6,7]. The currently available methods for diagnosis restrict testing to a few centralized laboratories. Further, the current standard of testing requires confirmation of a positive test result by a second test on whole blood sample [8], resulting in a long turn-around time and high attrition rate. We observed that a confirmed positive result could be given to only two-thirds of infants who were positive by the first test, and a long turn-around time resulted in an inappropriate delay in starting positive children on life-saving ART.

We had 5% discordance between the first and second test results. Laboratory contamination resulting from manual manipulation of sample cards was the most likely cause of false positivity in the initial test, underscoring the need for stringent quality control and confirmatory testing. Although guidelines recommend testing of exposed children at 6 weeks of age, we found that less than one-fifths of eligible infants were tested at this time. A multi-country review including 65 countries, found that only 28% of exposed children received an HIV-test within the first two months [9]. A study from South Africa reported that the early peak of pediatric HIV-related deaths occurred at three months of age [10], highlighting the importance of testing infants very early. Hence, factors responsible for the delay in getting tested need to be identified.

The major limitation of this study was that the analysis did not extend to examine the percentage of HIV-infected children who were subsequently initiated on treatment. Experience from other developing countries indicate that only about one-third of the confirmed positive infants end up receiving ART [11].

Knowing the overwhelming benefits of early ART, withholding treatment until confirmatory results are available is not appropriate. There have been suggestions to consider dried blood spot results as final, given the high level of concordance with the whole blood test results [12]. Alternatively, another blood spot from the original sample card could be tested [13]. Since laboratory contamination and technical problems have been frequently reported as causes for discordance between the initial and repeat specimens, this method could help in faster confirmation and reporting of positives, and at the same time check reporting of false positives. Realizing that occurrence of false positive results can undermine community trust in the EID program which is still in its infancy, we opine that the second option would be better suited for the current scenario.

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