Journal of HIV for Clinical and Scientific Research

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Dates: **Received:** 23 April, 2015; **Accepted:** 26 June, 2015; **Published:** 29 June, 2015

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www.peertechz.com

ISSN: 2455-3786

Keywords: EID; Algorithm; Turnaround Time; LTFU; PCR

Review Article

Adherence to Early Infant Diagnosis Testing Algorithm, a Challenge to Early Infant Diagnosis Program in Resource Limited Settings of Uganda

Abstract

Introduction: Early Infant Diagnosis (EID) targeting HIV exposed infants, happens over a period of time (6 weeks up to 18months), and employs different testing technologies at different testing time points. Being a process that is implemented over time and employing different testing technologies, a testing algorithm was designed to ensure reliable final diagnosis. This study was set out to estimate the level of adherence to the testing algorithm.

Methods: Retrospective EID data was collected from 24 health facilities that covered the entire tier of the health system, from 4 geographic regions of Uganda. From each study site, all exposed infants that were tested in 2012 were tracked from the 1st molecular test beginning at 6 weeks to the final rapid test at 18 months.

Results: From the 24 study sites, 4221 exposed infants were tested with 1st molecular test in 2012. Out of these, 3888 (92.1%) were HIV negative and 333 (7.9%) were HIV positive. Of the negative only 1543 (39.7%) did a 2nd molecular test representing a loss of 60.3%. A total of 14 babies converted to HIV with the 2nd molecular test, resulting in a total of 347 positive babies. Of the total positive babies, 212 (61.1%) initiated ART, representing a loss of 38.9%. Of the total who were screened with the 1st molecular test, 1130 (26.8%) were tested with the final rapid test at 18 months, representing a loss of 73.2%.

Discussion: The results indicate that, despite operational improvements, very poor adherence to EID testing algorithm was observed. This poor adherence may have an impact on the ultimate objectives of the whole program. Factors explaining high LTFU include; results long turnaround time (TAT), lack of patient follow-up mechanism, and poor patient counseling. There is therefore an urgent need to rethink the implementation of the EID program, not only in Uganda but also in other resource-limited countries. Mechanisms of patient follow-up and linkage to care should be integrated into the testing process.

Abreviations

EID: Early Infant Diagnosis of HIV; PMTCT: Prevention of Mother to Child Transmission of HIV; WHO: World Health Organization; UNAIDS: Joint United Nations Program on AIDS; MOH: Ministry of Health; HIV: Human Immune deficient Virus; AIDS: Acquired Immune deficiency Syndrome; HCT: HIV Counseling and Testing; ART: Anti-Retroviral Therapy; eMTCT: Elimination of Mother to Child Transmission; HC III: Health Center III; HC IV: Health Center IV; ANC: Antenatal Clinic; DBS: Dry Blood Spot; TAT: Turn Around Time; PCR: Polymerase Chain Reaction; DNA: Deoxy-ribose Nucleic Acid; CPHL: Central Public Health Laboratory; HCW: Health Care Worker; MCH: Maternal Child Health Dept; UNICEF: United Nations Children Education Fund; RRH: Regional Referral Hospital; POC: Point of Care; TAT: Turn Around Time; LTFU: Loss To Follow Up; HCF: Health Care Facility; CDC: Centers for Disease Control

Introduction

Globally, approximately 1.5 million infants are born to HIV infected women each year, majority of whom are not tested until it is too late for optimal antiretroviral therapy (ART) [1] . Despite the increase in effective methods to prevent mother-to-child transmission (PMTCT) of human immunodeficiency virus type 1 (HIV-1), there were an estimated 390,000 new pediatric HIV-1 infections in 2010, majority of which occurred in resource-limited settings [2]. Without treatment, the mortality rate in HIV infected infants can go as high as 40% by the first birthday and over 50% by the second birthday [3]. Recent studies have however shown that early HIV diagnosis and prompt ART intervention can reduce infant mortality by 76% and HIV progression by 75% [4]. These studies prompted a change in treatment guidelines by the World Health Organization (WHO) recommending initiation of ART in infants as soon as they are diagnosed as HIV infected [5]. However, the entry into care and treatment programs is dependent on early diagnosis.

Unfortunately, simple antibody-based diagnosis of HIV infection in infants is complicated by the passive transfer of maternal antibodies during pregnancy. Therefore, molecular assays such as polymerase chain reaction (PCR) technology are needed to distinguish HIV infected from HIV exposed but uninfected children during the first 1-2 years of life [6-8].

However, PCR-based technologies are too complex and expensive for widespread use in resource poor countries where 90% of exposed infants are found [9]. The other limitation is that PCR-based technologies require complex infrastructure, skilled manpower, stable supply of electricity and other utilities, which are scarce in developing countries, particularly in rural areas [9]. Therefore, testing is limited to centralized laboratories, posing other challenges such as sample transport and long turnaround time [8].

To promote EID in Uganda and other developing countries, WHO and the U.S. Centers for Disease Control and Prevention (CDC) convened a stakeholders meeting in 2006, following which the Amplicor HIV DNA PCR version 1.5 assay was recommended as the best option available for immediate scale-up of EID programs in the majority of African countries [8]. The report also recommended the use of DBS as a preferred sample type. Like many high burden HIV countries in SSA, Uganda responded by initiating EID services in 2007.

The program begun by using eight regional laboratories run by partners and a courier (Posta Uganda) was contracted to facilitate the referral of DBS samples from health facilities to the regional laboratories, and results back to health facilities. However, an in-country program review conducted in 2010 revealed high overhead costs, laboratory inefficiencies, and long turn-around times (TAT) [10].

In order to improve efficiency, lower operational costs, and improve oversight and coordination, the MOH consolidated the 8-partner run laboratories, to a single centralized laboratory managed by the MOH and based at the Central Public Health Laboratories (CPHL) [10]. This innovation was later enhanced by the introduction of the national hub-and-spoke system for DBS sample collection and transport from a network of health facilities to a lab hub from where samples were delivered to the central EID laboratory using the Posta Uganda courier services [11].

EID for exposed infants is not a one off test, but a series over time (6wks to 18months). This therefore required a national testing algorithm to ensure counter checks in testing process. The EID testing algorithm is outlined below and in appendix 3: exposed infants are tested with 1st HIV molecular test (1st PCR) at 6 weeks of age (coinciding with the 1st immunization visit), or at the earliest opportunity thereafter. If the 1st molecular test is positive, the infant should be initiated on ART the day they receive their results, on which day, a repeat sample for confirmatory PCR is collected and sent for retesting. If the 1st molecular test is negative, a 2nd molecular test (2nd PCR) is performed 6 weeks after cessation of breastfeeding (9-18 months). All children who were screened by molecular test should go through an exit rapid anti-HIV test at 18 months irrespective of results of the earlier tests.

Despite this well laid out testing algorithm in operational guidelines and on result forms sent back to the health facility, routine program data suggests poor adherence to the testing algorithm, though this has not been quantified and its impact to the final diagnosis is not yet known. This study was undertaken to assess adherence to the current testing algorithm.

Materials and Methods

Study sites and population

This evaluation focusing on adherence to the testing algorithm was cross-sectional, retrospective and outcome based. The target population was HIV exposed infants tested within Uganda's centralized EID laboratory in the year 2012 at selected study sites. Study sites included 24 health facilities, selected from six health regions in Uganda including: Gulu in northern region, Arua in northwest, Jinja in eastern region, Masaka in central region, Mbarara in southwest, and Fort Portal in Midwest. In each health region, 4 health care facilities (HCF) covering 4 levels of health care system were selected: one regional hospital (level VI), one general hospital (level V), one health center level IV and one health center level III. In total, there were 6 regional hospitals, 6 general hospitals, 6 health center IVs and 6 health center IIIs. Figure 1 shows the map indicating the location of the study sites and the central testing laboratory.

HIV testing

The molecular tests were performed using COBAS AmpliPrep Taqman Analyzer, manufactured by Roche Diagnostics Ltd. CH-6343 Rotkreuz, Switzerland. The rapid HIV tests were done on mothers using the national testing algorithm, which comprises three anti-HIV rapid tests, which include; Alere Determine HIV 1/2 as screening test (Alere Inc., Scarborough, UK), HIV 1/2 Stat-Pak Assay as confirmatory test (Chembio Diagnostic Systems Inc Medford NY, USA), and Uni-Gold Recombigen HIV ½ (Trinity Biotech PLC, Cowicklow, Rep Ireland), as the tie-breaker. These 3 test strips are used in series. The 1st test is the Alere Determine, should the results be positive, it is then retested with Stat-Pak for confirmation. Should the results of Determine and Stat-pack disagree, then Uni-Gold Recombigen would be used as a tie-breaker.

Data collection and analysis

We designed a data collection template in which we entered patient identification information, testing and follow-up information through the 18 months testing period. The primary data collection tool was the exposed infants' register, from which we captured patient identification and testing information. In case there were gaps, the clinical chart complemented this register. The dispatch form was also checked to fill in any missing information or where there were inconsistencies. The HIV counseling and testing (HCT) register was used to check for the 18 month HIV rapid test results and the pre ART and ART registers were used to check for treatment initiation. From the collection template, data was entered into an Excel spreadsheet developed for this study. It was then cleaned and imported into an access database for analysis. The major study limitation was the incompleteness of data, so some analyses could not be conducted.

Ethical consideration

The study received IRB approval and also approval by the Uganda National Council of Science and Technology. Since we used retrospective data, there was no direct interaction with patients. However to ensure confidentiality, study IDs were entered into the data collection template instead of patient names.

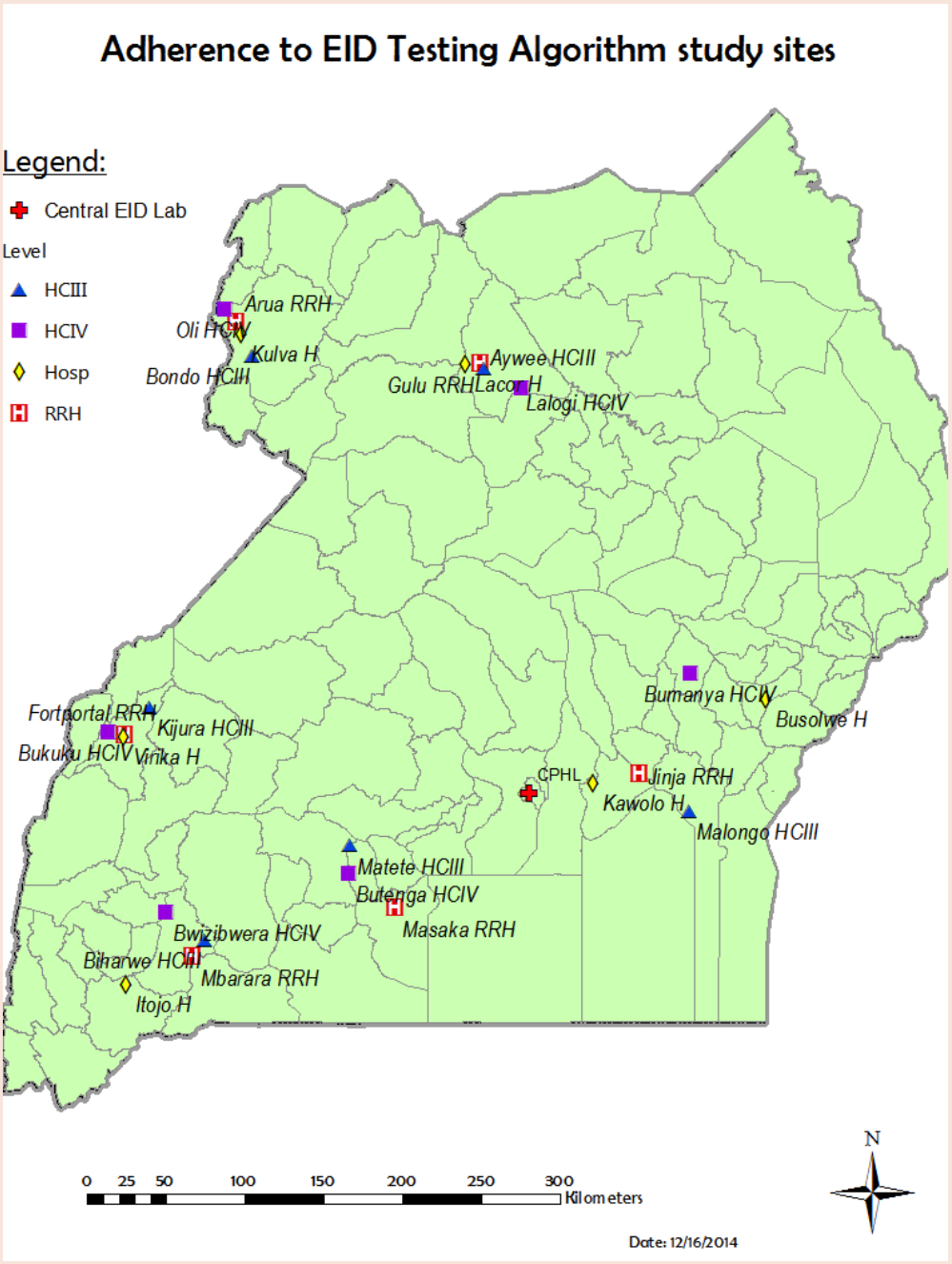

Figure 1: Map of Uganda showing the location of the study sites.
The red square with H represents regional referral hospital, the yellow diamond the general hospital, the magenta square Health care facility level IV and the blue triangle the health care facility level III. The Red Cross indicates the central public health laboratory (CPHL) where central molecular testing was performed.

Results

The 24 selected facilities covered the entire tier of the health system, stretching from health center III that is at sub county level to regional referral hospitals, which are at regional or provincial level. The selected health regions were fairly representative of the country (Figure 1). The data is presented in a consolidated form (Figure 2).

From the initial 4427 infants entered in the study, 206 (4.7%) were excluded for lack of results. Lack of results was due to one of the following; either samples were poorly collected and thus the lab requested for another samples, which was never sent, or samples were sent to the laboratory without any documentation and could therefore not be run by the lab, neither trace where they came from, or results were sent back and given to the patient without being

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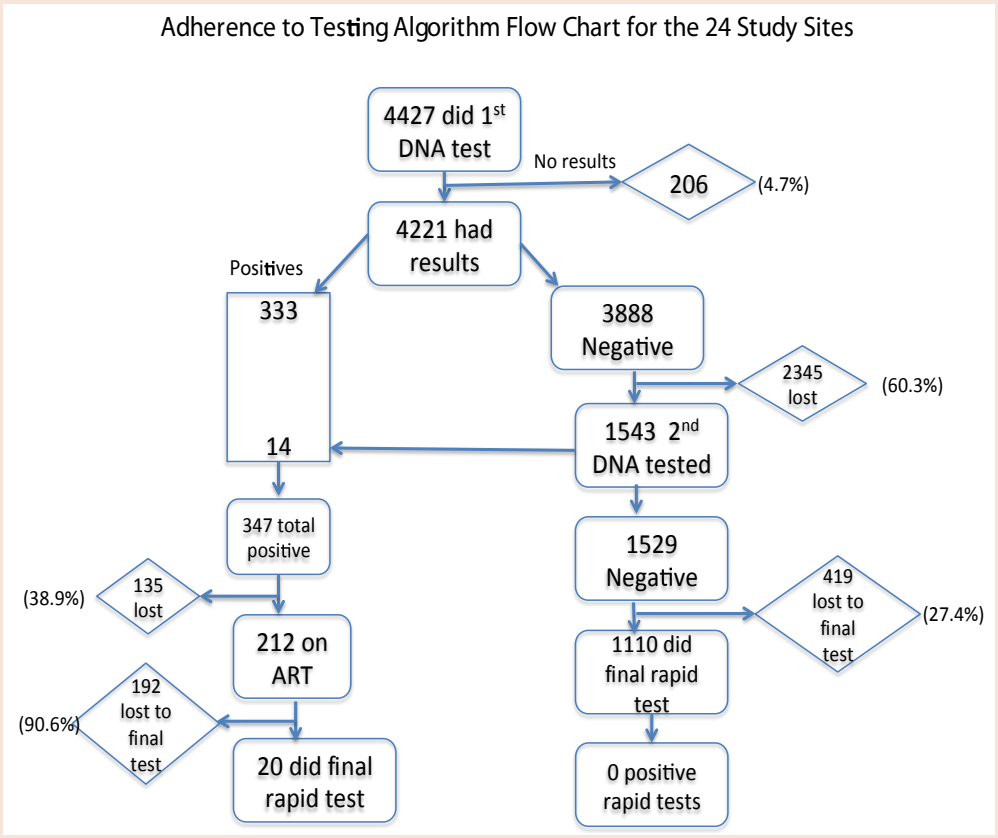

Figure 2: Flow chart that shows the key data that was collected from all the 24 study sites.
Consolidated data collected from all 24 sites, irrespective of health care facility grading. Number of LTFU and % are indicated at each step in a diamond. Refer to appendix 1 for more details.

entered anywhere at the facilities, therefore the research team found no record at the facility. A total of 4221 infants had results and were therefore included in the study. Table 1 represents the distribution between regions and health care facility levels. The northwest had the lowest number of infants, because it is also a low HIV prevalence region.

In order to critically analyze the data according to EID testing algorithm, three major testing and attrition time ranges were selected: 1) from 1st molecular test to final anti-HIV rapid test for all tested infants, 2) from 1st molecular test to 2nd molecular test for infants who tested negative at the 1st molecular test but still breastfeeding and 3) from receipt of HIV positive results to ART initiation. To better understand the factors associated with loss to follow-up (LTFU) at these time points, TAT of test results associated with each time point was collected.

The age range for 1st molecular test was 0.2 months to 22 months with a median of 2 months and an average of 3.5 months. The age range for 2nd molecular test was 1 month to 24 months with a median of 13.5 months and an average of 12.6 months. The age range for final rapid test was 2.5 months to 36 months with a median of 18 months and an average of 18.6 months.

Figure 2 shows that the prevalence of HIV infection in Ugandan EID program at 1st molecular test was 7.9% at an average age of 3.5 months (14 weeks). It further increased to 8.2% after 2nd molecular test at an average age of 12.6 months (54 weeks). However, this minor increase related to 2nd molecular test does not reflect epidemiology, since 60.3% of infants were LTFU between 1st and 2nd molecular testing.

Of the total 4221 infants who were tested and had 1st molecular test results, 2976 (70.5%) caretakers collected their infants' results, representing a loss of 29.5% and 1130 (26.8%) were brought back for the final rapid test, representing a LTFU of 62%. From the total 4221 infants who had a 1st molecular test, a cumulative loss of 73.2% was suffered between the 1st molecular test and the final rapid antibody test. In other words, only 26.8% adhered to the testing algorithm between 1st molecular test and final rapid test.

From Figure 2, 3888 infants tested negative at the 1st molecular test, and thus should have had a 2nd molecular test. However, of these, only 2645 caretakers collected their infants' results for the 1st molecular test, representing 32% LTFU. Of the 2645 who collected 1st molecular test results 1543 (58.3%) did a 2nd molecular test, representing 41.7% LTFU. Of the 1543 who did the 2nd molecular test, 1108 (71.8%) collected results, representing 28.2% LFTU. Overall, there was a cumulative loss of 71.5% among infants who had tested

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negative at the 1st molecular test. In other words, only 28.5% of those who were negative at 1st PCR adhered to the testing algorithm.

From Figure 2, on the infected infants' side, the vast majority of infections were identified by the first molecular test. However, when extrapolating the further infections identified in 40% of the population tested by second molecular test, a total of 35 new infections were predicted, reaching a total prevalence of HIV infections to 8.7%. Here again, 258 caretakers (74.4%) collected their test results, representing 25.6% LTFU. Of the 258 caretakers who collected results, 212 (82.2%) were initiated on ART, representing 17.8% LTFU. Overall, the cumulative LTFU for HIV positive infants stood at 38.9% (Figure 2). Unsurprisingly, LTFU related to caretakers' attention to infants' health was significantly higher in children identified as non-infected at the first molecular test step (P<0.0001).

The next step of this analysis was to examine the TAT at each of the three critical steps in the testing algorithm at different HCF levels. We defined TAT for the 1st molecular test as the time elapsed between sample collection from infant to caretaker receiving results. Table 2 shows the distribution of TAT for 1st molecular test between levels of health facilities and regions where they are located. These results indicate that distance from the testing laboratory did not have a major influence on TAT. This is seen from the fact that health facilities from the eastern region that had the shortest distance from the central laboratory (60km) had longer TAT than facilities from the northwestern region that had the longest distance from the lab (504km) and yet had the shortest TAT.

Table 3 shows the distribution of TAT for 2nd molecular test between different health care levels and regions. A key observation from these results is a marked increase of TAT for 2nd molecular test as compared to 1st molecular test at the same health facilities. For example, the average TAT for 1st molecular test in regional hospitals was 45.9 days (Table 2) as compared to 2nd molecular test where the average TAT was 73.6 days (Table 3). The same was true of general hospitals. This further emphasizes that TAT is not necessarily a factor of distance from the central testing lab. Other factors that might influence TAT need to be investigated.

Table 4 shows the distribution of TAT for ART initiation between different levels of health care facilities from the six regions. TAT for ART initiation was quite long for most facilities apart from those in the Midwest, which averaged at only 1.3 days. This shorter time to ART in the Midwest region might be due to the more efficient PMTCT services, related to the 'Save Mothers Give Life' Project established in the region.

Figure 3 shows the time elapsed between sample collection and receipt of results by the client for 1st molecular test (bar 1), between sample collection and receipt of results by the client for the 2nd molecular test (bar 2) and reception of results of first or second PCR and initiation of ART (bar 3) for positive infants at all study sites. The TAT was ranging between 49 and 72 days (mean 60.2d) for the 1st molecular test with regional referral hospitals having the least and other health centers the longest, between 45 and 75 days for the 2d molecular test (mean 68.3d) and between 18 and 45 days (mean 25.9d) between a diagnosis of HIV infection and initiation of ART. Therefore, the accumulation or overlap of caretakers' delay to collect results and delay between sampling and availability of results had a major impact on the massive percentage of LTFUs.

In order to understand the impact of TAT to clients collecting their results, we did an analysis for regional referral hospitals

Table 1: Distribution of patients according to region and type of health care facility.

	Northern	Northwest	Eastern	Central	Southwest	Midwest	Total
RRH	394	110	327	607	541	492	2471
GH	259	28	60	242	89	244	922
HCF IV	105	41	26	23	174	90	459
HCF III	20	18	62	76	46	147	369
Total	778	197	475	948	850	973	4221

Table 2: Distribution of TAT for 1st PCR Test between levels of health care facilities (HCF) in days.

HFC	RRH Level VI	GH Level V	HFC level III	HFC level IV	Distance from central lab (km)
Northern	36.7	52.4	37.0	68.4	346
Northwest	42.4	39.0	43.0	44.5	504
Eastern	41.9	86	112.5	67	60
Central	49.3	42.6	65.8	38.0	130
Southwest	62.8	68.4	38.4	93,2	266
Midwest	42.5	59.1	62.4	52.6	294
Average	45.9	57.9	59.9	60.6	267

By road, the speed of transport is variable ranging between 30 and 70 km/hour, depending on the region. Results are sent electronically using GSM printers to the hubs which are mainly level VI and V HCF but not in many of level III and IV.

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Table 3: Distribution of TAT for 2nd molecular test between levels of health care facilities (HCF) in days.

HFC	RRH level VI	GH GH level V	HFC level III	HFC level IV
Northern	72	50	32	33
Northwest	78	60	40	51.8
Eastern	60.3	91	105.3	77.6
Central	68	59.5	140	51
Southwest	100.8	62.5	16	12.6
Midwest	62.6	109.4	65.6	50
Average	73.6	72	66.5	46

Table 4: Distribution of TAT for ART initiation between levels of health care facilities (HCF) in days.

HFC	RRH level VI	GH level V	HFC level III	HFC level IV	Average N days
Northern	23	21	-	33	25.7
Northwest	20	-	-	1	10.5
Eastern	21	58	18	-	32
Central	15	12	68	221	79
Southwest	47	30	0	0	19.3
Midwest	3	0	0	2	1.3

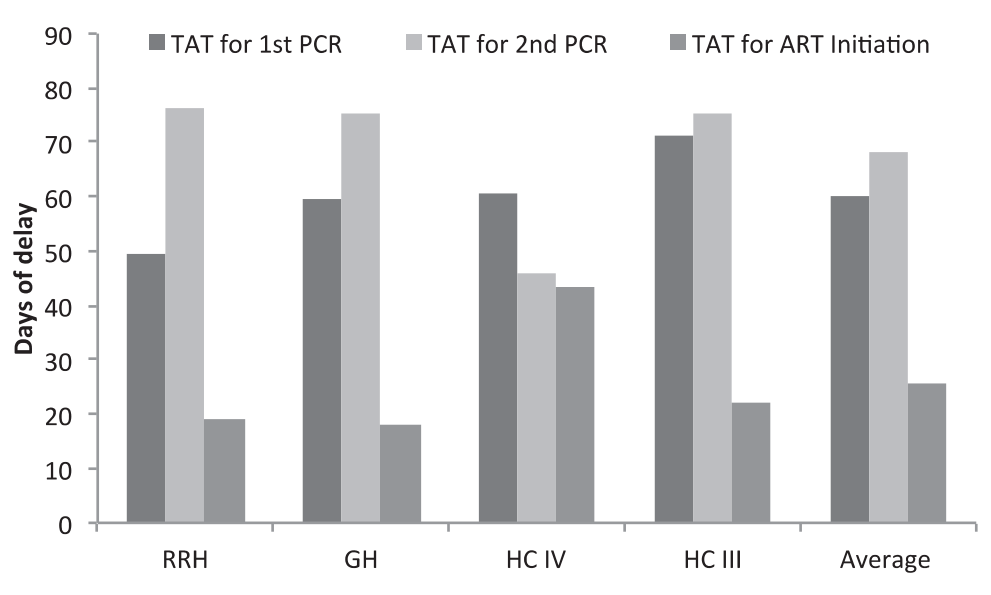

Figure 3: Turnaround time (TAT) in days for 1st and 2nd test as well as ART initiation at the 24 study sites.
The dark grey bar indicates TAT for 1st PCR at 6-8 weeks, the light grey bar the TAT of 2d PCR (10-15w) and the mid grey bar the TAT between HIV positive diagnosis and initiation of ART.

(Figure 4) (Tables 5, 6). This data shows that Fort Portal hospital with an average TAT of 42 days had 81% of clients who collected their results as compared to an average TAT of 63 days in Mbarara regional hospital with only 64% caretakers collecting results. Regional hospitals put together have a TAT of 45.9 days and have 72% of caretakers collecting results as compared to health center IIIs where TAT was 60 days with 62% caretakers collecting results (Table 7).

Discussion

The observed HIV positivity of 8.7% appears similar to the national average by then [12], but has of late gone down to about 5.6% due to option B+ being offered to HIV infected pregnant and lactating women [13]. The average age at first molecular of 14 weeks was higher compared to the recommended 6 weeks according to the

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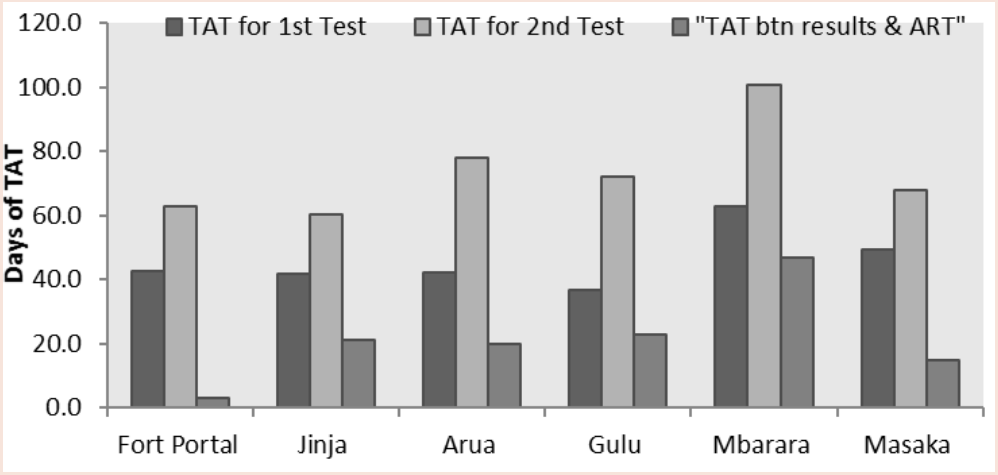

Figure 4: Comparison of turnaround time (TAT) in days for 1st and 2nd test as well as ART initiation between 6 regional referral hospitals. Dark grey bars represent TAT for 1st PCR, light grey bars represents TAT for 2d PCR and mid grey bar for rapid test TAT.

Table 5: Distribution of TAT for 1st PCR, 2nd PCR and ART Initiation at Regional Referral Hospitals (RRH).

RRH Level I	TAT for 1st mol test	TAT for 2nd mol. test	TAT for ART Initiation	Distance from Central lab (km)
Gulu	36.7	72	23	346
Arua	42.4	78	20	504
Jinja	41.9	60.3	21	60
Masaka	49.3	68	15	130
Mbarara	62.8	100.8	47	266
Fort Portal	42.3	62.6	3	294
Average	45.9	73.6	21.5	267

Table 6: Distribution of TAT for 1st PCR, and proportion who collected 1st PCR Results at Regional Referral Hospitals (RRH)

RRH Level I	TAT for 1st PCR	Proportion who picked 1st PCR Results
Gulu	36.7	68.3
Arua	42.4	73
Jinja	41.9	73.7
Masaka	49.3	73
Mbarara	62.8	64.4
Fort Portal	42.5	80.7
Average	45.9	72.2

testing algorithm. The HIV molecular testing was set up at 6 weeks to coincide with the first appointment for vaccination. Our data raises the issue of the connection between HIV testing and vaccination. If they remain linked, it poses a serious issue as to the adherence to the vaccination schedule. If it is not connected, the timing of 6 weeks can be challenged since testing earlier might be an advantage for controlling HIV morbidity in infants and newborn. In any case, the 8-14 weeks for first molecular test is a clear shifting from the algorithm that needs to be corrected given the vulnerability of these infants [4] in whom HIV tends to take a more aggressive mode as compared to adults [3].

Another weakness found with this part of the EID algorithm is that, not all tested infants' caretakers came back to collect their test results. As presented in the result section, the delay by caretakers to collect test results is multifactorial and shared between TAT of test results provided by the central testing laboratory, the appointment system of the clinics which may vary according to HCF level and region and the level of concern of families. According to the data, 29.5% of those who did a 1st molecular test and 32% of those who did a 2nd molecular test never came back to collect their results. The system of appointment adopted by the clinics to coincide with vaccination appointments may look justified for the first molecular test appointment using

Table 7: Distribution of TAT for 1st molecular test, and proportion of caretakers who collected 1st molecular test results at different levels of health facilities.

HF Level	TAT for 1st PCR	Proportion who picked 1st PCR Results
RRH	45.9	72.2
GH	57.9	79
HC IV	60.6	68.6
HC III	59.9	62.4

vaccination as an incentive at six weeks of age. However, evidence collected here suggests that the broad range of first molecular test samples collected might reflect a degree of disconnection between HIV and vaccination appointments. Instead of setting appointments at one-month intervals, a direct communication from the clinic to the family by mobile phone as soon as results are received might help the initiation of ART and limit LTFU.

Here we examined one of the three factors that appear the most critical: TAT for test results. One study reported that long TAT was one of the major reasons for failure to collect results [14]. It appears to be longer in the southwest region despite being in the mid distance from Kampala where the central testing laboratory is located (Table 2). Unsurprisingly, regional referral hospitals at level VI had the shortest TAT, with the smallest range between regions (Figure 4). This is likely due to the fact that all regional hospitals are hubs, and therefore receive results faster than non-hub health facilities. Lower HCF which are not hubs don't have access to electronic communication with the central lab, there by relying on bike riders to drop results, which may delay for a couple of days up to 1 week in the event results arrive on a day the rider is not visiting the site. The limited data available does not support that distance between HCF and central laboratory is a significant factor but distance between infants home and HCF might be, although we did not have the data to prove such hypothesis (Table 2). Other factors such as attitude of health workers and clients, lack of a patient follow-up mechanism at the facility, lack of transport for the caretakers, and others should be investigated.

The 2nd molecular test is intended to diagnose postpartum transmission through breastfeeding. To avoid nutrition-related deaths, mothers are encouraged to exclusively breastfeed for the first 6 months, after which they add supplementary feeding up to one year and then go for accelerated weaning [15]. Therefore, >98% of HIV infected mothers in Uganda are breastfeeding and the eMTCT agenda through option B+ aims at making breastfeeding safer. Given that background, we expect all HIV positive mothers, who had a non-infected baby at 1st molecular test, to bring the baby back for a second molecular test 6 weeks after cessation of breastfeeding.

From the data collected, 3888 babies tested negative at the 1st molecular test and mothers were thus expected to bring back their babies for 2nd molecular test after breastfeeding (Table 3). However, only 1543 (39.7%) brought back their infants for a 2nd molecular test, representing 60.3% LTFU in total. Of those babies tested, 14 (0.91%) were found HIV infected and added to the HIV positive cohort eligible for ART. These results are not very different from the 1.4% postpartum transmission reported in a previous study [16].

The LTFU after the 2nd molecular test was greater in health centers level III and IV than in hospitals (Level V and VI) (Table 4). It is a known fact that most post-partum MTCT occurs through breastfeeding [15], and failure to do a 2nd molecular test after breastfeeding, as stipulated in our testing algorithm, may lead to missed opportunities of early identification and ART initiation [4].

It is surprising to note that only 39.7% of caretakers brought back the infants to the clinic for a second molecular test after cessation of breastfeeding. It would be expected that having made the effort to come twice already to the clinic would have encouraged them to return a third time to potentially exonerate their child from HIV infection. It is also surprising that TAT for the 2nd molecular test is nearly one month longer than for the 1st molecular test. This is clear from Table 5 where the difference in TAT between 1st and 2nd molecular test is an average of 28 days within regional hospitals. The TAT at the central laboratory should be the same irrespective of the sample collected, and the rest of TAT should have remained the same, because the distances between the lab and the health facility and the health facility and the clients' homes remain the same. However, this indicates that there are other factors in play. The degree of involvement and dedication of the HCF staff might be one of them. In addition, the regular appointments set up for vaccination are no longer a factor after 4-5 months of age and this disconnection might make the clinic connection with the caretakers more problematic. Here again direct contact by mobile phone would seem a legitimate approach to improve the situation.

According to the EID testing and care algorithm; "Any HIV positive child under 2 years of age should be initiated on treatment the same day they get results irrespective of clinical or immunological staging". However, almost 40% of infants confirmed HIV positive were not initiated on ART. To find patients who are lost to follow-up can be difficult, costly and inefficient [17], which highlights the need to prevent losses. One option to improve the situation might be to establish better contact between the clinic staff and caretakers by telephone calls. Another probably more efficient option would be point of care (POC) testing, where the test can be performed and results given to the family on the visit day. However POC may solve the problem of returning results to care takers, but issues related to poor ART initiation go beyond return of results, since the data shows that there were some infants who got results but were not initiated on treatment.

According to the testing algorithm, the treatment initiation TAT should be 0 days, meaning that the same day caretakers receive results ART should be initiated. However according to Figure 3, data shows that it takes averagely 18.8days for regional and general hospitals, and 33 days for health center IIIs and IVs. The shorter interval in HCF level VI and V (18.8 days) than in HCF level III and IV (33 days)

might be due to lack of capacity for ART initiation at lower health facilities than higher ones [4]. The confidence and experience in such decisions is probably better for senior physicians than lower cadre health workers available in lower level HCF. If health workers were adhering to this part of the testing algorithm, the number of patients who initiate treatment would be equal to the number of infants who collect results.

The National EID testing algorithm stipulates that; "for all exposed infants under 18 months of age tested by a molecular test, the same will be retested by a rapid test after 18 months of age irrespective of the results of the earlier molecular test". This was put there as a counter check, to weed out any miss diagnosis that may have arisen due to human and technical errors in the earlier testing. However, data from this study reveals that, of the 4221 infants tested by 1st molecular assay, only 1130 (26.8%) ever did the final rapid test. This shows the lack of a system that ensures that the testing algorithm is adhered to. However, no new infection cases were identified through the rapid test (0/1130) suggesting a low risk of breastfeeding transmission beyond the first year of life.

A study conducted in Kenya [18] to assess discrepant test results in their EID program presented interesting findings. Over 2.5% of what was classified as positive and over 1.88% of what was classified as negative by manual PCR assay, tested otherwise on retesting using the automated assay. False positive and false negative results can arise from clerical errors, contamination, or from limitations of the technology used. It was against this background that this final rapid test was put within the testing algorithm. However, failure to operationalize this part of the testing algorithm leaves the program in a dilemma. We might be having infants on treatment who were wrongly diagnosed and have been committed to lifelong ART despite its deterring effects, discomfort, inconvenience and cost.

Conclusions

EID programs in resource limited settings face a lot of problems that start with identification of HIV positive mothers during pregnancy through PMTCT, identification of HIV exposed infants during the postnatal period and linking them to testing, retaining infants into the testing and care algorithm and initiating the positive infants on ART. However, this study concentrated on retaining the identified infants into testing and care algorithm and initiating positives onto ART.

The uniqueness of EID is derived from the fact that the testing is not a one off, but a series over a period of time, which facilitates loss, as long as there are no mechanisms of patient follow-up integrated into the testing process.

Results of this study show that it is one thing to have a testing algorithm but another thing to have it adhered to. There is already a discussion within WHO to revise EID testing algorithm by adding a PCR test at birth and a rapid test at 9 months to the existing algorithm. If the current algorithm is poorly adhered to, adding additional tests may not help the situation.

Uganda's EID program still faces challenges of poor retention of infants into the testing and care algorithm and poor ART initiation for the positives. However, these challenges may not be unique to Uganda but might be generalized among resource limited settings

Recommandations

In view of results from this study demonstrating poor adherence to testing algorithm, similar programs should undertake equivalent assessments.

Before revising the current testing algorithm by adding additional tests, the current algorithm should be strengthened by ensuring it is adhered to.

Since TAT is one of the major causes of LTFU at the different time points, efforts to reduce TAT especially when results reach the facility should be made by alerting clients through telephone calls when results come back.

To improve adherence to the 2nd PCR test and the final rapid test, patients may need to be reminded through telephone calls or other means.

Because of poor adherence to testing algorithm, spot checks should be done to assess discordance, like was done in Kenya by Kageha et al 2012.

More capacity for pediatric ART initiation should be built especially at lower level health facilities, where time to ART initiation was high.

There is need to integrate patient follow-up and care into the EID testing process.

Point of care EID testing when available should be used to complement centralized EID program, especially in hard to reach areas and other sites, which for one reason or another experience excessive TAT.

However, having analyzed the many challenges the current centralized program is facing, it is important to make serious considerations as we think of deploying point of care platforms. Being able to provide results the same day may not mean these results will automatically impact patient care. Just having a POC in itself may not translate into improved patient outcomes [19-24].

Acknowledgement

I acknowledge the help offered by the study site staff who assisted me during the protracted process of data collection. Thanks also go to the in charges of the study sites, who allowed me access to the site data records, and in most cases dedicated a staff to work with me.

I also acknowledge the support offered by the EID team based at the Central Public Health Laboratories, led by the lab manager Isaac Sewanyana, Chris Okira, Allan Kisakye and Rebecca Nakidde for all the support they offered me during the process of data collection, entry and analysis. Thanks also go to Mr. Aisu Steven the Head of Central Public Health Laboratories for his inspiration and guidance.

Overall thanks goes to Dr. Jane Ruth Aceng the Director General of Health Services who gave me authority letters to the study sites.

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Citation: *Kiyaga C, Lee HH, Allain JP (2015) Adherence to Early Infant Diagnosis Testing Algorithm, a Challenge to Early Infant Diagnosis Program in Resource Limited Settings of Uganda. J HIV Clin Scientific Res 2(2): 030-039. DOI: 10.17352/2455-3786.000011*