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Original Research Article

Trends in uptake of early infant diagnosis for HIV: implementation results of the Ugandan military PMTCT program

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ABSTRACT

Background: Early infant diagnosis (EID) is an important strategy of the Prevention of Mother-to-child transmission (PMTCT) and when implemented in combination with other strategies could eliminate HIV MTCT. We implemented a series of strategic interventions intended to improve EID at 9 Military facilities in Uganda and evaluated their impact on uptake of EID.
Methods: A retrospective cross-sectional design was adopted, following-up HIV Exposed Infants (HEI) at the study sites over a 2 year period, and using a data extraction tool to capture4 indicators of EID namely; number of HIV-positive mothers, number of HEI enrolled, number of PCR and rapid tests performed on HEI, and number of HIV-positive results of HEI. Scatter plots and simple linear regression were applied to demonstrate trends in EID uptake and estimate intervention impact over time. Statistical significance was assumed at $p<0.05$.
Results: We established incremental trends in numbers of first PCR ($f\ [1,6]=2.8$; $p=0.15$),third PCR ($f\ [1,6]=8.4$; $p<0.05$), rapid tests ($f\ [1,6]=16.1$; $p<0.05$) performed on HEI, and a modest decline in HIV-positivity among HEI over the study period. The intervention improved retention in PMTCT cascade to 80%, when contrasted with the national average of 70%.
Conclusions: We have demonstrated that interventions invoking pre-booking HIV-positive pregnant mothers during antenatal care, follow up of mother-baby pairs using telephone and mentor mothers and integrating EID in immunization programs can improve uptake of EID in a relatively short period, and with a positive impact on EID indicators.

Keywords: Early infant diagnosis, Intervention, Trends, Impact, Military facilities, Uganda

INTRODUCTION

There are multiple avenues for the transmission of Human immunodeficiency virus (HIV) from an HIV-positive mother to her infant, i.e. HIV-exposed Infant (HEI), namely through pregnancy, delivery as well as during the breastfeeding phase.[1] When a combination of strategies of Prevention of Mother-to-child transmission (PMTCT) is implemented, HIV Mother-to-Child transmission rates can drop to below 1%.[2] These strategies include providing Antiretroviral therapy (ART) for pregnant mothers living with HIV, ART initiation for HIV-Exposed Infants (HEI), testing infants at 18 months, and Early infant diagnosis.[3]

Early infant diagnosis (EID) prescribes a cascade of HIV testing for HEIs with the first test done at four to six weeks of age as a measure in PMTCT.[4] The rationale for adoption of EID in PMTCT can never be overemphasized. Firstly, HIV infection advances swiftly in the early months of life amongst infants who acquire HIV at delivery, and if undetected, often leads to death.[5] Secondly, data shows that thirty 35% of all HIV infected children will die in the first year of life, and 53% before their second birthday.[6] Evidence suggest further that HIV-infected infants and children initiating ART (antiretroviral therapy) late have a poor treatment prognosis, and without timely access to ART 20% of HIV-positive infants will die before 6 months, 35–40% will die before 1 year, and over 50% will die by 2 years.[3,6-8] In addition, EID reduces the waiting time for tests turnaround from months to hours, and ultimately increases the chances of access to early treatment for infants and children living with HIV.[9,10] Moreover, EID facilitates timely access to ART and thereby optimizes viral load suppression and improves the overall quality of life of HIV-positive children. Data indicates further that timely initiation of ART reduces the risk of infant mortality by 76% within the first 3 months of life and the progression to AIDS (Acquired Immunodeficiency Syndrome) by 75%.[11,12]

In Uganda the prevalence of HIV among children aged 0-14 is 0.5% which corresponds to approximately 95,000 children living with HIV.[13] In 2012, Uganda's Ministry of Health adopted Option-B plus, a strategy of starting all HIV-positive pregnant and lactating mothers on ART irrespective of their clinical and immunological stage in order to eliminate mother to child transmission of HIV (EMTCT).[14] In 2018, Ninety-three per cent of pregnant women living with HIV accessed antiretroviral medicine to prevent MTCT, resulting in the prevention of 17 000 new HIV infections among newborns. The percentage of HEI tested for HIV before eight weeks of age (an indicator of EID) stood at 45% in 2018.[15]

WHO recommends that all infants born from mothers who tested positive during pregnancy should have a blood sample collected for EID at 4-6 weeks of age.[16] This window has been selected because EID testing has >95% HIV sensitivity at this point, which also coincides with the period when most national guidelines recommend the first set of immunizations for infants. From birth to 18 months, HEIs undergo routine care. At birth, nevirapine syrup is introduced but the dose is adjusted according to weight and age bands until 6 weeks. At 6 weeks, nevirapine syrup is stopped, the first HIV test using Deoxyribonucleic acid-polymerase chain reaction (DNA-PCR) is performed between 4-6 weeks, and cotrimoxazole prophylaxis is introduced (also adjusted according to age and weight bands) until 18 months. The second DNA-PCR is performed at 9 months when the child turns up for measles vaccine. The third PCR is done for HEI who breastfeed beyond 1year and it is done 6 weeks after cessation of breastfeeding. For HEI above 18months of age a final HIV antibody test is done. Should a HEI test HIV-positive at any time point, ART is initiated alongside cotrimoxazole prophylaxis. Regarding breastfeeding, HEIs exclusively breastfeed for the first 6 months before commencing complementary feeding, and breastfeeding ceases at 1 year.[16,17] Despite these recommendations, merely two in every five HEIs access EID by DNA-PCR tests within two months of birth (first DNA-PCR) in Uganda.[18]

While the EID testing is steadily increasing across the continents of Africa and Asia, it is crucial for National Governments to set up programs and systems to support and ensure that HIV-positive pregnant mothers and HEI pairs are systematically followed up to enhance early testing services for HEI and if tested positive initiate early treatment as per World Health Organization recommendations. Some of the key challenges in the implementation of EID faced by low-income countries, specifically in Africa include suboptimal retention along the PMTCT cascade, a lack of sufficient linkages to care, inadequate testing efficiency (Rapid sample referral and result delivery), Point-of-care (POC) diagnostics, and data systems to improve the cascade of care, resource mobilization, laboratory networks and management. Uganda has put in place systems such as the Rapid sample referral and result delivery (i.e. short message system (SMS) printers and dashboards) systems to increase the access to EID by 50% while reducing sample transport costs by 50%.[19] The efficiency of such initiatives are demonstrated by the 86% reduction in new infections among children between 2010 and 2016 [18]. However, the proportion of HEI tested for HIV at 18 months after delivery remains low at 38% due to low retention of mother-and-baby pairs in PMTCT programmes.[20] Nonetheless, windows of opportunity are forthcoming to close up these gaps through collaborative initiatives such as the URC-DHAPP Early Infant Diagnosis strategy undertaken in Military PMTCT programmes in the country.

The Ugandan military PMTCT program

The University Research Co., LLC - Department of Defense HIV/AIDS Prevention Program (URC-DHAPP) provides technical support to Uganda's military health facilities to provide quality, sustainable, integrated and comprehensive HIV prevention and treatment services with a goal of reducing the number of new HIV infections among the military, their families and communities. The program currently supports 28 ART sites and 12 HTS only sites. In phase 3, the program plans to accredit three more HTS high volume sites to offer comprehensive HIV care.

The program implementation started in March 2019 and based on performance in year 1, there was suboptimal performance in most of the PMTCT indicators especially PMTCT EID. In order to improve on EID performance, the program devised targeted strategies to improve on EID testing coverage which included; pre-booking HIV-positive pregnant mothers coming for the final ANC visits for I PCR based on their expected date of delivery (EDD), active follow up of mother-baby pairs in the communities with the help of telephone calls and mentor mothers in addition to integrating EID in child immunization (EPI).

Aim, objectives and hypotheses

The aim of the current assessment was to evaluate the program impact on uptake of EID. Specifically, the objectives were: to demonstrate trends in the uptake of early infant diagnosis of HIV among HEI as a result of key interventions in military facilities; and to estimate the impact of key interventions on the uptake of early infant diagnosis of HIV among HEI in the military facilities.

Four hypotheses related to three key indicators of uptake of EID were tested. We hypothesized that following strategies adapted to improve PMTCT EID:

Hypothesis 1 (H1): The number of HIV-positive mothers enrolled in the program would increase over time (i.e. during the intervention period).

Hypothesis 2 (H2): The number of HIV-exposed Infants (HEI) enrolled in the program would increase over time (i.e. during the intervention period).

Hypothesis 3 (H3): The number of HEI tested for HIV would increase over time (i.e. during the intervention period).

Hypothesis 4 (H4): The percentage of HIV positive HEI detected would decrease over time (i.e. during the intervention period).

METHODS

Study design, sites, inclusion criteria and measures

We carried out a quantitative retrospective cross-sectional study, where (HEIs, defined as infants born to mothers with HIV and aged between 4 weeks to 24 months, were followed up through breastfeeding periods to ascertain whether PCR and Rapid tests were done at 6 weeks from birth, at 9 months of age, 6 weeks after cessation of breastfeeding and at 18 months respectively from 9military facilities namely General military hospital-bombo, Nakasongola military hospital, Rubongi military hospital, 4th Division military hospital-Gulu, 5th division HCIV-Acholpii, 2nd division HCIV-Makenke, Moroto Army HCIII, CMRC- Mubende and Luwunga HCIV.

The facility selection criteria were based largely on total number of active clients at the facility, level of the facility, location/distribution, and availability of a functional mother-baby care point in maternal and childcare centers.

A data extraction tool capturing 4 indicators of uptake of EID: number of HIV-positive mothers enrolled; number of HEI enrolled; number of PCR and Rapid tests performed on HEI; and Number of HIV-positive HEI diagnosed. These indicators were retrieved over 8 consecutive quarters starting October 2020.

The patient inclusion criteria was HEIs aged between 4 weeks to 24 months who were delivered in the 9 selected facilities in the last two years from October 2018 to September 2020, or were delivered elsewhere but sought care and were tested for HIV at the facilities during the study period.

Statistical analysis

Raw data was compiled in excel and cleaned before being exported to statistical package for social sciences (SPSS) for analysis. Scatter plots were used to visualize observed data and trend. Simple linear regression was applied to determine linear trends in observed data over time. Trends were considered statistically significant if the F-statistic testing for linearity in observed data over time exhibited a $p<0.05$. The impact of the interventions was predicted based on the estimated regression equation.

For each of the EID uptake indicators, we specified the following regression model to estimate trends (study objective 1) and make predictions regarding impact of interventions (study objective 2):

Regression model: $Y= b\pm mX$

Where m represents the rate of change in outcome (i.e. uptake of EID indicators) over time, b represents the y-intercept of the linear model, Y represents the outcome of interest and X represents time (i.e. quarter).

Ethical considerations

Ethical approvals were obtained Institutional Review Board of TASO REC and Uganda National Council of Science and Technology. We obtained waiver of informed consent since this was program data, and no identifiable patient details were collected.

RESULTS

Distribution of EID indicators

Over the study period (i.e. October 2018 to October 2020), a total of 872 mothers and 872 HEI were enrolled in the study, of which 620 (71%) had been enrolled at birth at any of the 9 military health facilities selected for the study (Table 1). Twenty nine percent (29%) of HEI had been delivered elsewhere but sought care at the selected facilities and were tested during the study period. Of the HEI, 73% (n=640) had documented a first PCR results, 95% (n=832) a second PCR results, 17% (n=147) a third PCR, and 62% (n=540) a rapid test results over the study period. An overall retention of 80% of HEI was observed in the data.

Table 1: Quarterly data (Q1-Q8) on key indicators of EID uptake.

Variables	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total
Total number of HIV positive mothers and HEI enrolled	97	86	80	76	84	292	56	101	872
Total number of HEI enrolled at birth at study site	89	86	69	73	82	84	65	72	620
Nr. 1 PCR done	40	29	30	25	41	196	143	136	640
Nr. HIV Positive	1	1	1	2	2	2	0	0	9
Nr. 2 PCR done	100	113	117	112	106	122	71	91	832
Nr. 3 PCR done	0	0	0	0	0	48	40	59	147
Total rapid test done	45	52	40	59	49	84	105	106	540
Nr. HIV Positive	2	1	2	0	3	2	2	2	14

Trends in number of mothers and children enrolled over time (October 2018 to October 2020)

As exhibited in figure 1 by the regression equation (i.e., the straight line) and the equation's 95% Confidence Interval (i.e., the curves), the estimated trend in the number of HIV-positive mothers enrolled over time (i.e., the straight line) was statistically non-significant at p<0.05 (see footnote to Figures 1 for visual interpretation).

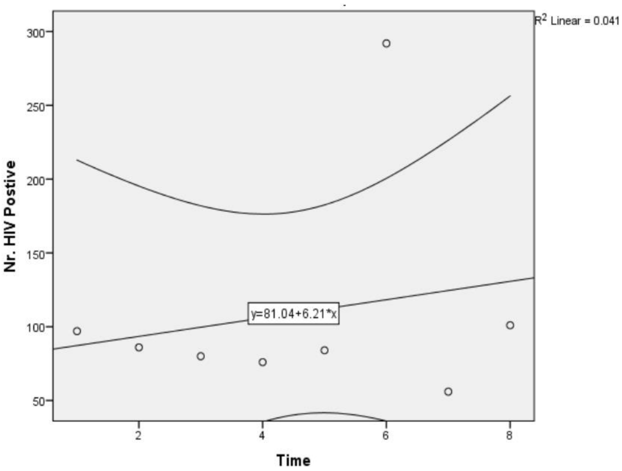

Figure 1: Trends in HIV positive mothers (Nr. HIV positive) enrolled from October 2018 to September 2020.

Visually interpreted, if a straight horizontal line can be drawn within the Confidence Intervals without touching the curves, then this represents the first signal for statistical non-significance. However, robust confirmatory tests e.g. F-test must be done to confirm significance status.

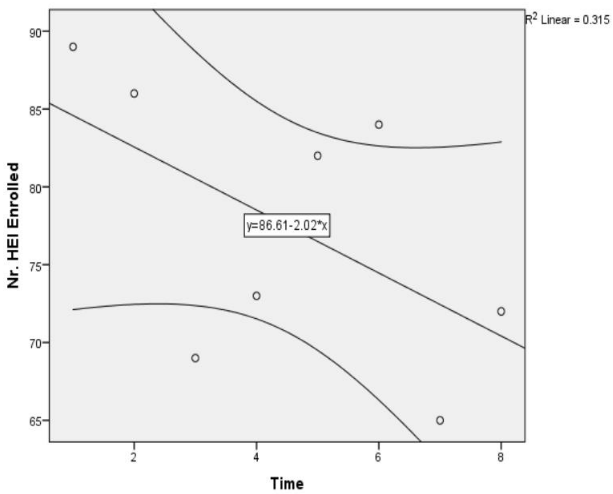

Figure 2: Trends in HIV exposed infants (Nr. HEI enrolled) enrolled from October 2018 to September 2020.

Visually interpreted, if a straight horizontal line can be drawn within the Confidence Intervals without touching the curves, then this represents the first signal for statistical non-significance. However, robust confirmatory tests e.g. F-test must be done to confirm significance status.

The F-test for linearity (f [1,6]=0.2; p=0.63) further confirmed that the estimated trend over time was statistically non-significant at p<0.05. Similarly, the trend in number of HEI enrolled at birth over time (Figure 2) was statistically non-significant at p<0.05 as observed by the regression equation and it's 95% confidence interval, and confirmed by the F-test for linearity (f [1,6]=2.8; p=0.15).

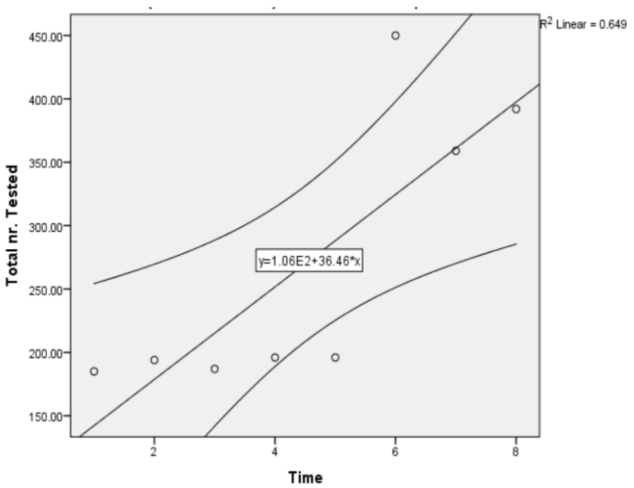

Figure 3: Trends in number of HIV exposed infants tested for HIV (Total nr. Tested) from October 2018 to September 2020.

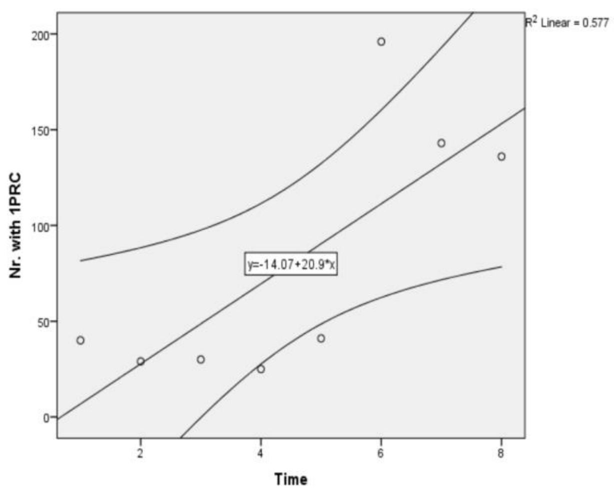

Figure 4: Trends in number of HIV exposed infants with one PCR test (Nr. With 1PCR) done from October 2018 to September 2020.

Visually interpreted, since a straight horizontal line cannot be drawn within the Confidence Intervals without touching the curves, this represents the first signal for statistical significance. However, robust confirmatory tests e.g. F-test must be done to confirm significance status.

Trends in number of HEI tested over time (October 2018 to October 2020)

As exhibited in figure 3 by the regression equation and the equation's confidence interval, there was a statistically significant incremental trend (f [1,6]=11.1; p<0.05) in number of HEI tested over time (see also footnote to figure for visual interpretation). Further, the r-square statistic indicated that time explained 65% of the variation in number of HEI tested over time. The linear equation suggested that on average the number of HEI tested increased by 36 infants per quarter, which translate to 288 additional infants tested over the 8 quarters studied.

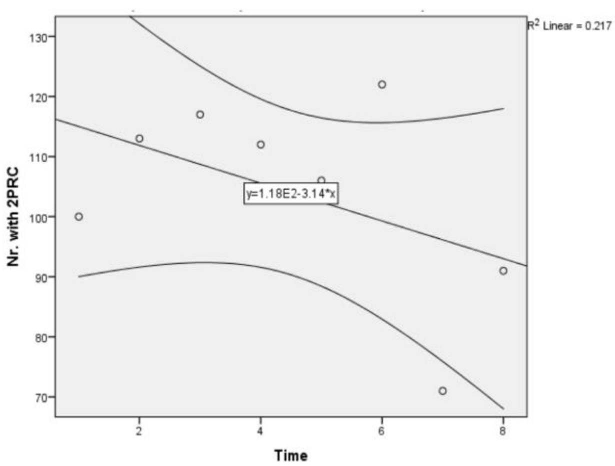

Figure 5: Trends in number of HIV exposed infants with two PCR test (Nr. With 2PCR) done from October 2018 to September 2020.

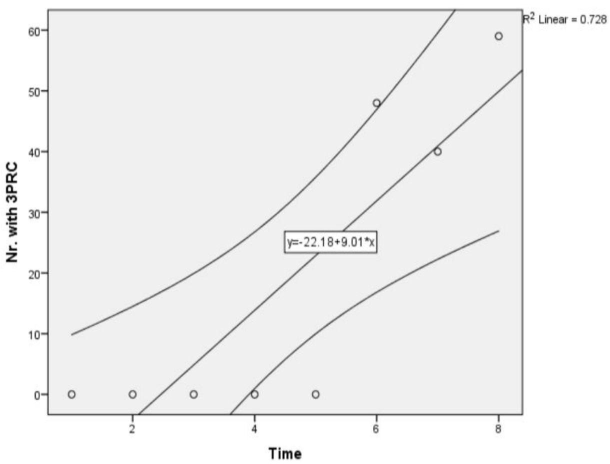

Figure 6: Trends in number of HIV exposed infants with three PCR test (Nr. With 3PCR) done from October 2018 to September 2020.

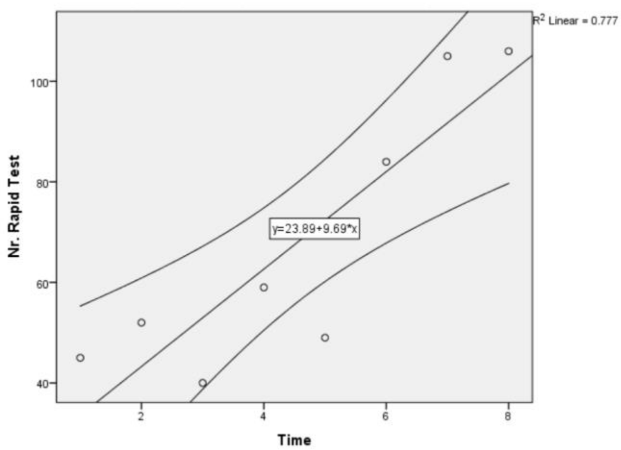

Figure 7: Trends in number of HIV exposed infants with rapid tests (Nr. Rapid test) done from October 2018 to September 2020.

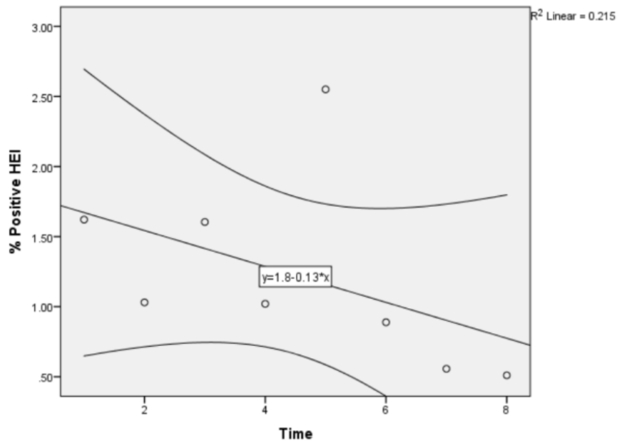

Figure 8: Trends in percentage of HIV exposed infants testing positive for HIV (% positive) from October 2018 to September 2020.

Visually interpreted, since a straight horizontal line cannot be drawn within the Confidence Intervals without touching the curves for Figures 6, 7 and 8, this represents the first signal for statistical significance. However, robust confirmatory tests e.g. F-test must be done to confirm significance.

Similarly, there was a statistically significant incremental trend (f [1,6]=8.4; p<0.05) in number of HEI tested once using PCR over time (figure 4). Further the r-square statistic indicated that time explained 58% of the variation in 1 PCR tests done over time. The linear equation suggested that on average the number of single PCR test done over time increased by 21 per quarter, resulting in 168 additional infants tested over the studied 8 quarters.

As exhibited in Figure 5 by the regression equation (i.e. the straight line) and the equation's 95% confidence interval (i.e. the curves), the estimated trend in the number of second PCR tests done over time was statistically non-significant at p<0.05 (see footnote to figure for visual explanation). The F-test for linear trend (f [1,6]=1.6; p=0.24) further confirmed that the estimated trend over time was statistically non-significant at p<0.05.On the other hand, there was a statistically significant incremental trend (f [1,6]=16.1; p<0.05) in number of third PCR tests done over time. Further the r-square statistic indicated that time explained 73% of the variation in number of third PCR tests done over time (Figure 6). The linear equation suggested that on average, the number of HEI with 3 PCR tests done increased by 9 per quarter (Figure 6), translating to 72 additional HEI tested with 3 PCR over the study period.

Similarly, there was a statistically significant incremental trend (f [1,6]=20.9; p<0.05) in number of HEI tested using the rapid test method at 18 months over time. The r-square statistic indicated that time explained 78% of the variation in number of rapid tests done over time (Figure 7). Furthermore, the linear equation suggested that on average, such tests increased by almost 10 in number per quarter (Figure 7), translating to additional 80 HEI with rapid tests done over the assessment period.

Trends in percentage of HEI testing HIV positive

Overall14 (2.5%) babies tested positive of the 540 babies tested (Table 1). As exhibited in figure 8 by the regression equation and the equation's 95% Confidence Interval (see figure footnote for visual interpretation), and confirmed by the f-test for linear trend (f [1,6]= 1.6; p<0.24), the estimated trend in the percentage of HEI testing positive for HIV over time was statistically non-significant change, even though a tendency to reduction was observed the last three quarters of the study (Figure 8).

DISCUSSION

We studied trends in uptake of EID following a series of interventions implemented in 9 Military facilities in Uganda, with technical support by the URC-DHAPP program. The interventions aimed at strengthening the PMTCT cascade performance (enrollment, retention to final EID test) and included; pre-booking HIV-positive pregnant mothers coming for the final ANC visits for I PCR based on their expected date of delivery (EDD), strengthening retention by active follow up of mother-baby pairs in the communities with the help of telephone calls and mentor mothers in addition to integrating EID in expanded program for immunization (EPI). Four indicators of uptake of EID namely number of HIV-positive mothers enrolling in the program, number of HEI enrolling in the program, number of HEI tested for HIV at final rapid test, and percentage of HEI testing positive were investigated. We hypothesized that these percentages would increase over time (i.e. during the intervention period).

Trends in enrolment of HIV-positive mothers and enrolment of HEI (October 2018 to September 2020)

Our findings could neither confirm an increase in number of HIV-positive mothers nor number of HEI enrolled over time as a result of these interventions. Pre-booking of HIV positive mothers during last ANC visit was expected to have resulted in increased HEI enrollment. Though a major part of the intervention activities were designed to strengthen retention of mother-HEI pairs in PMTCT program through active follow up mothers who had given birth in the study facilities, our expectation was that enrollment into the program would increase over time as information of the program and its benefits begin to take root in the served communities. Even though the program managed to attract HIV-positive mothers and HEI who had not been born at the study sites (i.e. almost 30% HEI enrolled) the total number of mothers with HIV and HEI did not increase significantly over time. This runs contrary to studies elsewhere like in Thailand where community enrolment in EID programs tended to increase during a similar initiative.[21] While previous evidence from Low Income Countries have pointed to facility related factors such as the long turnaround time for receipt of PCR results and poor reliability of PCR machine hindering EID service delivery and leading to non-completion of the EID process by clients, the facilities in the current study have largely been supported by the program to ensure these challenges are addressed.[22,23] Therefore, we are able to rule out such challenges as explanation to the stagnated trend observed in our data. On the other hand, community and individual level factors including negative perceptions on the importance of EID, financial difficulties and denial of HIV status have in previous research been advanced to explain poor EID uptake and could explain the stagnated enrolment of mother-infant pairs observed in our data.[23] The lack of increased enrollment of HIV positive mothers could have been due to other factors like stigma, low male involvement, low family members engagement which have been identified elsewhere as key barriers to enrollment in PMTCT. These were not among the implemented interventions in this program.[24] Another possible explanation for non-significant increase in enrollment in HIV-positive mothers and HEIs could be due to already saturated program coverage regarding enrollment by the start of the program. Uganda Ministry of Health (MoH) reports show high ANC coverage and near universal testing in ANC since about 2016.[25]

Trends in number of HEI tested and impact over time (October 2018 to September 2020)

Our data exhibited statistically significant incremental trends in number of HEI tested and retained in PMTCT cascade over the study period, number HEI completing third PCR and number of HEI tested at end of PMTCT cascade using rapid tests methods all increased. Overall 80% of the HEI completed the cascade contrary to previous research demonstrating higher (>30%) losses to follow-up as a challenge to EID in Uganda and other LDCs.[22,23] Additionally, our findings are inconsistent with previous works suggesting that the impact of birth-PCR could lead to loss to follow up of HEI, i.e. neonates testing HIV-negative at first PCR may be less prone to present for subsequent EID testing.[26]. The mentioned works are however observational studies. Therefore, our findings are likely demonstrating efficacy of the active follow-up strategy of the URC-DHAPP program in turning around these observations. It appears that the strategy of pre-booking HIV incremental pregnant mothers coming for the final ANC visits for Ist PCR based on their expected date of delivery (EDD), active follow up of mother-baby pairs in the communities with the help of telephone calls, engaging lay providers (mentor mothers) and integrating EID in expanded program for immunization (EPI) impacted positively on the numbers of HEI tested over time. These is in keeping witha recent review of studies about interventions for improving retention in PMTCT.[24].

The linear regression equation estimated the total number of HEI retained over the study period to increase by 288 HEI, number of single PCR test done over time to increase by 168 infants, number of HEI with 3 PCR done to increase by 72 HEI and number of HEI tested with rapid tests by 80 HEI over the study period. These figures demonstrate the potential impact of the program in promoting Prevention of mother-to-child transmission (PMTCT) through strategic EID interventions.

Trends in percentage of HEI testing HIV-positive and impact over time (October 2018 to September 2020)

The overall HIV positivity rate of 2.5% found in our study is comparable with the national average of 2.4%. The estimated trend in the percentage of HEI testing positive for HIV over time was statistically non-significant, even though a tendency to reduction was observed in the last three quarters of the study. Observational studies have previously alluded to facility and individual level factors as barriers to EID uptake.[22-24] With these factors not fully addressed by the interventions, a poor prognosis, reflected among others in an increasing number of positive tests, would be expected for HEI. The combination of interventions in the DHAPP program consisting of pre-booking of HIV positive mothers during last ANC visit, activities designed to strengthen retention of mother-HEI pairs in PMTCT program through active follow up mothers who had given birth in the study facilities and integration of EID in expanded programs for immunization, were envisioned to at the very minimum break this trend or even reverse it. There is some support for this argument in our data for the last three quarters as the percentage HEI testing positive fell to below 1%. Additional data from beyond the study endpoint would however be required for statistical analysis to support this observation. Another explanation for the insignificant reduction HEI positivity rates could be that most of the positive babies were identified during the postnatal period among women who had not been on ART. Community level interventions to ensure such women are identified early are needed in reducing transmission for such HEI.

Limitations

Though our study appears to provide relatively robust findings, some limitations of the methodology deserve acknowledgement. Firstly, the study adopted a design without control periods/groups. Assessment of intervention effects neither considered information from the period before the intervention as a control nor did it consider facilities that were not included in the URC-DHAPP program as plausible control groups. Therefore, causality cannot be entirely ruled out, i.e. we cannot rule out the possibility that the trends and impacts observed overtime in our study are due to external factors not measured or included in our interventions. On the other hand, the initial observations (i.e. observations from quarters Q1-Q5) show a rather constant development with no significant changes in our EID indicators, supporting the plausibility of a similar trend during quarters proximal to the intervention initiation. Therefore, that our intervention started giving an impact around Q6, could rule out the plausibility of potential unmeasured effects prior to the intervention accounting for the trends, as these would have reflected on the Q1-Q5 data. Nonetheless comparing trends between control and program facilities could have provided more robust data to confirm our conclusions.

Secondly we applied linear regression in estimation of trend. This analysis assumes linearity which may not always be the case. Other more sophisticated methods e.g. fractional polynomial and spline regression models are especially valuable when nonlinear associations are anticipated in the data. However, interpretational challenges may limit their application in the real world of implementation, as well as their usefulness for policy formulation and informing program adaptability. Another limitation of regression modeling in trend analysis stems from its reliance on linear calibration supported by r2, which may mask hitherto unexplained or shared variances in the data due to confounding. This is particularly problematic for models with a single or only few independent variables in the model. Our results thus should be interpreted with relative caution, particularly the impact estimates, as they could represent overestimates in light of confounding.

CONCLUSION

Using conventional statistical modeling, we have demonstrated incremental trends in number of HEI tested for HIV, retained in PMTCT cascade and tendencies towards a reduction in percentage of HEI testing positive for HIV as a result of a multi-prong programmatic intervention consisting of pre-booking HIV-positive pregnant mothers coming for the final ANC visits for I PCR based on their expected date of delivery (EDD), active follow up of mother-baby pairs in the communities with the help of telephone calls and engagement of lay providers (mentor mothers), in addition to integrating EID in childhood immunization clinics. These interventions did not however improve enrolment of HIV-positive mothers and HEI into the program over time.

Recommendations

As opportunity for program continuation is promising, it is recommended that these results inform strategies for phase 3 of the program, particularly considering incorporation of measure to improve enrolment of expectant HIV-positive mothers in the communities into the program.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: recommendations for a public health approach-2010 version. World Health Organization; 2010. https://www.who.int/hiv/pub/mtct/antiretroviral2010/en/. Accessed on 20 February 2021.
2. World Health Organization. 'Mother-to-child transmission of HIV'. https://www.who.int/hiv/topics/mtct/about/en/#:~:text=ThetransmissionofHIVfrom,from20152520to204525. Accessed on 20 February 2021.
3. UNAIDS. Miles to go. Global AIDS update 2018. https://www.unaids.org/en/20180718_GR2018#:~:text=Miles%20to%20go%20%2D%20Global%20AIDS%20update%202018%20%7C%20UNAIDS&text=GENEVA%2C%2018%20July%202018%E2%80%94UNAIDS,is%20at%20a%20precarious%20point. Accessed on 20 February 2021.
4. Katabira ET, Kamya MR, Kalyesubula I, Namale A. National antiretroviral treatment guidelines for adults, adolescents, and children. ed. Kampala, Uganda. 2009.
5. Mphatswe W, Blanckenberg N, Tudor-Williams G, Prendergast A, Thobakgale C, Mkhwanazi N et al. High frequency of rapid immunological progression in African infants infected in the era of perinatal HIV prophylaxis. Aids. 2007;21(10):1253-61.
6. Mirkuzie AH, Hinderaker SG, Sisay MM, Moland KM, Mørkve O. Current status of medication adherence and infant follow up in the prevention of mother to child HIV transmission programme in Addis Ababa: a cohort study. Journal of the International AIDS Society. 2011;14(1):1-0.
7. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. The Lancet. 2004;364(9441):1236-43.
8. Cook RE, Ciampa PJ, Sidat M, Blevins M, Burlison J, Davidson MA et al. Predictors of successful early infant diagnosis of HIV in a rural district hospital in Zambezia, Mozambique. Journal of acquired immune deficiency syndromes (1999). 2011;56(4):e104.
9. Francke JA, Penazzato M, Hou T, Abrams EJ, MacLean RL, Myer L et al. Clinical impact and cost-effectiveness of diagnosing HIV infection during early infancy in South Africa: test timing and frequency. The Journal of infectious diseases. 2016;214(9):1319-28.
10. Jani I, Meggi B, Loquiha O, Tobaiwa O, Mudenyanga C, Mutsaka D et al. Effect of point-of-care testing on antiretroviral-therapy initiation rates in infants. InConference on Retroviruses and Opportunistic Infections (CROI 2017), Seattle, USA. Abstract 2017;26.
11. Motswere-Chirwa C, Voetsch A, Lu L, Letsholathebe V, Lekone P, Machakaire E et al. Follow-up of infants diagnosed with HIV—Early infant diagnosis program, Francistown, Botswana, 2005–2012. MMWR. Morbidity and mortality weekly report. 2014;63(7):158.

12. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA et al. Early antiretroviral therapy and mortality among HIV-infected infants. New England Journal of Medicine. 2008;359(21):2233-44.
13. MoH. Uganda Population-Based HIV Impact Assessment (UPHIA) 2016-2017.
14. Izudi J, Auma S, Alege JB. Early diagnosis of HIV among infants born to HIV-positive mothers on option-B plus in Kampala, Uganda. AIDS research and treatment. 2017;2017.
15. Uganda/UNAIDS. 2018. https://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf. Accessed on 20 February 2021.
16. World Health Organization. WHO recommendations on the diagnosis of HIV infection in infants and children. World Health Organization. 2010. http://apps.who.int/iris/bitstream/handle/10665/44275/9789241599085_eng_Annexes.pdf;jsessionid=EDCABF59B151EBF71FA59A7333DF742E?sequence=2. Accessed on
17. Katabira ET. The Integrated National Guidelines for Antiretroviral Therapy, Prevention of Mother to Child Transmission of HIV and Infant & Young Child Feeding. Kampala, Uganda: Ministry of Health-Uganda. 2011.
18. UAC. Uganda HIV/AIDS country progress report July 2016-2017.
19. Kiyaga C, Sendagire H, Joseph E, McConnell I, Grosz J, Narayan V et al. Uganda's new national laboratory sample transport system: a successful model for improving access to diagnostic services for early infant HIV diagnosis and other programs. PloS one. 2013;8(11):e78609.
20. Pandey A, Galvani AP. The global burden of HIV and prospects for control. Lancet HIV. 2019;6(12):e809-11.
21. Naiwatanakul T, Voramongkol N, Punsuwan N, Lolekha R, Gass R, Thaisri H et al. Uptake of early infant diagnosis in Thailand’s national program for preventing mother-to-child HIV transmission and linkage to care, 2008–2011. Journal of the International AIDS Society. 2016;19(1):20511.
22. Anaba UC, Sam-Agudu NA, Ramadhani HO, Torbunde N, Abimiku AL, Dakum P et al. Missed opportunities for early infant diagnosis of HIV in rural North-Central Nigeria: A cascade analysis from the INSPIRE MoMent study. PloS one. 2019;14(7):e0220616.
23. Ankrah AK, Dako-Gyeke P. Factors influencing the delivery and uptake of early infant diagnosis of HIV services in Greater Accra, Ghana: A qualitative study. PloS one. 2021;16(2):e0246876.
24. Vrazo AC, Firth J, Amzel A, Sedillo R, Ryan J, Phelps BR. Interventions to significantly improve service uptake and retention of HIV-positive pregnant women and HIV-exposed infants along the prevention of mother-to-child transmission continuum of care: systematic review. Trop Med Int Health. 2018;23(2):136-48.
25. Uganda AIDS Commission. Uganda Annual Joint Aids Review Report 2019/2020
26. Dunning L, Kroon M, Fourie L, Ciaranello A, Myer L. Impact of birth HIV-PCR testing on the uptake at follow-up Early Infant Diagnosis (EID) services in Cape Town, South Africa. The Pediatric Infect Dis J. 2017;36(12):1159.

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