

Early diagnosis in infants born to HIV-positive adolescent compared to HIV-positive adult mothers in Kisumu, Kenya

Margaret Wanja Mburu

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Committee:

Carey Farquhar

Elizabeth Anne Bukusi

R. Scott McClelland

Barbra Richardson

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Margaret Wanja Mburu

University of Washington

Abstract

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Margaret Wanja Mburu

Chair of the Supervisory Committee:

Carey Farquhar

Department of Epidemiology

Although many countries have made great efforts to establish prevention of mother to child HIV transmission (PMTCT) services, globally 160,000 children are newly infected with HIV each year. Early infant diagnosis (EID) of HIV is critical to the survival of HIV-positive infants. While adolescent girls, defined by WHO as 10-19 years olds, represent a growing proportion of persons living with HIV, accumulating data show that adolescents have poor engagement in HIV care, retention, antiretroviral adherence, and treatment outcomes. Less is known about adolescent uptake of PMTCT of HIV services including early infant diagnosis.

A retrospective cohort study was conducted among 967 HIV positive pregnant women in Kisumu, Kenya followed up between October 2016 and September 2018 to assess EID uptake. Early infant HIV diagnosis completion rates were measured by linking maternal HIV exposed infant (HEI) data with antenatal care (ANC) data using mothers' unique patient identifiers. Completion of the six-week EID testing, which has been standard of care since 2006, was compared between adolescent and adult mothers using a generalized linear model with a Poisson link.

A total of 967 HIV positive pregnant women were included in the study, of whom 63 (6.5%) were adolescent mothers aged 10-19. The mean age for adolescent mothers was 17.8 years (Standard Deviation (SD) 1.6) and that of adult mothers was 28.3 years (SD 4.9). Twenty-four (38.1%) of the adolescent mothers were not married, while 97 (10.7%) of older women were not married. The rate of EID uptake was not significantly different for adolescent mothers compared to adult mothers (risk ratio (RR): 0.977; 95% Confidence Interval [CI] 0.875, 1.090). HIV positive mothers on ART for a longer period of time had a higher rate of EID uptake compared to those on ART for a shorter period of time after controlling for facility type, mothers age, parity and nevirapine use by infants, (adjusted RR (aRR)= 1.056; 95% CI 1.002, 1.114). Use of nevirapine by the infants born to these women trended toward statistical significance in the rate of EID uptake after adjusting for facility type, mothers age, parity and mother's number of years on ART, (aRR = 1.152; 95% CI 0.994, 1.335, p=0.061)

Results showed that being an adolescent mother was not associated with failure to access early infant HIV diagnosis 6 weeks after birth. An infant taking nevirapine and a mother on ART for a longer period of time had a higher likelihood of EID uptake, showing that linking HIV-positive women and retaining them in HIV care for treatment may have an impact on improving early infant HIV diagnosis for their exposed infants.

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INTRODUCTION

Worldwide, more than three million children are infected with HIV and 90% of these live in sub-Saharan Africa [1]. Mother to child transmission causes more than 90% of HIV infections in infants and children [2]. Many countries have made great efforts to establish prevention of mother to child transmission (PMTCT) services. These programs have had considerable success, but there remains a need for greater scale up of coverage to 100% and higher rates of early infant diagnosis (EID) after birth [3-6]. The PMTCT coverage has increased from 61% in 2010 to 89% in 2016 globally. Although there has been significant reduction (at least by 47%) in the number of new HIV infections among children [7], AIDS-related illnesses are still among the leading causes of infant mortality among children living with HIV [8].

Early Infant Diagnosis of HIV

Early infant diagnosis in Kenya and other low-resource settings faces a number of challenges [9]. First, pregnant women may fail to complete HIV testing. A review of 2016 demographic and health survey data in Ethiopia reported that at least 60% of pregnant mothers might fail to complete HIV testing during pregnancy [10]. However, in some parts of Saharan Africa in particular, this number is even higher. A study including pregnant women from four countries (Congo, Mozambique, Nigeria and Uganda) in 2016 reported HIV testing to range between 45% and 82% [11].

Second, infants born to women known to be HIV-positive may fail to complete early infant diagnosis for HIV testing [12]. Beginning in 2006, World Health Organization (WHO) and the Kenyan government's National AIDS and STI Control Programme (NASCOP) recommended infant HIV testing at six weeks after birth for babies born to HIV-positive mothers [13-15]. Despite this recommendation, the first HIV testing for infants born to HIV-positive mothers has been reported to occur at an average age of 3.1 months in Kenya and other low income countries [9,16]. In 2018, a global information and education on HIV and AIDS report showed that only 43% of HIV-exposed infants were tested in the first two-months of life globally [17]. A recent global review in 2017 of early infant diagnosis and innovative practices reported only 49% of infants receiving an EID test by the WHO-recommended 6-week window and only a fraction of these retested at 9 and 18 months [18]. Other studies in Africa and Asia have shown significant attrition (22-70%) in the EID cascade [16,19]. A study carried out in South Rift Valley, Kenya in 2017 showed 42% uptake of early infant diagnosis at 6 weeks [20], which confirmed findings from an earlier multi-country review of implementation of EID services from 2007-2009 in Nigeria, Uganda and Namibia that reported < 50% of EID uptake within 8 weeks of life [21]. To address this problem, in 2016, WHO recommended infant HIV testing at birth [18,22,23]. To date, this recommendation has not

been fully implemented [24]. Recently, Kenya revised EID guidelines to include birth testing (currently a pilot) in addition to 6 weeks, 6 months, 12 months and 18 months testing time points [25].

Even when infants are tested, turnaround times for their HIV test results can be long. A review in 2017 on the progress and challenges with EID scale-up in global plan countries, reported that EID results to mother-infant pairs took weeks [26]. A study done in Malawi (2017) to compare management and outcomes of HIV exposed infants reported 5 weeks turnaround time for EID results [27], while that conducted in Kenya earlier (2011-2014) reported 4 weeks from the time the sample was obtained to the time available to the clinician [28]. Inadequate transport of specimen from testing sites to processing laboratories and undocumented HIV status once results are back also contribute to loss or delayed HIV results [29-31]. A review of seven sub-Saharan countries in 2015 by Centers for Disease Control and Prevention (CDC) revealed difficulty in transporting samples in Kenya among other four countries [32]. Poor transport and distance may prevent whole blood samples from reaching processing laboratories in good time while still viable for testing.

Individual Challenges

Individual barriers for pregnant mothers may limit the use of EID process. In a study to examine loss to follow-up among HIV exposed infants in Western Kenya, some mothers were unaware of the importance of EID services, some lacked money for transport to the hospital and others were fearful of disclosing their HIV status [33]. Other women are not ready to start ART treatment. In Malawi, a study carried out between 2008 and 2010 reported challenges with EID implementation; 5.5% of the mothers did not give consent for their infants to be tested for HIV and never went back for EID, and among those who were tested, only 60% returned to receive results [34,35]. The delayed care and missed opportunities may be attributed to lack of follow-up of the mother.

Program challenges also affect HIV exposed infants. Poor coordination between the stakeholders limit accountability and efficiency [16,36]. In addition, high patient to caregiver ratio and loss to follow up among pregnant HIV positive mothers, are system barriers associated with EID uptake. To achieve the target of 90-90-90 by 2020, innovative approaches are needed to address these limitations [16].

HIV in Adolescent Girls

In 2014, women represented 59% of adults living with HIV in sub-Saharan Africa [37]. In the year 2017, the newly infected among 15-24 years old were 590,000, of whom 42% were adolescents

15-19 years [38]. According to this report, only 23% of girls (15-19 years) in Eastern and Southern Africa tested for HIV within a year. The Kenya AIDS Indicator Survey (KAIS) 2012 reported that; overall HIV prevalence among 15-19 years adolescents was 1.1% for females and 0.9% for males [39]. This proportion is expected to be higher in Kisumu County, which has higher HIV prevalence (above 16.3%) compared to 5.9% in the country. Adolescents diagnosed with HIV face overwhelming challenges related to emerging sexuality and concerns about relationships and future family [40]. They experience hormonal, emotional, cognitive and behavioral changes. It is at this stage when they strive to become independent from their families and identify more with their friends just like any other normal adolescent. Sometimes they can experience poor confidence and low self-esteem due to their HIV status [41]. Many of them (an estimate of 6 million in sub-Saharan Africa), have been orphaned due AIDS and act as family heads coupled with taking care of their infants [42-44]. Past reports show that HIV-positive adolescents have poor adherence to ART and clinic visits [40,45].

Although several studies have been done in sub-Saharan Africa on the effectiveness of PMTCT programs [35], little is known about adolescent uptake of PMTCT of HIV services including early infant diagnosis [46]. Few national AIDS strategies explicitly program adolescents and therefore they are largely invisible in global, regional and country HIV and AIDS reports making it hard to assess their progress [47]. This study provides information to HIV programs on the current services for adolescent pregnant women and their infants in terms of accessing care and EID uptake and adherence, as an essential component to child survival. The study took place at Family AIDS Care and Education Services (FACES) supported health care facilities, in Kisumu, Kenya. Using the combined demographic and clinical variables for mother and baby, we explored whether adolescent mothers (≤ 19 years old) are at higher risk for failure to complete EID for their infants compared to adult mothers (> 19 years old).

METHODS

Population and Procedures

This was a retrospective cohort study utilizing data from Kisumu County between October 2016 and September 2018. The FACES program that provided the data for this project, works collaboratively with Ministry of Health (MOH) and it is the only implementing partner providing HIV services in Kisumu County since October 2016 under President's Emergency Plan for AIDS Relief (PEPFAR) funding. This information was abstracted from the Antenatal Care (ANC) register and linked to infant testing information from the HIV Exposed Infants (HEI) register to determine

whether their infants received EID within eight weeks following birth. Because of recent changes in PMTCT guidelines to include HIV testing at birth in addition to testing at six weeks, we evaluated whether infants received HIV testing between four and eight weeks post-partum. This incorporated the recommended 6 week testing time point +/-2 weeks by WHO. Information on HIV testing at birth as a pilot in one site was included in the primary outcome, since the EID testing time point in this site was the same as the other sites. To facilitate linkage to HIV related information, mothers' Comprehensive Care Clinic (CCC) patient identifiers are manually documented in the ANC register during their first ANC visit or subsequent visits. Their infants are also assigned unique identifiers, documented in the HEI file together with the respective mother's CCC patient identifier. This system means that the HEI file provided a key for linking mother-infant pairs. Family AIDS Care and Education Services program assign unique CCC patient identifiers to HIV-positive patients receiving care at their facilities and the same is used to identify mothers who become pregnant and attend MNCH facilities during pregnancy instead of the usual routine HIV care and treatment clinic offered by FACES. All data required for the study was available in ANC and HEI registers in hard copy and in electronic medical records (OpenMRS and KenyaEMR). The study included 10 high-volume FACES supported HIV care facilities in the County; Lumumba Health Centre, Kisumu County Hospital, Railways Dispensary, Rabuor Health Centre, Nyang'ande Dispensary, Ahero Sub-County Hospital, Nyang'oma Health Centre, Katito Health Centre, Nyakach County Hospital and Sondu County Hospital.

We included data for all HIV-positive pregnant mothers who visited ANC clinic during the period of interest. The corresponding data for their infants covered the period from birth to the most current information documented in the HEI register. If the mother-baby pair could not be linked using mother's CCC patient identifier, they were excluded from the analysis and this information documented. In addition, women with miscarriage, stillbirth, or early infant death (prior to 8 weeks) were excluded.

A data collection tool was created in MS Excel to collect ANC data for the HIV-positive pregnant women who received antenatal care at the 10 MNCH facilities, and their infants' information recorded after birth in the HEI register. The study obtained Institutional Review Board (IRB) approval from Kenya Medical Research Institute (KEMRI) Scientific Ethics Review Unit and University of Washington. Additional data on routine HIV care for the women was extracted from OpenMRS and KenyaEMR databases. The variables collected included; age, marital status, gestation, parity, date first diagnosed with HIV, Antiretroviral Therapy (ART) initiation date, most recent viral load, ANC visits, HIV disclosure to sexual partner, use of nevirapine (NVP) by the

baby, infant date of birth, gender and four HIV testing time points. This information was de-identified. The primary outcome variable for this study was the infant age at first HIV testing point (4-8 weeks) using mother's age as the exposure variable.

Study power:

We did a study of independent cases (adolescents) compared to controls (adults), and anticipated that about 13% of infant deliveries would be adolescents; a ratio of 7 adults per adolescent. Overall EID testing uptake at FACES was 88% for the period since 2016. Assuming that the EID rate was 92% in adults (unexposed) and 84% in adolescents (exposed), the Type 1 error of 0.05, and a two-sided test, we calculated we needed at least 158 adolescents and 1,106 adults to be able to reject the null hypothesis that the EID rates in these groups are equal with 80% power. The actual sample size obtained for this study was 967 women, in a ratio of 14 adults per adolescent. Using the same assumptions above, the power of our study to detect the assumed differences was actually 66%, significantly lower than if our sample size ratio had been what we had originally assumed.

Statistical Analysis:

Information on patients' demographics and clinical characteristics was exported from MS Excel to STATA Version 15 to perform all the analyses. Descriptive statistics were used; mean (standard deviation - SD) for normally distributed continuous variables and median (inter-quartile range - IQR) for non-normally distributed continuous variables. For categorical variables, we used counts and proportions.

To determine if being an adolescent mother was associated with uptake of early infant HIV diagnosis at six weeks, we fit a generalized linear model with a Poisson link to compare the difference in EID uptake between infants born to adolescent mothers versus adult mothers. The exposure variable, mother's age, was dichotomized to indicate mothers who were 10-19 years old (adolescents), versus mothers who were 20-47 years old. Models were adjusted for facility type as a confounder since type of facility could be associated with both age of mothers attending ANC clinic and women's likelihood of bringing their children for HIV diagnosis. The 10 facility sites were divided into three categories of facility type; urban/city sites (Lumumba, KCH, Railways), peri-urban sites (Sondur, Rabuor, Ahero) and rural sites (Katito, Nyang'oma, Nyakach and Nyang'ande).

To evaluate other risk factors associated with failure to complete six-week EID testing among HIV-positive mothers, we conducted similar univariate models as was done for mother's age comparing the risk of failure to complete EID testing across groups defined by marital status (married versus not married (single, divorced, separated or widowed)), parity (nulliparous versus multiparous), time on ART drugs (continuous) and number of ANC visits (< 4 visits versus ≥ 4 visits). Length of time on ART was calculated as the difference between first ANC visit date and ART initiation date. Each univariable model adjusted for the type of facility. We then built a multivariable model that included variables that had a univariate p-value ≤ 0.250 . The facility type covariate was included based on *a priori* clinical knowledge, and age remained the exposure variable in the model.

We tested the significance of interaction terms between mothers' age; and marital status, gestational age at the ANC visit, HIV disclosure to sexual partner, number of ANC visits and length of time on ART. A 95% confidence interval and p-value of the hypothesis that the risk ratio of EID uptake is equal to 1, was reported. A p-value < 0.05 was considered significant.

RESULTS

The summary characteristics of the women are presented in Table 1 and stratified by facility type and age group. A total of 967 HIV positive pregnant women were included in the study, with 63 (6.5%) adolescent mothers. The mean age for adolescent mothers was 17.8 years (standard deviation [SD] 1.6) and that of adult mothers was 28.3 years (SD 4.9). More than a third (38.1%) of the adolescent mothers were not married while 97 (10.7%) of older women were not married. Forty percent (388) of participants were from the urban sites, 321 (33.2%) from peri-urban and 258 (26.7%) from the rural sites. Adolescent mothers had a median of 0 (minimum 0, maximum 5) children during pregnancy and adult mothers had 2 (minimum 2, maximum 7). Thirty-eight (60.3%) of the adolescents gave birth to male children while almost half 441 (49%) of the adult mothers gave birth to male children. The median time on ART was 32.8 months (IQR 3.7, 64.8) for adult women compared to 3.2 months (IQR 0, 21.7) for adolescents. Early infant diagnosis uptake was 53 (84.1%) among adolescents and 786 (87.0%) among adult mothers. See figure 2 and 3.

Though the follow up data on infant HIV status was not complete for all infant participants, 1% (9/918) of the infants tested HIV positive of which 4.8% (3/62) of the infants were born to adolescent mothers. Six (6/924) of the infants who tested HIV positive were diagnosed at week 6

and the remaining 3/924 were diagnosed between 11 and 20 weeks documented as first HIV test in HEI register. Eight (0.8%) infants died from the study population of which 1/63 infant was born to an adolescent mother (result not shown).

Several factors were associated with EID uptake in univariable and multivariable models (Table 2). In the unadjusted model, the rate of EID uptake was not significantly different for adolescent mothers compared to adult mothers (risk ratio [RR]: 0.968; 95% confidence interval (CI) 0.867, 1.080, $p=0.558$). In a multivariable model to estimate additional risk factors associated with EID uptake, HIV positive mothers on ART for a longer period had a higher rate of EID uptake compared to those on ART for a shorter period of time after controlling for facility type, mothers age, parity and nevirapine use by infants, (RR per one month increase = 1.001; 95% CI 1.000, 1.001, $p=0.039$). The administration of nevirapine to the infant showed a trend toward statistical significance for the rate of EID uptake after adjusting for facility type, mothers age, parity and mother's number of years on ART, (RR = 1.152; 95% CI 0.994, 1.335, $p=0.061$).

There was no statistically significant interaction between mothers' age and marital status, gestational age at the ANC visit, HIV disclosure to sexual partner, number of ANC visits or time on ART.

DISCUSSION

In this cohort study of HIV-positive pregnant women, early infant HIV diagnosis uptake was higher than what is reported globally at 84% for adolescent girls and women aged 10-19 and 87% for women >19 years, however, both the results were suboptimal compared to the 100% target for EID uptake. This study shows that adolescent uptake of HIV services for their infants was no different from that of adult mothers, which was in contrast to what was expected. Past HIV studies focusing on adolescents, have shown poor clinical outcomes for adolescents including low viral suppression, lack of clinic visit, ART adherence and poor retention [40,45]. A self-report study in Zimbabwe amongst HIV positive adolescents reported sub-optimal adherence to ART [48]. Similar results were shown in a prospective study in South Africa; older adolescents (15-19 years) were less likely to be retained in HIV care compared to adults (>24 years) [49].

HIV positive mothers on ART for a longer period of time had a higher rate of EID uptake compared to those on ART for a shorter period. Similar findings have been reported in a previous study to determine reasons for vertical HIV transmission in South Africa, 2015 [50]. In addition, past

research shows that mothers on ART predict EID follow-up and uptake [51-53]. Use of nevirapine by the infant also showed slightly higher uptake of EID. This finding is in agreement with a study carried out to investigate factors determining HIV viral testing of infants in South Africa, which reported association between polymerase chain reaction (PCR) test participation; and maternal and infant nevirapine adherence [54].

The findings from this study on higher EID uptake (87%) compared to <50% reported in the country, could be attributed to FACES current practices; the program has invested to ensure positive clinical outcomes to all its HIV infected patients with specialized services for adolescent patients. New practices in HIV care recommend having adolescent clinics for routine HIV care for easier follow up; these measures were in place; and one site had specialized ANC adolescent clinic. Future studies should include data from other HIV programs to have more generalizable findings. To reach the 13% infants missing EID uptake, the program needs to come up with ways to track every HIV positive pregnant mother at first ANC visit, take their current contacts, location and obtain consent from the mothers to trace them should they miss follow-up ANC visits and EID testing time points for their babies after birth. The program should strengthen the community team to do these follow-ups and also work with traditional birth attendants (TBAs) in the community to help link back mother-baby pairs to PMTCT for the mothers who would prefer to give birth at home. Challenges facing EID birth testing should be addressed at National and County level.

The main reason for EID testing is to detect HIV virus in infants as early as possible and start treatment immediately. Out of the nine infants who were confirmed to be HIV-positive, six were identified at week 6 of early infant HIV diagnosis testing. Almost 5% (3/63) of infants born to HIV positive adolescent mothers tested HIV positive compared to less than 1% infected among adult mothers. In addition, 8/967 of infants died from the study population compared to 1/63 infant from adolescent mother (result not shown). The causes of these deaths are unknown. This calls for more interventions for adolescent mothers to prevent mother to child HIV transmission and achieve the global target of zero HIV infection rate among HIV exposed infants.

The most recent studies recommend birth and EID point of care testing since it has proved to improve EID uptake and outcomes [18]. One study site was a pilot for birth testing but the results showed no difference in time to EID testing uptake compared to other study sites that were following the usual six-week time point. This shows there are still existing system or individual gaps acting as a barrier to implement birth testing in low and middle-income regions, specifically Kenya. Barriers to implementation of infant HIV diagnosis at birth should be identified so that any infant testing positive at birth can start treatment early. Birth testing also provides an opportunity

for the mother to get more education and counseling on how to prevent HIV transmission to the baby.

Data was collected from urban, peri-urban and rural facilities, which was a good representation of EID uptake in Kisumu County. In addition, we were able to link data for HIV-positive pregnant mothers and their infants from ANC and HEI registers respectively, and then to mothers' routine HIV care data in electronic form. The findings from this study adds to the literature in PMTCT comparing EID uptake between adolescents and adults, an area that has not been researched on extensively.

The study had some limitations. The study sample had lower power to detect differences between adolescent and adult mothers than was originally projected. The study assumed one HIV positive pregnant adolescent per seven adult mothers, but the actual sample had double adults per adolescent. Although there was no bias in getting more mothers that are adolescent into the study than adult mothers, some sites lacked antenatal care registers for significantly long periods of time. This meant we could not link infant information even if this information existed. Developing electronic data capture for the maternal, newborn, and child health registers could help resolve this problem. Some sites had missing data reflecting the previous nurses strike period. There were also mothers who visited ANC clinics without carrying their to-come-again (TCA) card where mother's CCC identifier details are documented and which help the care provider capture this information into the register. This study included only women with CCC number identification to allow data linkage.

CONCLUSION

Within the facilities from which the sample was drawn in Kisumu County, being an adolescent mother was not associated with failure to take early infant HIV diagnosis at recommended 6 weeks after birth. An infant taking nevirapine and a mother being on ART for a longer period had a higher likelihood of EID uptake, showing that linking HIV-positive women and retaining them in HIV care for treatment may have an impact on improving early infant HIV diagnosis for their HIV exposed infants.

REFERENCES:

1. Bwana, Veneranda M., Michelo, Charles et al. (2016). Accessibility of services for early infant diagnosis of Human Immunodeficiency Virus in sub-Saharan Africa: A systematic review. *Tanzania Journal of Health Research*, 18(3).
2. Joint United Nations Programme on HIV/AIDS. "progress report on the global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive." Geneva: UNAIDS (2013).
3. HIV and AIDS. UNICEF Worldwide Eastern and Southern Africa. Preventing mother-to-child transmission (PMTCT) of HIV. Available from: https://www.unicef.org/esaro/5482_pmtct.html.
4. Chigevenga, Rosemary. "Constraints to Rural women's Participation in PMTCT Programmes in Zimbabwe." Available from: www.academia.edu/7660954/
5. Ruark, Allison. (2015) Prevention of mother to child transmission and pediatric HIV in Low and middle income countries. Available from: www.bing.com/cr?IG=AA6A7D68071947F0A81DD446052E59D5&CID=070E1AE222FB647D3121119C235465D3&rd=1&h=ZL4PbiBKjYgYzDsm4Tw1kMSSaVpWMRCQfQhnwOQPtVM&v=1&r=http%3a%2f%2fwvi.org%2fsites%2fdefault%2ffiles%2fLiterature%2520Review_PMTCT_0.docx&p=DevEx,5041.1
6. Essajee, Shaffiq, et al. "Scale-up of early infant HIV diagnosis and improving access to pediatric HIV care in global plan countries: past and future perspectives." *JAIDS Journal of Acquired Immune Deficiency Syndromes* 75 (2017): S51-S58.
7. UNAIDS Report on the Global AIDS epidemic (2013). Available from: <https://www.unric.org/en/latest-un-buzz/28702-52-reduction-in-new-hiv-infections-among-children>
8. Children, HIV and AIDS. AVERT, 6 Dec. 2017. Available from: www.avert.org/professionals/hiv-social-issues/key-affected-populations/children.
9. Finocchiaro-Kessler, Sarah, et al. "Improving early infant HIV diagnosis in Kenya: study protocol of a cluster-randomized efficacy trial of the HITSystem." *Implementation Science* 10.1 (2015): 96.
10. Ejigu, Yohannes, and Biniyam Tadesse. "HIV testing during pregnancy for prevention of mother-to-child transmission of HIV in Ethiopia." *PloS one* 13.8 (2018): e0201886.
11. Gunn, Jayleen KL, et al. "Antenatal care and uptake of HIV testing among pregnant women in sub-Saharan Africa: a cross-sectional study." *Journal of the International AIDS Society* 19.1 (2016): 20605.
12. "Early diagnosis of HIV in infants - Home | UNICEF." UNICEF, UNICEF, Dec. 2008. Available from: www.unicef.org/devpro/files/Actions_for_Children_2_EN_112508.pdf.

13. Hassan, Amin S., et al. "Dynamics and constraints of early infant diagnosis of HIV infection in rural Kenya." *AIDS and Behavior* 16.1 (2012): 5-12.
14. Finocchiaro-Kessler, Sarah, et al. "If you text them, they will come: using the HIV infant tracking system to improve early infant diagnosis quality and retention in Kenya." *AIDS* (London, England) 28.0 3 (2014): S313.
15. Kenya Ministry of Health. Algorithm for early diagnosis of HIV in children. Ministry of Public Health and Sanitation; Nairobi, Kenya: Dec, 2009.
16. Thiha, Soe, et al. "Early infant diagnosis of HIV in Myanmar: call for innovative interventions to improve uptake and reduce turnaround time." *Global health action* 10.1 (2017): 1319616.
17. "Testing rates in infants exposed to HIV." Avert, 2018. Available from: <https://www.avert.org/infographics/testing-rates-infants-exposed-hiv/>.
18. Celletti, Francesca, Gayle Sherman, and Ahmad H. Mazanderani. "Early infant diagnosis of HIV: review of current and innovative practices." *Current Opinion in HIV and AIDS* 12.2 (2017): 112-116.
19. Chatterjee, Anirban, et al. "Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries." *BMC public health* 11.1 (2011): 553.
20. Ashiono, Everline, et al. "Vertical HIV transmission in perinatally-exposed infants in South-Rift region of Kenya: a retrospective cross sectional study." *BMC public health* 17.1 (2017): 207.
21. Chatterjee, Anirban, et al. "Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries." *BMC public health* 11.1 (2011): 553.
22. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. World Health Organization, 2016.
23. "HIV & children - HIV testing." www.aidsmap.com/HIV-testing/page/1060202/.
24. "World Health Organization. HIV diagnosis and ARV use in HIV-exposed infants: a programmatic update. No. WHO/CDS/HIV/18.17. World Health Organization, 2018. Available from: <https://www.who.int/hiv/pub/paediatric/diagnosis-arv-infants/en/>.
25. Sandbulte, Matthew R., et al. "Infant HIV testing at birth using point-of-care and conventional HIV DNA PCR: an implementation feasibility pilot study in Kenya." *Pilot and feasibility studies* 5.1 (2019): 18.

26. Essajee, Shaffiq, et al. "Scale-up of early infant HIV diagnosis and improving access to pediatric HIV care in global plan countries: past and future perspectives." *JAIDS Journal of Acquired Immune Deficiency Syndromes* 75 (2017): S51-S58.
27. Phiri, N. A., et al. "Early infant diagnosis and outcomes in HIV-exposed infants at a central and a district hospital, Northern Malawi." *Public health action* 7.2 (2017): 83-89.
28. Wexler, Catherine, et al. "Evaluating turnaround times for early infant diagnosis samples in Kenya from 2011-2014: A retrospective analysis of HITSystem program data." *PloS one* 12.8 (2017): e0181005.
29. Ciaranello, Andrea L., et al. "Early infant HIV-1 diagnosis programs in resource-limited settings: opportunities for improved outcomes and more cost-effective interventions." *BMC medicine* 9.1 (2011): 59.
30. Creek, Tracy L., et al. "Infant human immunodeficiency virus diagnosis in resource-limited settings: issues, technologies, and country experiences." *American journal of obstetrics and gynecology* 197.3 (2007): S64-S71.
31. Woldesenbet, Selamawit A., et al. "Missed opportunities for early infant HIV diagnosis: results of a national study in South Africa." *Journal of acquired immune deficiency syndromes (1999)* 68.3 (2015): e26.
32. Lecher, Shirley, et al. "Scale-up of HIV viral load monitoring—seven sub-Saharan African countries." *Morbidity and Mortality Weekly Report* 64.46 (2015): 1287-1290.
33. Braitstein, Paula, et al. "'Wamepotea' (They have become lost): Outcomes of HIV-positive and HIV-exposed children lost to follow-up from a large HIV treatment program in western Kenya." *Journal of acquired immune deficiency syndromes (1999)* 57.3 (2011): e40.
34. Ciampa, Philip J., et al. "Improving retention in the early infant diagnosis of HIV program in rural Mozambique by better service integration." *JAIDS Journal of Acquired Immune Deficiency Syndromes* 58.1 (2011): 115-119.
35. Adebimpe, Wasiu O. "Challenges facing early infant diagnosis of HIV among infants in resource poor settings." *African journal of reproductive health* 17.1 (2013): 122-129.
36. Braun, Maureen, et al. "Inadequate coordination of maternal and infant HIV services detrimentally affects early infant diagnosis outcomes in Lilongwe, Malawi." *Journal of acquired immune deficiency syndromes (1999)* 56.5 (2011): e122.
37. UNAIDS, UNAIDS. "The gap report." Geneva, Switzerland(2014). Available from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf.

38. "Adolescents and Young People." UNICEF data, Nov. 2017. Available from: <https://data.unicef.org/topic/hivaids/adolescents-young-people/>.
39. NASCOP. "Welcome to CDC stacks | Kenya AIDS indicator survey 2012: KAIS : final report - 26189 | Stephen B. Thacker CDC Library collection." Centers for Disease Control and Prevention, June 2014, stacks.cdc.gov/view/cdc/26189.
40. Willis, N., et al. "'My story'—HIV positive adolescents tell their story through film." *Children and Youth Services Review* 45 (2014): 129-136.
41. Lowenthal, Elizabeth D., et al. "Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges." *The Lancet infectious diseases* 14.7 (2014): 627-639.
42. Bekker, Linda-Gail, et al. "Building our youth for the future." *Journal of the International AIDS Society* 18 (2015): 20027.
43. "Children, HIV and AIDS." AVERT, 6 Dec. 2017. Available from: www.avert.org/professionals/hiv-social-issues/key-affected-populations/children.
44. Available from: <http://uis.unesco.org/country/KE>.
45. Olds P.K, Kiwanuka JP, Nansera D, et al. Adherence to antiretroviral therapy in children and adolescents living with HIV. Last updated April 27, 2017. Available from: https://aidsinfo.nih.gov/contentfiles/glchunk/glchunk_83.pdf.
46. Musarandega, Reuben, et al. "PMTCT service uptake among adolescents and adult women attending antenatal care in selected health facilities in Zimbabwe." *Journal of acquired immune deficiency syndromes* (1999) 75.2 (2017): 148.
47. Kasedde, Susan, et al. "Reducing HIV and AIDS in adolescents: opportunities and challenges." *Current HIV/AIDS Reports* 10.2 (2013): 159-168. Available from: www.ncbi.nlm.nih.gov/pubmed/23563990.
48. Mavhu, Webster, et al. "Enhancing psychosocial support for HIV positive adolescents in Harare, Zimbabwe." *PloS one* 8.7 (2013): e70254.
49. Evans, Denise, et al. "Treatment outcomes of HIV-infected adolescents attending public-sector HIV clinics across Gauteng and Mpumalanga, South Africa." *AIDS research and human retroviruses* 29.6 (2013): 892-900.
50. Technau, Karl-Günter, et al. "Timing of maternal HIV testing and uptake of prevention of mother-to-child transmission interventions among women and their infected infants in Johannesburg, South Africa." *Journal of acquired immune deficiency syndromes* (1999) 65.5 (2014): e170.

51. Cook, Rebecca E., 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)* 56.4 (2011): e104.
52. Wettstein, Celina, et al. "Missed opportunities to prevent mother-to-child-transmission in sub-Saharan Africa: systematic review and meta-analysis." *AIDS (London, England)* 26.18 (2012): 2361.
53. Vrazo, Alexandra C., et al. "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." *Tropical Medicine & International Health* 23.2 (2018): 136-148.
54. Peltzer, K., and G. Mlambo. "Factors determining HIV viral testing of infants in the context of mother-to-child transmission." *Acta paediatrica* 99.4 (2010): 590-596.

LIST OF FIGURES AND TABLES

Figure 1. Flow chart of study participants abstracted from files

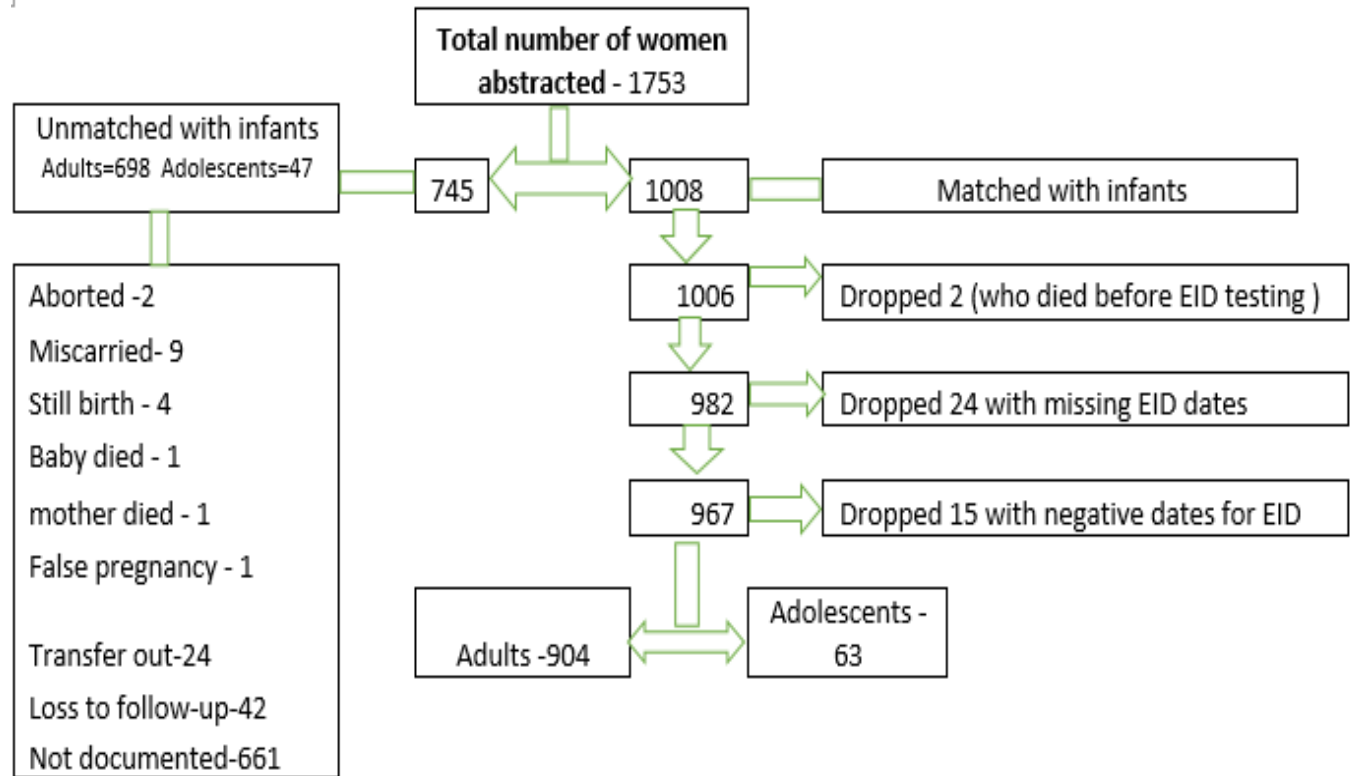


Table 1: Women and infant demographic and clinical characteristics

	Variable / Facility type	City n=388	Peri-Urban n=321	Rural n=258	Adults n=904	Adolescents n=63	Overall n=967
Mother	Mean age yrs (SD)	28.4(5.3)	27.0(5.4)	27.3 (5.4)	28.3 (4.9)	17.8 (1.6)	27.6 (5.4)
	Marital Status n(%)						
	Married	335 (86.6)	26 (86.0)	234 (90.7)	806 (89.3)	39 (61.9)	845 (87.5)
	Not Married	52 (13.4)	45 (14.0)	24 (9.3)	97 (10.7)	24 (38.1)	121 (12.5)
	Median ANC visits (min, max)	2 (1,11)	3 (1,7)	3 (1,7)	2 (1,11)	2 (1,5)	2 (1,11)
	<4 ANC visits n(%)	272 (75.8)	194 (66.9)	168 (66.1)	592 (70.1)	42 (72.4)	1273 (77.1)
	≥4 ANC visits n(%)	87 (24.2)	96 (33.1)	86 (33.9)	253 (29.9)	16 (27.6)	378 (22.9)
	Median gestation weeks (IQR) (last ANC)	32 (25,36)	32 (28,36)	32 (28,36)	32 (27,36)	30 (26, 34)	32 (27,36)
	Median gestation weeks (IQR) (1 st ANC)	20.6 (13.9, 26.9)	21.9 (17.3, 29.1)	22.3 (17.3, 28.7)	21.4 (15.9, 28.1)	22.5 (15.1, 27.9)	21.6 (15.7, 28.1)
	Attended ANC after week 16 n(%)	223 (64.5)	207 (76.7)	174 (76.7)	564 (71.5)	40 (74.1)	1,037 (67.7)
	Attended ANC by week 16 n(%)	123 (35.6)	63 (23.3)	53 (23.4)	225 (28.5)	14 (25.9)	495 (32.3)
	Parity n(%)						
	Nulliparous	48 (12.6)	51 (16.1)	28 (11.0)	89 (10.0)	38 (61.3)	253 (14.6)
	Multiparous	334 (87.4)	266 (83.9)	227 (89.0)	803 (90.0)	24 (38.7)	1,475 (85.4)
Median months since HIV diagnosis (IQR)	34.7 (0.9,69.6)	35.6 (1.5,73.0)	21.7 (2.4,71.8)	34.7 (2.6,73.0)	1.5 (0,19.3)	32.5 (1.5,71.1)	
Median months since ART initiation (IQR)	29.1 (1.3,62.2)	32.8 (2.7, 61.5)	29.8 (7, 69.1)	32.8 (3.7, 64.8)	3.2 (0, 21.7)	32.4 (2.8, 63.1)	
Disclosure n(%)							
No	60 (16.2)	70 (36.5)	27 (20.2)	137 (20.9)	20 (47.6)	157 (22.5)	
Yes	311 (83.8)	122 (63.5)	107 (79.9)	518 (79.1)	22 (52.4)	540 (77.5)	
Last viral load during pregnancy n(%)							
<LDL copies/ml	201 (71.3)	128 (56.6)	93 (46.5)	396 (60.0)	26 (54.2)	422 (59.6)	
<1000 copies/ml	56 (19.9)	74 (32.7)	77 (38.5)	190 (28.8)	17 (35.4)	207 (29.2)	
≥1000 copies/ml	25 (8.9)	24 (10.6)	30 (15)	74 (11.2)	5 (10.4)	79 (11.2)	
Infant	Gender n(%)						
	Female	184 (47.8)	158 (49.2)	141 (54.9)	458 (50.9)	25 (39.7)	483 (50.2)
	Male	200 (52.0)	163 (50.8)	116 (45.1)	441 (49)	38 (60.3)	479 (49.7)
	Male/Female	1 (0.3)			1 (0.1)		1 (0.1)
	On NVP n(%)						
	No	12 (3.7)	11 (3.5)	39 (15.1)	61 (7.3)	1 (1.7)	62 (6.9)
	Yes	314 (96.3)	304 (96.5)	219 (84.9)	778 (92.7)	59 (98.3)	837 (93.1)
	Median weeks at EID testing (IQR)	6.1 (6,6.4)	6.3 (6,7)	6.1 (6,6.7)	6.1 (6,6.6)	6.1 (6,6.9)	6.1 (6,6.6)
	HIV status n(%)						
	Negative	362 (98.9)	309 (98.0)	247 (99.2)	859 (99.3)	59 (95.2)	918 (99.0)
Positive	4 (1.1)	3 (1.0)	2 (0.8)	6 (0.7)	3 (4.8)	9(1.0)	
Number tested for HIV							
once	126 (32.5)	69 (21.5)	67 (26.0)	247 (27.3)	15 (23.8)	262 (27.1)	
2 times	123 (31.7)	95 (29.6)	97 (37.6)	290 (32.1)	25 (39.7)	315 (32.6)	
3 times	72 (18.6)	83 (25.9)	61 (23.6)	201 (22.2)	15 (23.8)	216 (22.3)	
4 times	67 (17.3)	74 (23.1)	33 (12.8)	166 (18.4)	8 (12.7)	174 (18.0)	
EID Uptake n(%)							
No	42 (10.8)	48 (15.0)	38 (14.7)	118 (13.1)	10 (15.9)	128 (13.2)	
Yes	346 (89.2)	273 (85.1)	220 (85.3)	786 (87.0)	53 (84.1)	839 (86.8)	

*no missing data where not indicated

Table 2: Factors associated with EID uptake in univariable and multivariable analysis

Variable	Univariate analysis*			Multivariable analysis		
	Crude RR	95% CI	p-value	Adjusted RR	95% CI	p-value
Women	Adults	ref				
	Adolescents	0.977	(0.875, 1.090)	0.675		
Mother's age (years)		1.002	(0.998, 1.007)	0.373	1.001	(0.995, 1.006) 0.855
Facility type	urban/City	ref				
	Peri-Urban	0.954	(0.900, 1.010)	0.106	0.989	(0.931, 1.050) 0.713
	Rural	0.956	(0.899, 1.017)	0.153	0.996	(0.936, 1.059) 0.887
Parity	Nulliparous	ref				
	Multiparous	1.072	(0.984, 1.167)	0.111	1.004	(0.916, 1.100) 0.933
Months since ART initiation		1.001	(1.000, 1.001)	0.003	1.001	(1.000, 1.001) 0.039
Infant on NVP	No	ref				
	Yes	1.18	(1.017, 1.366)	0.029	1.152	(0.994, 1.335) 0.061
Marital status	Married	ref				
	Unmarried	0.999	(0.928, 1.075)	0.979		
ANC Visits	< 4 visits	ref				
	≥ 4 visits	0.991	(0.938, 1.047)	0.750		
Gestation in weeks at last ANC		1.000	(0.997, 1.003)	0.983		
Gestation in weeks at 1st ANC	Attended ANC after week 16	ref				
	Attended ANC by week 16	0.980	(0.925, 1.039)	0.495		
Last VL result	< LDL copies/ml	ref				
	< 1000 copies/ml	0.978	(0.916, 1.044)	0.505		
	≥ 1000 copies/ml	1.029	(0.953, 1.112)	0.466		
HIV disclosure to partner	No	ref				
	Yes	0.999	(0.935, 1.067)	0.969		

*Facility type is adjusted for in all univariate analysis

Figure 2: Early infant HIV diagnosis uptake across different facilities

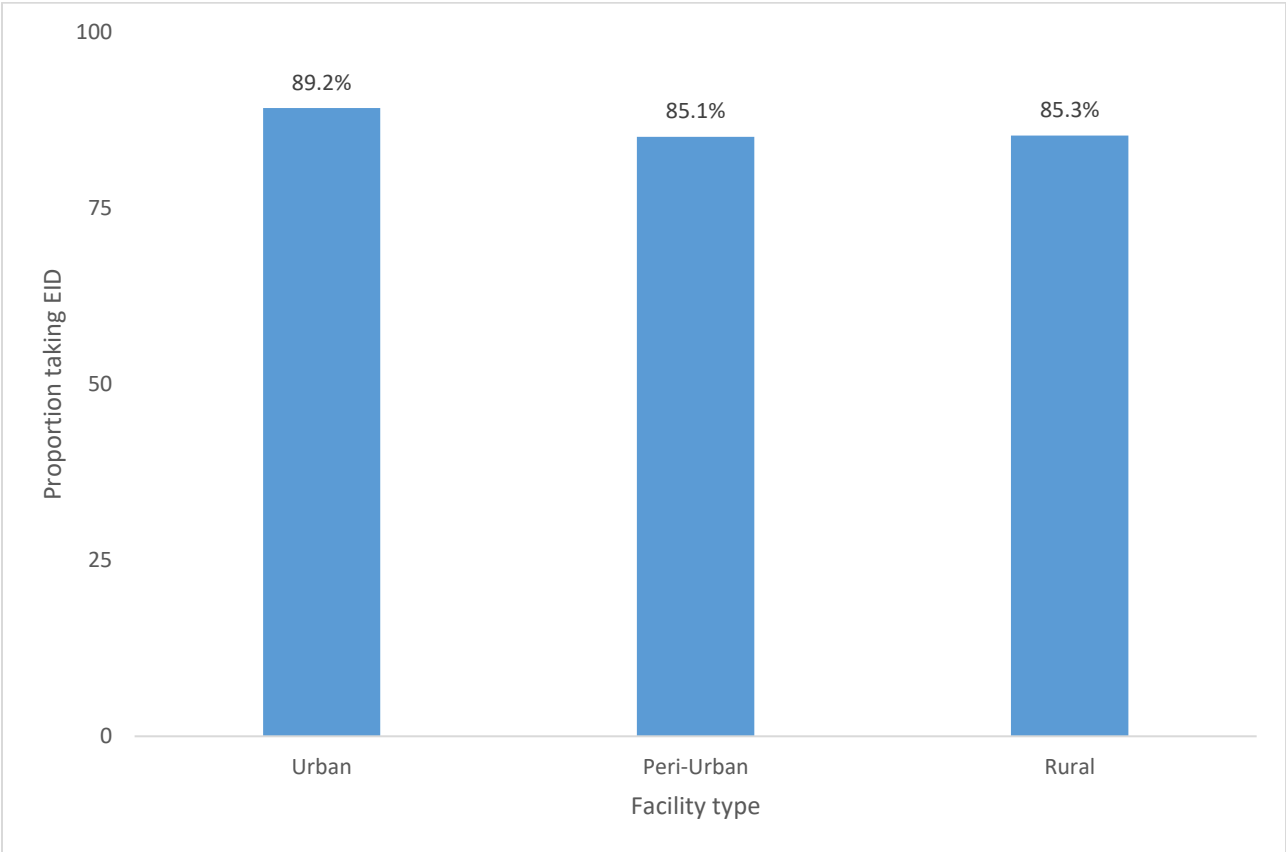


Figure 3: Early infant HIV diagnosis uptake between adolescents and adult mothers

