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ORIGINAL ARTICLE | PEDIATRIC HIV

Associations of Sociodemographic and Clinical Factors with Late Presentation for Early Infant HIV Diagnosis (EID) Services in Kenya

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ABSTRACT

Background: Understanding the missed opportunities in early infant HIV testing within the PMTCT program is essential to address any gaps. The study set out to describe the clinical and sociodemographic characteristics of the infants presenting late for early infant diagnosis in Kenya.

Methods: We abstracted routinely collected clinical and sociodemographic characteristics, in a cross-sectional study, on all HIV-infected infants with a positive polymerase chain reaction (PCR) test from 1,346 President's Emergency Plan for AIDS Relief (PEPFAR) supported health facilities for the period October 2016 to September 2018. We used multivariate logistic regression to examine the association of sociodemographic and clinical characteristics with late (>2 months after birth) presentation for infant HIV testing.

Results: Of the 4,011 HIV-infected infants identified, the median infant age at HIV diagnosis was 3 months [interquartile range (IQR), 1-16 months], and two-thirds [2,669 (66.5%)] presented late for infant HIV testing. Factors that were associated with late presentation for infant testing were: maternal ANC non-attendance, adjusted odds ratio (aOR) 1.41 (95% confidence interval (CI) 1.18 -1.69); new maternal HIV diagnosis, aOR 1.45, (95%CI 1.24 -1.7); and lack of maternal antiretroviral therapy(ART), aOR 1.94, (95% CI 1.64 - 2.30). There was a high likelihood of identifying HIV-infected infants among infants who presented for medical services in the outpatient setting (aOR 18.9; 95% CI 10.2 - 34.9) and inpatient setting (aOR 12.2; 95% CI 6.23-23.9) compared to the infants who presented late in maternity.

Conclusion and Global Health Implications: Gaps in early infant HIV testing suggest the need to increase maternal pre-pregnancy HIV diagnosis, timely antenatal care, early infant diagnosis services, early identification of mothers who seroconvert during pregnancy or breastfeeding and improved HIV screening in outpatient and inpatient settings. Early referral from the community and access to health facilities should be strengthened by the implementation of national PMTCT guidelines.

Keywords: • Antenatal Care • EID • HIV • Early Infant Testing • PMTCT • Antiretroviral Treatment • Kenya

1. Introduction

Prevention of mother-to-child transmission (PMTCT) of Human Immuno-deficiency Virus (HIV) is among the highest priorities of national HIV programs in sub-Saharan Africa. While PMTCT services have greatly reduced mother-to-child transmission of HIV (MTCT) since the beginning of the global HIV response, over 90% of the new pediatric infections result from MTCT.[1] In 2019, there were over 150,000 new pediatric infections worldwide, with 110,000 of these within the 21 focus countries (prioritized under the Global Plan) and; >90% are estimated to occur in sub-Saharan Africa.[2] Kenya contributes around 6,600 (6%) of the cases among the Joint United Nations Programme on HIV/AIDS (UNAIDS) Start Free, Stay Free, AIDS-Free twenty-one focus countries.[2]

In 2011, UNAIDS/World Health Organization (WHO) launched the "Global Plan Towards the Elimination of New HIV Infections Among Children and Keeping Their Mothers Alive," [3] followed in 2015 by "Start Free, Stay Free, AIDS-Free framework for ending AIDS in children, adolescents, and young women by 2020."[2] Both initiatives focus on universal access to lifelong maternal antiretroviral therapy (ART), provision of ART prophylaxis to HIV-exposed infants (HEI), and timely access to early infant diagnosis by 2 months of age and initiation of ART treatment among HIV-infected infants. With the adoption of these frameworks, Kenya prioritized rapid scale-up of PMTCT and pediatric HIV services, aiming to reach and sustain 95% of pregnant women living with HIV accessing lifelong HIV treatment by 2030, and to reach 95% of HIV-exposed infants with early infant diagnosis services within 2 months of birth.[4] Between 2015 and 2019, ART coverage among pregnant women in Kenya increased from 59% to 94%, while infant infections subsequently declined by 26% from 9,200 in 2015 to 6,800 in 2019.[5,6] Early infant diagnosis (EID) coverage at 2 months also increased from 53% in 2015 to 69% in 2019;[6] falling short of Kenya's ambitious targets.

EID among HIV-exposed infants is a critical component of the PMTCT program. HIV-infected infants have a 35% risk of death in the first year and a 50% risk in the second year of life and hence, WHO recommends that national programs establish the capacity to provide early virologic testing of infants for HIV.[7] The goal of early infant HIV testing is to identify infected infants and start them on treatment early to reduce their morbidity and mortality.[7]

As global stakeholders focus on the elimination of mother-to-child transmission of HIV (EMTCT) and syphilis goals, a systematic approach to learning from cases of missed opportunities within a PMTCT program will be essential to address remaining gaps in coverage of key services.[2] These persistent gaps in PMTCT program performance prompted us to identify a need for further understanding of where the "leaks" occur in the PMTCT cascade.[8,9] This paper set out to describe the clinical and sociodemographic characteristics of the infants presenting late for EID to provide a deeper understanding of the delays of early infant HIV testing in Kenya.

2. Methods

2.1. Setting and Population

We implemented a cross-sectional study at 1,346 Government of Kenya health facilities that offer PMTCT services. These facilities were chosen because they offer services to approximately 80% (62,477) of the HIV-infected pregnant population and receive support through PEPFAR.[10] The country is further divided by the Ministry of Health, into three groups of counties – high, medium, and low-HIV burden counties based on geographical disparities in HIV incidence and the proportion of people living with HIV where these facilities are located, for more focused strategies for epidemiological control.[11]

2.2. Study Design

We abstracted clinical and sociodemographic data for both mother and infant pairs from the facility-based HIV exposed infant (HEI) registers and maternal medical records that are used by the Kenya Ministry of Health (MOH) for routine data collection at the PMTCT health facilities. We included all infant records that had an HIV-infected infant with a positive polymerase chain reaction (PCR) test result between October 2016 and September 2018.

Infant records that did not have a date of birth were excluded from the analysis.

2.3. Routine Procedures/Standard of Care

Standard PMTCT care for HEI and their mothers in Kenya is provided through integrated maternal child health (MCH)-PMTCT clinics for antenatal (ANC) and postnatal services (PNC). The standard package of care includes: a) HIV testing for pregnant and breastfeeding women who are not already known to be HIV-positive; b) ART for all HIV-positive pregnant women; c) EID by 2 months and initiation of ART for HIV-infected infants; d) provision of ARV prophylaxis, cotrimoxazole; and e) immunization at an appropriate age for the HEI. In Kenya, EID is done at 6 weeks and this aligns with 6 weeks immunization program. A mother bringing her infant 2 weeks later, at 8 weeks is still considered to fall under this timeline of early EID by 2 months. Kenya's national guidelines have supported same-day or the rapid start of ART for pregnant and breastfeeding women (PBFW) since 2014,[12] also referred to as Option B+. Infant testing is done as soon as the caregiver brings an HIV-exposed infant to the MCH-PMTCT clinic in accordance with the national guidelines.

During clinical visits, data are recorded on the relevant MOH tools, including PCR tracking log registers, HEI and ANC registers, clinical cards, and medical records. PEPFAR implementing partners provide mentorship and technical assistance to the facility health care workers to complete the MOH tools during their monthly supervision visits, assessing the quality of data collected and using it to assess gaps.

2.4. Study Variables

2.4.1. Dependent variable

The primary outcome of interest was time at presentation for early infant HIV testing. It can be used as an indicator of achievement of other cascade components and represents the final entry point for PMTCT services. Early infant testing is defined as a first HIV PCR test at or less than two months. Late infant testing was defined as any PCR testing done after 2 months of age.

2.4.2. Independent variables

Age of infant at enrollment for HEI services, entry point to care for other medical services, maternal age, mother's attendance to ANC, HIV status of the mother at presentation for MCH services, provision of maternal ART, timing of maternal ART initiation, disclosure of HIV status and location of delivery were examined as independent variables. Mothers' HIV status at presentation to MCH clinic was classified in the clinic registers as "known HIV positive" if she was diagnosed before this pregnancy and documented as "newly diagnosed" if she was diagnosed with HIV at her first visit (presentation) to the MCH clinic for this pregnancy.

2.5. Data Collection and Processing

A structured data extraction tool was developed and used to collect data from the medical charts, clinical cards (HEI card, HIV clinic cards), and registers (HEI, PCR, tracking log/antenatal registers). We abstracted sociodemographic characteristics, maternal ANC attendance, data on maternal ART and infant ARV prophylaxis. No personally identifiable information from medical registers was included. The data were cleaned and imported into Stata version 14.0 (Stata Corporation, College Station, Texas) for processing and analysis.

2.6. Statistical Analysis

We used descriptive statistics to show the distribution of sociodemographic and key clinical outcome data for the HIV-infected infants and their mothers. To assess the difference between the infants who received early versus late testing**,** we tested for the independence of proportions for categorical variables using Pearson's Chi-square test. We used the Little's test to determine if data were missing completely at random. Since the data were missing completely at random, we performed multinomial logistic regression through a Bayesian process to impute missing values by running 10 iterations conducted using Markov Chain Monte Carlo (MCMC) simulations implemented in Stata's *mi impute chained (mlogit)* procedure.[13] This procedure assumes that all the variables in the imputation model have a joint multivariate

normal distribution. For the unadjusted logistic regression model, the factors were selected *a priori* for comparability because they were relevant for programmatic interpretation. Significant covariates at $p<0.05$ level were then fitted into a multivariable logistic regression model. We additionally assessed for collinearity of factors and determined that the factors included in the multivariate model were not collinear. The protocol for the study was approved by the Kenya Medical Research Institution Scientific Ethical Review (KEMRI) Unit protocol # KEMRI/SERU.CCR/0108/3705 and the Regional Committee for Medical and Health Research Ethics West in Norway (2018/943/REK West). It was also reviewed in accordance with the U.S. Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined as research, but the CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes. Waiver of consent for this analysis was received from KEMRI.

3. Results

3.1. Sociodemographic Characteristics

A total of 4,091 HIV-infected infants were identified, 4,011 (98.0%) had a date of birth recorded and were included in the analysis. Of these, 2,109 (52.6%) were females and 1,790 (44.6%) of the infants came from 496 facilities in high HIV burden counties, 1,359 (33.9%) from 512 facilities in medium HIV burden counties, and 862 (21.5%) from the 338 facilities in low HIV burden counties.

3.2. Characteristics of the HIV-Infected Infants

Of the 4,011 HIV-infected infants, two-thirds [2,669 (66.5%)] presented late for infant HIV testing and the median infant age at initial presentation for infant HIV testing was 3 months [interquartile range (IQR), 1-16 months].

Most of the HIV-infected infants (2,783 or 69.4%) were identified from the integrated MCH-PMTCT clinic with an additional 13.3% (533) identified in other outpatient departments (OPD), 6.3% (251) identified in the pediatric inpatient wards and 269 (6.7%) were identified through the HIV clinic. Most of the infants received cotrimoxazole (3,060 or 76.3%), and infant ARV prophylaxis 2,592 (64.6%). Many of the infants were on schedule for their immunization as age-appropriate, 3,054 (76.1%). Almost seventy-nine percent [3,159 (78.8%)] were linked to HIV clinics and started on ART; 6.6% (264) were documented as lost to follow-up in the clinic records and 6.1% (245) were reported as dead (Table 1).

3.3. Characteristics of the Mothers of the HIV-Infected Infants

Almost 60% of the mothers of HIV-infected infants (2,398/4,011 or 59.8%) were newly diagnosed as HIV-infected (Figure 1). Slightly over half 52.4% [1,993/3,806] of the mothers with age recorded infants were aged 25-34 years and a median age of 27 years (23 -31 IQR). Only 55.3% (2,220/4,011) had attended antenatal care (ANC) and 44.9% (1,800/4,011) had received maternal ART in the antenatal period. Of the mothers who were started on ART, 50.2% (2,012/4,011) were started on ART in the postnatal period (Table 2).

3.4. Factors Associated with Late Presentation for Infant HIV Testing

Factors that were independently associated with late presentation for infant testing among the population of HIV-infected infants were maternal ANC non-attendance, adjusted odds ratio (aOR) 1.41 [95% confidence interval (CI) 1.18 -1.69]; new maternal HIV diagnosis, aOR 1.45, (95% CI 1.24 -1.7); and lack of maternal ART, aOR 1.94, (95% CI 1.64 - 2.30). There was a higher odds of identifying HIV-infected infants among infants who presented for medical services in the outpatient (aOR 18.9; 95% CI 10.2 - 34.9) and inpatient (aOR 12.2; 95% CI 6.23-23.9) compared to the infants who presented late in the maternity and also those late for immunization (aOR 1.57, 95% CI:1.26-1.95) (Table 3).

4. Discussion

Two-thirds of the HIV-infected infants in our study presented late to the health facility for infant HIV testing. Our findings indicate that they were late to access the healthcare system, as shown through the late maternal presentation to ANC, new maternal HIV diagnoses during pregnancy, late presentation of infants

Table 1: Characteristics of HIV-infected infants and timing of infant HIV testing, 2016-2018 Kenya

Characteristic	Overall N= 4,011	Early infant HIV testing (< 2 months)	Late infant HIV testing (>2 months)	p-value
	n (%)	N= 1,342 (33.5%) n (%)	N=2,669 (66.5%) n (%)	
County HIV-burden group				0.31
High	1,790 (44.6)	606 (45.2)	1,184 (44.4)	
Medium	1,359 (33.9)	466 (34.7)	893 (33.5)	
Low	862 (21.5)	270 (20.1)	592 (22.2)	
Entry point to infant testing				<0.001
Maternity	74 (1.8)	52 (3.9)	22 (0.8)	
MCH-PMTCT clinic*	2,783 (69.4)	1,127 (84.0)	1,656 (62.0)	
HIV clinic	269 (6.7)	84 (6.3)	185 (6.9)	
Outpatient	533 (13.3)	37 (2.8)	496 (18.6)	
Inpatient ward	251 (6.3)	23 (1.7)	228 (8.5)	
Other	86 (2.1)	12 (0.9)	74 (2.8)	
Missing	15 (0.4)	7 (0.5)	8 (0.3)	
Received infant cotrimoxazole				<0.001
Yes	3,060 (76.3)	1,202 (89.6)	1,858 (69.6)	
No	914 (22.8)	132 (9.8)	782 (29.3)	
Missing	37 (0.9)	8 (0.6)	29 (1.1)	
Received infant ARV prophylaxis				<0.001
Yes	2,592 (64.6)	1,149 (85.6)	1,443 (54.1)	
No	1,314 (32.8)	152 (11.3)	1,162 (43.5)	
Missing	105 (2.6)	41 (3.1)	64 (2.4)	
Immunization status				<0.001
On schedule	3,054 (76.1)	1,131 (84.3)	1,923 (72.0)	
Not on schedule	663 (16.5)	145 (10.8)	518 (19.4)	
Missing/Not done	294 (7.0)	66 (4.9)	228 (8.5)	
Infant outcome**				0.03
Discharged	31 (0.8)	16 (1.2)	15 (0.6)	
Linked to HIV clinic	3,159 (78.8)	1,076 (80.2)	2,083 (78.0)	
Transfer out	213 (5.3)	66 (4.9)	147 (5.5)	
Lost to follow up	264 (6.6)	89 (6.6)	175 (6.6)	
Dead	245 (6.1)	67 (5.0)	178 (6.7)	
Other	42 (1.0)	9 (0.7)	33 (1.2)	
Missing	57 (1.4)	19 (1.4)	38 (1.4)	

*MCH-PMTCT Maternal Child Health-Prevention of mother to child transmission clinics; **infant outcome at the time of data collection

for HIV testing. In this sense, they were 'late-comers' to the health system after the recommended 2 months of age in the Kenya PMTCT guidelines.[4] The median age of infant presentation for testing was 3 months, which is an improvement from a similar study in Kenya done in 2008, in which the median age at enrollment to the HEI program was 5.0 months.[14] Beginning in 2005 Kenya has scaled up a robust EID program, and by the end of 2019, the number of HIV-exposed infants tested for HIV using PCR had increased from 52% to 69%[2,5]; however, less than 65% of those tested received EID within the recommended 2 months.[6]

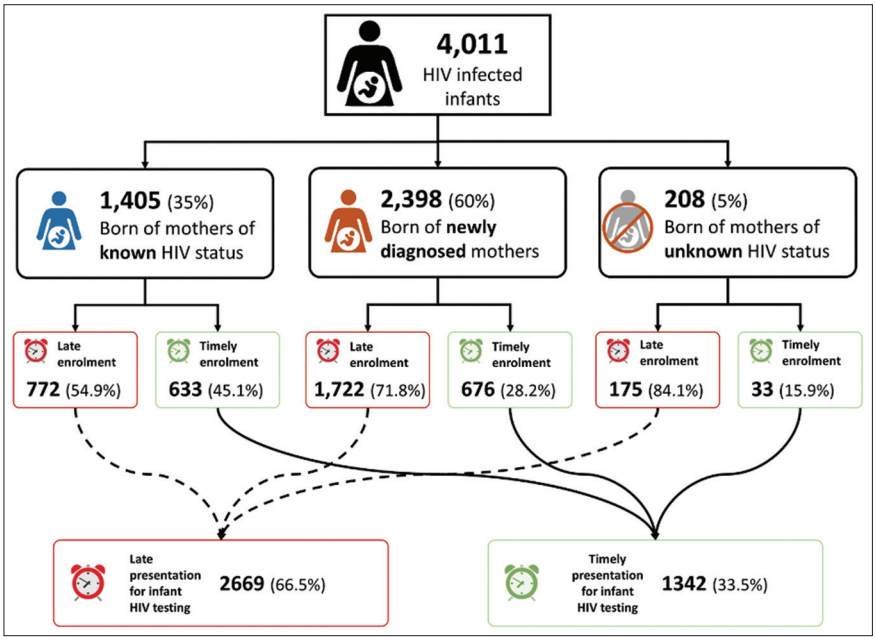

Figure 1: Mothers' HIV status at enrollment of HIV-infected infants into the HIV Exposed Infants (HEI) program and timing of infant HIV testing, 2016-2018, Kenya

While most Kenyan mothers attended ANC, with overall ANC attendance of at least one visit (~96%), only 20% had their first ANC in the first trimester.[15] The remaining 4% in the demographic survey may be contributing to the significant number of HIV-infected infants. Our study found that just under half of mothers with HIV-infected infants were late or did not attend an ANC during their last pregnancy. Mothers who have been engaged in PMTCT by attending the ANC services early benefit from receiving antenatal counseling that would underscore the importance of infant services and maternal re-testing during follow-up among mothers who are HIV-negative.[16] A study in Kenya found that the odds of very late infant testing (>3 months of age) were nearly 70% lower among mothers whom a healthcare provider had counseled during pregnancy. Counseling of mothers in the antenatal period provides important information for the mother for her care during pregnancy and for the infant on breastfeeding and early infant testing.[9,17] Our findings are consistent with a similar study done in Kenya and Uganda, which reported missed opportunities to prevent MTCT and diagnose HIV-infected children, including gaps in ANC attendance, re-testing during pregnancy and breastfeeding, initiation of maternal ARVs, and delays in HIV testing for the HIV exposed children.[8] This underscores the need for strategies to improve ANC access during the earlier stages of pregnancy among women that have not been reached by PMTCT services.

The Kenya guidelines advocate for early and repeat HIV testing of mothers in ANC and those found to be HIV-infected should start on ART immediately, even as early as 14 weeks.[12] However, if mothers are not accessing health services, they do not benefit from these services. Many of the mothers of HIV-infected infants were started on ART in the postnatal period indicating that these mothers were newly diagnosed during this period. Such late presentation demonstrates a combination of missed diagnosis from previous infections and incidents of HIV infections during breastfeeding in the postpartum period which increases the risk of HIV transmission to their infants when compared to women with chronic infection.[18,19] This indicates the importance of additional efforts to encourage the

Table 2: Characteristics of the mothers of HIV-infected infants, 2016-2018 Kenya

Characteristics	Overall N = 4,011		Early infant HIV testing (< 2 months)		Late infant HIV testing (>2 months)		p-value
	n (%)		N = 1,342 (33.5%) n (%)		N = 2,669 (66.5%) n (%)		
Mother's age							0.003
<20 years	263	6.6%	97	7.2%	166	6.2%	
20-24 years	1,077	26.9%	322	24.0%	755	28.3%	
25-34 years	1,993	49.7%	702	52.3%	1,291	48.4%	
>=35 years	473	11.8%	180	13.4%	293	11.0%	
Missing	205	5.1%	41	3.1%	164	6.1%	
Mother attended antenatal clinic							<0.001
Yes	2,220	55.3%	962	71.7%	1,258	47.1%	
No	1,587	39.6%	340	25.3%	1,247	46.7%	
Missing	204	5.1%	40	3.0%	164	6.1%	
Mother's HIV status							<0.001
Known HIV positive	1,405	35.0%	633	47.2%	772	28.9%	
Newly diagnosed	2,398	59.8%	676	50.4%	1,722	64.5%	
Missing/unknown	208	5.2%	33	2.5%	175	6.6%	
Mother had ART in antenatal (ANC)							<0.001
Yes	1,800	44.9%	903	67.3%	897	33.6%	
No	1,831	45.6%	362	27.0%	1,469	55.0%	
Missing	380	9.5%	77	5.7%	303	11.4%	
Timing of mother's ART initiation							<0.001
Before Pregnancy	54	1.3%	27	2.0%	27	1.0%	
1st trimester	401	10.0%	221	16.5%	180	6.7%	
2nd trimester	332	8.3%	192	14.3%	140	5.2%	
3rd trimester	436	10.9%	244	18.2%	192	7.2%	
Labor & delivery	114	2.8%	60	4.5%	54	2.0%	
Postnatal	2,012	50.2%	397	29.6%	1,615	60.5%	
Missing	662	16.5%	201	15.0%	461	17.3%	
Maternal/neonatal PMTCT regimen							0.002
Option B+ (HAART)[1]	3,512	87.6%	1,230	91.7%	2,282	85.5%	
sdNVP[2]	6	0.1%	1	0.1%	5	0.2%	
Option A (AZT + NVP + 3TC)[3]	31	0.8%	15	1.1%	16	0.6%	
Option B4	10	0.2%	1	0.1%	9	0.3%	
None	103	2.6%	19	1.4%	84	3.1%	
Other	73	1.8%	22	1.6%	51	1.9%	
Missing	276	6.9%	54	4.0%	222	8.3%	
Place of delivery							<0.001
Facility delivery	2,299	57.3%	893	66.5%	1,406	52.7%	
Home	1,494	37.2%	403	30.0%	1,091	40.9%	
Missing	218	5.4%	46	3.4%	172	6.4%	

[1]HAART-Highly Active Antiretroviral Therapy; [2]sdNVP-single dose Nevirapine; 3AZT – Zidovune NVP- Nevirapine [3]TC – Lamivudine; [4]Option B- interrupted HAART

Tables 3: Factors associated with late infant HIV testing among HIV-infected infants in Kenya, 2016-2018

Characteristic	Total (n=4011)	%	Unadjusted odds ratios		Adjusted odds ratios	
			OR (95% CI)	p-value	aOR (95% CI)	p-value
County HIV- level burden classes						
High	1,790	45%	Ref.			
Medium	1,359	34%	0.98 (0.85-1.14)	0.79		
Low	862	21%	1.12 (0.94-1.34)	0.19		
Entry point to infant testing						
Maternity*	77	2%	Ref.		Ref.	
MCH/PMTCT1 clinic	2,791	70%	3.24 (1.99-5.27)	<0.001	3.47 (2.07-5.81)	<0.001
HIV clinic	270	7%	4.89 (2.83-8.45)	<0.001	4.85 (2.72-8.67)	<0.001
Outpatient	535	13%	29.72 (16.5-53.4)	<0.001	18.9 (10.2-34.9)	<0.001
Pediatric inpatient ward	252	6%	20.98 (11.1-39.8)	<0.001	12.2 (6.23-23.9)	<0.001
Other	86	2%	13.62 (6.26-29.6)	<0.001	10.3 (4.56-23.2)	<0.001
Received Cotrimoxazole						
Yes*	3,090	77%	Ref.		Ref.	
No	921	23%	3.85 (3.16-4.69)	<0.001	1.01 (0.77-1.32)	<0.95
Received Infant ARV prophylaxis						
Yes*	2,674	67%	Ref.		Ref.	
No	1,337	33%	5.83 (4.86-6.99)	<0.001	3.3 (2.60-4.20)	<0.001
Immunization status						
On schedule*	3,129	78%	Ref.		Ref.	
Not on schedule	690	17%	2.07 (1.70-2.51)	<0.001	1.57 (1.26-1.95)	<0.001
Unknown	192	5%	2.01 (1.42-2.84)	<0.001	1.21 (0.81-1.80)	0.34
Mother's age						
<20 years	284	7%	Ref.			
20-24 years	1,129	28%	1.40 (1.07-1.84)	0.01		
25-34 years	2,100	52%	1.13 (0.87-1.46)	0.35		
>=35 years	498	12%	0.98 (0.73-1.33)	0.91		
Mother attended antenatal clinic						
Yes*	2,326	58%	Ref.		Ref.	
No	1,685	42%	2.70 (2.34-3.12)		1.41 (1.18-1.69)	<0.001
Mother's HIV status						
Known HIV positive*	1,468	37%	Ref.		Ref.	
Newly diagnosed positive	2,543	63%	2.07 (1.82-2.39)	<0.001	1.45 (1.24-1.70)	<0.001
Mother had ART in antenatal (ANC)						
Yes*	1,945	48%	Ref.		Ref.	
No	2,066	52%	3.93 (3.42-4.53)	<0.001	1.94 (1.64-2.30)	<0.001
Place of delivery						
Hospital*	2,420	60%	Ref.		Ref.	
Home	1,591	40%	1.73 (1.50-1.98)	<0.001	1.1 (0.93-1.30)	0.26

[1]MCH-PMTCT Maternal Child Health-Prevention of mother to child transmission clinics **infant outcome at the time of data collection

mothers to come for early ANC services, as they would receive health counseling about the benefits of early ART in pregnancy, early infant testing, and prophylaxis for prevention.[20]

The majority (70%) of the HIV-infected infants were identified at the MCH-PMTCT clinics where immunization services are provided as part of the integration of services. A large proportion of HIV-infected infants diagnosed late were on schedule for age-appropriate immunizations. This could suggest there may be opportunities to improve EID with strategies to better integrate immunization services with early infant HIV testing in Kenya.[21] Some studies have shown that HEI services integrated within the immunization timepoints are optimal for healthcare workers to identify any missed opportunities for maternal testing/re-testing and infant HIV testing.[22,23] Despite many of the HIV-infected infants being identified at the MCH in our study, other infants were still being identified at other service entry points in the health facilities like the OPD and IPD. Infants enrolled from OPD and IPD service points are likely to be symptomatic infants and may have missed earlier testing and ART initiation opportunities, and these care costs may be averted if the early diagnosis had been made.[24,25] In areas where PMTCT programs are successful, most of the HIV-infected infants identified in the OPD and IPD will be born from mothers who do not access PMTCT services.[26,27] This indicates room for improvement in the screening strategies of clinical departments that serve children to enhance the identification of HIV-infected infants.

There are some limitations to our study. First, we analyzed data of mother-infant pairs who came to the healthcare facilities. Therefore, we missed infants who were not delivered at health facilities or brought in for other health services post-delivery. Consequently, we cannot estimate the actual number of HIV-infected infants who did not come into the facility at all. Secondly, we only collected data from an HIV-infected population, and therefore, we did not have an HIV-exposed but HIV-negative population as a comparison group. Thirdly, the use of secondary data abstracted from records has its limitations with missing data. While insights may be limited due to the constraints of information collected in routine program documentation, the aggregate information from these case reviews has the potential to inform strategic program shifts, improve overall quality in the delivery of services, identify system improvements to further strengthen services, and ultimately, contribute to the achievement of the Kenyan EMTCT goals.

5. Conclusion and Global Health Implications

Gaps in early infant HIV testing suggest, more attention is needed on the mother-infant dyad 'late-comers' to the Kenyan healthcare system. There is a need to increase early attendance in antenatal care, maternal pre-pregnancy HIV diagnosis, early identification of mothers who seroconvert during pregnancy or breastfeeding, and early infant diagnosis during the first 2 months after birth, in addition, there is a need for interventions like pre-exposure prophylaxis in breastfeeding women who have an increased risk of acquiring HIV.[27] PMTCT programs may need to address this by working with community programs to improve linkages between the community and the health facilities.[28,29] There is also a need for wider HIV screening in outpatient and inpatient clinical care settings to identify infants living with HIV who were previously missed in the MCH clinics. PMTCT programs should aim to reduce any missed opportunities to identify mothers and infants in the community, offer early referral and enable access to the health facilities by strengthening the implementation of the national PMTCT guidelines.[4,30]

Compliance with Ethical Standards

Conflicts of Interest: *The authors declare no conflict of interest.* ***Financial disclosure:*** *The authors had no financial disclosure to declare.* ***Funding/Support:*** *This study was supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Centers for Disease Control and Prevention (CDC), Division of Global HIV and TB (DGHT) under the cooperative agreement [NU 2GG H001953-02-00].* ***Ethics Approval:*** *The protocol for the study was approved by the Kenya Medical Research Institution Scientific Ethical Review Unit # KEMRI/SERU.CCR/0108/3705, and the Regional Committee for Medical and Health Research Ethics West in Norway (2018/943/REK West). It was also reviewed in accordance with CDC human research protection procedures and was determined as research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.*

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Key Messages

- Many mothers who had an HIV-infected infant had missed opportunities for critical services in PMTCT programs, hence more attention is needed on these 'late-comers.'
- More efforts are needed for women to know their HIV status before getting pregnant and identify women living with HIV who and do not come for early antenatal services and counseling on EID services for their infants.
- Facility services need to provide wider HIV screening in outpatient and inpatient clinical care settings to identify infants living with HIV who were previously missed in the MCH clinics.

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