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Determinants of Late Sero-Conversion Time among HIV Exposed Infants Aged 6 Weeks-24 Months in Homabay County, Kenya: A 7-Year Retrospective Analysis

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Abstract – Background: **Despite the scale-up and proven efficacy of the prevention of mother to child transmission (PMTCT), the intervention has failed to achieve virtual elimination of HIV infection among exposed infants in Kenya. This study investigated the determinants of late sero-conversion time among a retrospective cohort of HIV exposed infants who subsequently seroconverted between 2010 and 2017.** ***Methods:*** **Institution based retrospective follow up study was carried out at nine health facilities in Mbita and Suba sub-counties. The maternal child health registers and electronic databases were used to identify the mother-baby pair. Data abstraction was done using a tool developed by adopting the Kenya Ministry of Health's national HIV exposed infant follow-up card. Data entered in an excel spreadsheet, checked for completeness, imported and analyzed using STATA version 14. Chi-square ($\chi 2$) followed by binary and multivariate logistic regression were carried out to identify the association.** ***Results:*** **Out of 254 infant-mother-pair information, most (53.4%) of infants were aged between 0-6 months and the majority (52%) seroconverted late. Maternal secondary level of education reduced the risk of sero-conversion by 83% (aOR = 0.17; 0.34-0.87 p<0.034) while parity of 3-5 (aOR = 3.48; 1.22-9.93 p<0.020), late infant diagnosis time (aOR = 19.36; 3.5-105.57 p<0.001) and home delivery though not statistically significant (aOR = 1.66; 0.60- 4.60 p<0.327) increased the risk of sero-conversion.** ***Conclusion:*** **There is a high risk of MTCT among children exposed to HIV in Homabay County. The findings reveals that maternal education, parity, late infant diagnosis time and home delivery are determinants of late sero-conversion. This study provides valuable information for policymakers to strengthen and upscale PMTCT especially targeting community and facility linkage for retention of both mother and baby in care.**

Keywords **– HIV Epidemiology, Virtual Elimination Challenges, Late Sero-Conversion, Prevention of Mother to Child Transmission, HIV Exposed Infants, Kenya Option B+, Lost to Follow-Up, Pediatric Prophylaxis.**

I. INTRODUCTION

Estimates indicate that Mother-To-Child Transmission (MTCT) is the major route of new pediatric HIV infections, an estimated 370,000 were newly infected, pausing a serious challenge to public health systems globally [1]. There is an increased risk of MTCT in both breastfeeding (15-30%) and non-breastfeeding (5-20%) HIV-infected mothers without intervention[2]. Sub-Saharan Africa bears the brunt of this infection with 59% of children below 14 years living with HIV found in East and South Africa [3, 4]. For example, Kenya has the fifth- highest HIV-incidences among children in Sub-Saharan Africa [5]. Thus to mitigate the effects of MTCT in low and middle - income countries the World Health Organization (WHO) issued various PMTCT strategies [2, 6].

To ensure reduction and move towards elimination of vertical transmission, Kenya adopted UNAIDs four-pronged strategy that entails; preventing HIV infection among women of reproductive; preventing unintended pregnancies in women living with HIV; prevention of mother-to-baby HIV transmission; and provision of treatment and support to mothers living with HIV and their babies [7, 8]. Additionally, the country initiated Early Infant Diagnosis (EID) in 2004 and the lifelong use of ART (Option B+) for all HIV-infected pregnant and breastfeeding women in 2014 [2, 9]. The implementation of these programs has significantly reduced incidences of HIV infections among 0–14-year-olds leading Kenya to be ranked 10th in Eastern and Southern Africa in terms of reduction of HIV incidence [10]. More importantly, MTCT rate reduced by half from 17% in 2010 to 8% in 2015 [11], but this is still below the virtual elimination of new HIV infections in children targeted by the UNAIDS 2016–2021 second e-MTCT strategy that also targets improved survival of HIV positive mothers by 2020 [4].

Kenya has reported progress in HIV testing and treatment coverage that stands at 84% and 75% for children aged 0-14 years and adults respectively [12, 13]. Prior to 2016, EID uptake was low especially in rural areas due to prolonged turnaround time and weak referral systems [12]. However, the number of accredited laboratories performing HIV viral load measurements and EID has been increased from 7 to 10 thereby strengthening both early- detection of HIV infected children and their initiation on ART [12, 14]. Despite this progress, there are geographical variations in the decline of MTC rates in Kenya in spite of uniform policy and resource allocation [12, 14], suggesting that there are context-specific drivers of these variations. In addition, despite the initiation of Option B+, there are still higher infection rates among infants tested after eight weeks after birth indicating high postnatal transmission during the breastfeeding period [10]. Therefore, a critical analysis of the factors underlying late sero-conversion in infants despite increasing availability of PMTCT services will inform further targeted efforts towards eMTCT targets. We thus sought to determine the prevalence and factors associated with late HIV sero-conversion among HIV exposed infants in Homabay County, which is one of the HIV hyper-endemic regions in western Kenya.

II. Material and Methods

2.1. *Study Design*

A retrospective longitudinal review of secondary data which involved abstraction of both maternal PMTCT and HEI data for the period January 2010 to December 2017.

2.2. *Study Setting*

This study was conducted in nine health facilities in Homabay County; two private (Humanist and Med25) and seven public of which three are Sub-county hospitals (Mbita, Suba and Ogongo), three were health centers (Kitare, Sena and Tom Mboya) and one dispensary (Obalwanda), the choice of the facilities was based on the availability of routine PMTCT services prior to the roll-out of Option B+ in the year 2014, electronic data management systems either open medical records system (Open MRS) or electronic medical records system (EMR). In our setting, HIV positive pregnant and lactating mothers were initiated on long term ART for their own health and for the benefit of their exposed babies. After delivery, exposed babies were initiated on Nevirapine syrup prophylaxis for six weeks. The first PCR test for the baby is carried out six weeks after completion of the Nevirapine prophylaxis.

2.3. *Ethical Consideration*

We sought for ethical approval from Baraton University ethics committee (BARATON REC: UEAB/ 06/1/ 2018), and approval from both Jaramogi University of Science and Technology and the Director of medical services Homabay county. The study involved retrospective data therefore individual level consent was not obtained. De-identified data were collected using the patient's unique identification number and coded using random numbers.

2.4. *Study Population and Sample Determination*

Records of mothers and their HIV exposed infants who subsequently seroconverted between 2010 and 2017 were included in the study. A purposive sample size of 254 was estimated to detect a 8.5% decline in sero-conversion rates from a baseline of 16.8% in 2013 to 8.3% in 2015 for Homa-bay County[15] for a retrospective longitudinal cohort study. Assuming a power of 80%, 5% level of precision, 95% confidence intervals, and design effect of 1.5 the formula below was used to calculate the sample size [16-18] $n = \frac{r+1}{r} \frac{(\bar{p})\,(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$

Where n is the minimum sample size, r is the ratio expected between exposed and non-exposed infants to the exposure variables, we assume equal ratio of 1:1 hence r = 1. P is the current prevalence (2017) of sero-conversion estimated to be 8.3% [15], Z_{β} is the Z score for 80% power (0.84), Z_{α} is the Z score for a 5% type 1 error (Z = 1.96), p_1-p_2 is the expected change (10%) in sero-conversion rate expected between the year 2013 and 2016 and between those exposed to the independent factors and those not exposed.

2.5. *Data Collection Procedures*

Data abstraction was done using a tool developed by adopting the Ministry of Health's national HIV exposed infant follow-up card. The data collected captured information of both mother and infant with DNA PCR positive results using their unique identification numbers. The data collection involved a review of medical records on antenatal, intrapartum, postpartum, PMTCT and comprehensive care records. The Kenyan HIV testing guideline provides for routine testing to pregnant women attending antenatal and postnatal within the health facility to facilitate entry for eMTCT. Serological HIV test for mothers was done using Determine™ HIV-1/2, and Uni-Gold™ HIV. Those missed during antenatal care were offered tests at delivery, labor and post-natal. Those testing positive were linked and initiated on ART. After delivery, exposed babies were captured during routine immunization visits at birth or at 6 weeks, a dry blood spot sample obtained for HIV PCR testing and initiated on Nevirapine. The second PCR was done six weeks after cessation of breastfeeding, a follow-up for HIV exposed infants were followed up to 18 months of age when the antibody test for HIV test was done. Those testing positive at any stage of care continuum were enrolled for care and treatment at the ART clinic. Confirmed HIV negative children were discharged from care while their mothers continued receiving treatment at the ART clinic.

2.6. *Statistical Analysis*

Data cleaning was undertaken at the point of collection to ensure completeness and consistency, after validation exported to STATA (v.14). Sero-conversion time a binary dependent variable defined as early (< 6 months) and late (>6 months). The independent variable Early infant HIV virological test time measured as on

time (≤6 weeks), late (>7-12 weeks) and very (late >12 weeks) [19]. A descriptive of the socio-demographic and medical characteristics of HIV exposed infant and their mothers, univariate logistic regression analysis was performed for all the predictor variables against the sero-conversion time. The dependent variable – sero-conversion time was coded as a binary outcome, with early sero-conversion coded as "0" and late sero-conversion coded as "1". The alpha level of significance assessed at p-values <0.05. We conducted Bivariate analysis by cross-tabulation of independent variables time of early infant diagnosis, antenatal and postnatal service uptake, infant breastfeeding practice and infant antiretroviral prophylaxis with seroconversion time using Chi-square ($\chi 2$), then univariate binary logistic regression done, unadjusted Odds Ratios with 95% Confidence intervals (95% CI) reported to measure the magnitude of effect, all variables significant at the bivariate analysis ($p<0.05$) were included in the multivariate logistic regression analysis. Adjusted Odds Ratios with 95% Confidence intervals (95%CI) were reported, variables with p-values <0.05 were considered statistically significant results. In the multivariate analysis confounding factors such as maternal, infant and socio-demographic factors were controlled for.

III. Results

3.1. *Sociodemographic Characteristics of the Study Participants*

As shown in table 1, a dataset of 254 mother-baby pair was available for analysis, below is a description of their socio-demographic characteristics. The mothers' average age was 28.19 ± 5.96 years. Majority 141 (55.5%) were aged between 25-35 years, most 149 (58.7%) had primary education. One hundred and seventy-one (67.3%) were in monogamous marriage while 159 (62.6) had a parity of 3-5 children. The infant had a mean weight of 2.97 ± 0.65 kilograms. Most 135 (53.4%) infants were aged between 0-6 months while 118 (46.6%) were aged between 7-24 months at the time of DNA PCR for early infant diagnosis. Most of the infants 143 (56.3%) were males and 243 (95.7%) of the infants (OR = 1.67; 95% CI, 0.47-5.83) had no history of TB contact within the household.

Table 1. Sociodemographic characteristics of the participants.

Variable		**Sero-conversion time**			**Sero-conversion time**		
		Early n (%)	**Late n (%)**			**Early n (%)**	**Late n (%)**
Total	Overall N = 254	48%	52%		Overall N = 254	48%	52%
Mean Maternal Age	28.19 ± 5.96	28.24 ± 6.10	28.14 ± 5.84		Infant Mean Weight in Kgs	2.97 ± 0.65	2.96 ± 0.63
Age Category:					Infants Age (Months):		
15 – 24 years	73 (28.7)	34 (46.6)	39 (53.4)		0 – 6	135 (53.4)	121 (89.6)
25 – 34 years	141 (55.5)	70 (49.6)	69 (50.4)		7 – 24	118 (46.6)	1 (0.9)
35 – 44 years	40 (15.8)	19 (47.5)	21 (52.5)				
Education level:					Infant history of TB contact		
None	49 (19.3)	19 (38.8)	30 (61.2)		Yes	11 (4.3)	4 (36.4)
Primary	149 (58.7)	74 (49.6)	75 (50.4)		No	243 (95.7)	119 (49.0)

Variable		Sero-conversion time			Sero-conversion time		
		Early n (%)	Late n (%)			Early n (%)	Late n (%)
Secondary	41 (16.1)	23 (56.1)	18 (43.9)				
College	15 (5.9)	7 (46.7)	8 (53.3)				
Marital Status:							
Single	14 (5.5)	4 (28.6)	10 (71.4)				
Married Polygamous	46 (18.1)	18 (39.1)	28 (60.9)				
Married Monogamous	171 (67.3)	93 (54.4)	78 (45.6)				
Divorced/Widow	23 (9.1)	8 (34.8)	15 (65.2)				
Parity:							
0 – 2	86 (33.9)	53 (61.6)	33 (38.4)				
3 – 5	159 (62.6)	63 (39.6)	96 (60.4)				
6 and Above	9 (3.5)	7 (77.8)	2 (22.0)				
Missing (n = 12)							

3.2. *Uptake of Antenatal and Postnatal Services for PMTCT Intervention*

Table 2 shows that 126 (49.6%) of the mothers attended 4 antenatal care clinics (ANC) and most 156 (61.4%) reported for their first ANC visit between 16-28 weeks of gestation. The uptake of postnatal care (PNC) was low since 163(64.2%) did not attend any postnatal care (PNC) clinic. One hundred and forty-eight (58.2%) had a CD4+ T cell counts between 100-500/mm and 149 (57.7%) of the mothers were HIV positive at the time of their first ANC visit. Most of the mothers 130 (51.2%) had undergone couple counseling; 102(49.5%) were initiated on HAART and were adhering to the regimen while 41 (19.9%) mothers were on interrupted HAART. One hundred and fifty-seven (53.5%) mothers were on HAART at the time of EID and most mothers 248 (97.6) had given birth through spontaneous vertex delivery. Most mothers 144 (56.7%) delivered in health facilities with most mothers 151 (59.5%) residing within 0-5 Km from the health facilities. This data shows that 100 (39.4%) underwent EID on time and a majority of 121 (89.6%) of infants aged between 0-6 months were exclusively breastfed. Data further shows that 108 (53.2%) of the infants did not receive ARV prophylaxis, 57 (28.1%) were on NVP for six months; 38 (18.7%) received NVP during breastfeeding and 51 had missing data probably due to lost to follow during PMCT cascade. Overall 52% of the infants seroconverted late; the study finding shows that late seroconversion rate increased from 30% for infants referred for PMTCT intervention at antenatal clinics as compared to 70% referred from the ward. Eighty-five percent (85.6%) of these infants were captured very late (>12 weeks) for early infant diagnosis compared to 29% captured on time.

3.3. *Predictors of Seroconversion Time*

Through bivariate analyses the following factors were identified as predictors of seroconversion time; delivered in the hospital (OR = 0.54; 95% CI, 0.33-0.99 p<0.019), received NVP for 6 weeks (OR = 0.28; 95% CI, 0.14-0.55, p<0.001) and during breastfeeding (OR = 0.34; 95% CI, 0.16 –0.73, p<0.006), were less likely to experience late seroconversion. The following factors were associated with increased risk of late sero-

conversion: very late infant diagnosis time (OR = 14.53; 95% CI, 7.23 – 29.16, p<0.001), Infants whose mothers' had a parity of 3-5 (OR = 2.51; 95% CI, 1.45-4.33, p<0.001) and were on replacement feeding between 0-6 months (OR = 33.3; 95% CI, 3.16 – 35.9, p<0.004) on further analysis, the multivariate model revealed that that maternal secondary level of education reduced the risk of seroconversion by 83% (aOR = 0.17; 0.34-0.87 p<0.034) while parity of 3-5 (aOR = 3.48; 1.22-9.93 p<0.020) and late infant diagnosis time (aOR=19.36; 3.5-105.57 p<0.001) increased the risk of sero-conversion. (Table 1-3)

Table 2. Uptake of Antenatal and Postnatal services for PMTCT intervention.

Variable	Sero-Conversion Time				
	Overall N = 254	Early n (%)	Late n (%)	Crude cOR (95% CI)	p[a]-Value
Number of ANC visits					
None	14 (6.5)	8 (57.1)	6 (42.9)	Ref.	Ref.
1.	33 (15.3)	12 (36.4)	21 (63.6)	2.33 (0.65-8.34)	0.192
2	35 (16.2)	17 (48.6)	18 (51.4)	1.41 (0.40-4.92)	0.588
3	46 (21.3)	27 (58.7)	19 (41.3)	0.93 (0.28-3.15)	0.918
4+	126 (49.6)	59 (46.8)	67 (53.2)	1.51 (0.49-4.61)	0.466
Gestation at 1st ANC:					
None	12 (4.7)	6 (50.0)	6 (50.0)	Ref.	Ref.
< 16 Weeks	12 (4.7)	8 (66.7)	4 (33.3)	0.50 (0.09-2.60)	0.410
16-28 Weeks	156 (61.4)	79 (50.6)	77 (49.4)	0.97 (0.30-3.15)	0.966
29-32 Weeks	74 (29.1)	30 (40.5)	44 (59.5)	1.47 (0.43-4.98)	0.539
PNC visit attendance:					
None	163 (64.2)	59 (36.2)	104 (63.8)	Ref.	Ref.
1	81 (31.9)	56 (69.14)	25 (30.9)	0.25 (0.14-0.45)	<0.001*
2	10 (3.9)	8 (80.0)	2 (20.0)	0.14 (0.03-0.69)	0.016
Mother HIV Status at first ANC					
Unknown	40 (16.1)	15 (37.5)	25 (62.5)	Ref.	Ref.
New Positive	57 (23.0)	26 (45.6)	31 (54.4)	0.72 (0.31-1.63)	0.426
Negative	8 (3.2)	6 (75.0)	2 (25.0)	0.20 (0.04-1.12)	0.067
Known Positive	149 (57.7)	76 (51.0)	73 (49.0)	0.59 (0.28-1.18)	0.132
Couple Counselling					
Yes	130 (51.2)	66 (50.8)	64 (49.2)	Ref.	Ref.
No	124 (48.8)	57 (46.0)	67 (54.0)	0.82 (0.50-1.35)	0.444
Maternal viral load:					
Not Done	12 (12.6)	5 (41.7)	7 (58.3)	Ref.	Ref.
0-1000	38 (40.0)	21 (55.3)	17 (44.7)	0.58 (0.55-2.15)	0.414

Variable	Sero-Conversion Time				
	Overall N = 254	Early n (%)	Late n (%)	Crude cOR (95% CI)	p^a-Value
Above 1000	45 (47.4)	23 (51.1)	22 (48.9)	0.68 (0.19-2.47)	0.562
Missing (n = 159)					
CD4 Count					
Not Done	28 (14.2)	12 (42.9)	16 (57.1)	Ref.	Ref.
<100/ mm	7 (3.6)	4 (57.1)	3 (42.9)	0.56 (0.11-2.99)	0.531
100-500/ mm	148 (58.2)	73 (49.3)	75 (50.7)	0.77 (0.34-1.74)	0.500
>500/ mm	71 (36.0)	34 (47.9)	37 (52.1)	0.81 (0.34-1.97)	0.652
Mode of delivery:					
Caesarean section	6 (2.4)	4 (66.7)	2 (33.3)	Ref.	Ref.
Spontaneous Vertex	248 (97.6)	119 (48.0)	129 (52.0)	2.17 (0.38-12.05)	0.377
Delivery					
Distance from Health Facility					
0-5 km	151 (59.5)	70 (46.4)	81 (53.6)	Ref.	Ref.
6-10 km	76 (29.9)	37 (48.7)	39 (51.3)	0.91 (0.52-1.58)	0.740
>10 km	27 (10.6)	16 (59.3)	11 (40.7)	0.59 (0.26-1.36)	0.220
Age of Infant:					
0-6 months	135 (53.4)	121 (89.6)	14 (10.4)	N/E	0.827^t
7-27 months	118 (46.6)	1 (0.9)	117 (99.1)		
History of TB contact					
Yes	11 (4.3)	4 (36.4)	7 (63.6)	Ref.	Ref.
No	243 (95.7)	119 (49.0)	124 (51.0)	1.67 (0.47-5.83)	0.425

Ref. Reference category, OR odds ratio, * = significant (p<0.05), CI 95%): 95% confidence interval NE not estimable, aOR = adjusted odds ratio, t-Independent t-test statistics, p^a – statistical significance based on bivariate logistic regression, p^b - statistical significance based on multivariate logistic regression; EXB: exclusive breastfeeding MF: Mixed feeding; RF: Replacement feeding.

Table 3. Multivariate Logistic Regression Analysis of Predictors of Late sero-conversion time.

Variable		Sero-Conversion Time					
		Early n (%)	Late n (%)	Crude cOR (95%CI)	p^a-value	Adjusted aOR (95%CI)	p^b-value
Total	**Overall N = 254**	**48%**	**52%**				
Age Category:							
15 – 24 years	73(28.7)	34 (46.6)	39 (53.4)	Ref.	Ref.	Ref.	Ref.
25 – 34 years	141 (55.5)	70 (49.6)	69 (50.4)	0.88 (0.50-1.56)	0.636	0.52 (0.16-1.65)	0.263
35 – 44 years	40 (15.8)	19 (47.5)	21 (52.5)	0.96(0.44-2.09)	0.925	0.48(0.09-2.65	0.403

Variable		Sero-Conversion Time					
		Early n (%)	Late n (%)	Crude cOR (95%CI)	p[a]-value	Adjusted aOR (95%CI)	p[b]-value
Total	**Overall N = 254**	**48%**	**52%**				
Education level:							
None	49 (19.3)	19 (38.8)	30 (61.2)	Ref.	Ref.	Ref.	Ref.
Primary	149 (58.7)	74 (49.6)	75 (50.4)	0.64(0.33-1.25)	0.192	0.34(0.09-1.20)	0.093
Secondary	41 (16.1)	23 (56.1)	18 (43.9)	0.49(0.21-1.15)	0.103	0.17(0.34-0.87)	0.034*
College	15 (5.9)	7 (46.7)	8 (53.3)	0.72(0.22-2.32)	0.587	3.19(0.13-78.60	0.477
PNC visit attendance:							
None	163(64.2)	59 (36.2)	104 (63.8)	Ref.	Ref.	Ref.	Ref.
1	81(31.9)	56 (69.14)	25 (30.9)	0.25(0.14-0.45)	<0.001*	1.67(0.40-6.90)	0.481
2	10(3.9)	8 (80.0)	2 (20.0)	0.14(0.03-0.69)	0.016		
Parity:							
0 – 2	86 (33.9)	53 (61.6)	33 (38.4)	Ref.	Ref.	Ref.	Ref.
3 – 5	159 (62.6)	63 (39.6)	96 (60.4)	2.44(1.43-4.19)	0.001*	3.48(1.22-9.93)	0.020*
6 and Above	9 (3.5)	7 (77.8)	2 (22.0)	0.46(0.09-2.34)	0.349	0.46(0.03-8.21	0.600
Missing (n = 12)							
Place of Delivery							
Health Facility	144 (56.7)	79 (54.9)	65 (45.1)	0.54 (0.33-0.91)	0.019*	Ref.	Ref.
Home	110 (43.3)	44 (40.0)	66 (60.0)	Ref.	Ref	1.66 (0.60-4.60)	0.327
PMTCT Regimen							
None	63 (30.6)	25 (39.7)	38 (60.3)	Ref.	Ref.	Ref.	Ref.
HAART	102 (49.5)	58 (56.9)	44 (43.1)	0.50 (0.26-0.95)	0.033*	1.44 (0.43-4.87)	0.557
Interrupted HAART	41 (19.9)	20 (48.8)	21 (51.2)	0.69 (0.31-1.53)	0.361	1.39 (0.30-6.42)	0.677
Infant ARV Prophyalaxis							
None							
NVP for 6 weeks	108 (53.2)	37 (34.3)	71 (65.7)	Ref.	Ref.	Ref.	Ref.
NVP during BF	57 (28.1)	37 (64.9)	20 (35.1)	0.28 (0.14-0.55)	<0.001*	0.37 (0.11-1.25)	0.109
Missing (n = 51)	38 (18.7)	23 (60.5)	15 (39.5)	0.34 (0.16-0.73	0.006*	0.85 (0.21-3.50)	0.829
Time of Early infant diagnosis:							
On Time	100 (39.4)	71 (71.0)	29 (29.0)	Ref.	Ref.	Ref.	Ref.
Late	50 (19.7)	37 (74.0)	13 (26.0)	0.86 (0.40-1.84)	0.700	0.39 (0.08-1.89)	0.241
Very Late	104 (40.9)	15 (14.4)	89 (85.6)	14.53 (7.23-29.16	<0.001*	19.36 (3.5-105.57	0.001*

Variable		Sero-Conversion Time					
		Early n (%)	Late n (%)	Crude cOR (95%CI)	p^a-value	Adjusted aOR (95%CI)	p^b-value
Total	**Overall N = 254**	**48%**	**52%**				
Mother on HAART at time of EID							
Yes	157 (53.5)	84 (53.5)	73 (46.5)	0.58 (0.35-0.98)	0.040*		
No	97 (39.1)	39 (40.2)	58 (59.8	Ref.	Ref		
Infant feeding practice 0 – 6 months							
EBF	121 (89.6)	111 (91.7)	10 (8.3)	Ref.	Ref.		
MF	10 (7.4)	9 (90.0)	1 (10.0)	1.23(0.14-10.75)	0.849		
RF	4 (3.0)	1(25.0)	3(75.0)	33.3(3.16-35.0)	0.004*		
7 – 24 months							
MF	88 (74.6)	1(1.1)	87 (98.9)				
RF	30 (25.4)	0(0.0)	30 (100.0)	N/E			

Ref: reference category, OR odds ratio, *= significant (p<0.05), CI 95%): 95% confidence interval NE not estimable, aOR= adjusted odds ratio, t- Independent t-test statistics, p^a - statistical significance based on bivariate logistic regression, p^b - statistical significance based on multivariate logistic regression; EXB: exclusive breastfeeding MF: Mixed feeding; RF: replacement feeding. Available online at https://doi.org/10.6084/m9.figshare.9974540

IV. Discussion

Kenya has made significant progress in PMTCT intervention as HIV incidence among children declined threefold from 26% in 2009 to 8.3% in 2015 [20, 21]. But this is still below the virtual elimination of new HIV infections among children targeted by the UNAIDS 2016–2021 the second e-MTCT strategy [4], and this may be due to low PMTCT and HAART coverage. This study reveals low PMTCT and HAART coverage as only 49.6% of the mothers attended up to fourth antenatal clinics visit, 61.4% reported for their first ANC visit between 16-28 weeks of gestation, 64.2% did not attend any postnatal visit, slightly above fifty percent of women received drug for PMTCT and highly active antiretroviral drugs (HAART) at the time of early infant diagnosis despite the simplified treatment approaches of Option B and Option B+, widespread use of ART that can reduce the rate of vertical transmission to < 5% in breastfeeding population [22]. The low uptake of PMTCT services has been previously associated with health system structural factors such as distance from the health facility, cited as a barrier to access to these services [22]. In our study, however, 59.5% of mothers were reportedly residing within 5 kilometers from the health facility and the poor antenatal service utilization observed would be due to social barriers such stigma since more than half of women in this study had not disclosed their HIV status despite being either in monogamous or polygamous marriage relationships. Stigma has previously been shown to influence the uptake of PMTCT services due to violence, rejection, and denial by husbands [23]. These findings suggest a need to further intervene for early identification of HIV positive mothers for initiation and monitoring in care, it's important that healthcare providers inform the mothers at any point of contact on the availability of the HIV care services and integrating the same in other child health programs.

Understanding the challenges that affect the elimination of mother-to-child transmission (eMTCT) including uptake of PMTCT is important in accelerating efforts towards eMTCT. One of these formidable challenges is late seroconversion among HIV exposed infants. In this study, we found that 52% of HIV exposed infants seroconverted late suggesting that there are several underlying factors that predispose the HIV exposed infants to seroconvert late. Our multivariate logistic regression analysis revealed that late HIV seroconversion is associated with parity of 3-5 children, home delivery, late time of EID and late initiation to ARV therapy. In addition, the results revealed that mothers' having secondary education reduced the risk of late seroconversion among HIV exposed infants. Our findings are similar to previous studies in Kenya, Uganda, and Ethiopia that revealed that home delivery and late initiation to ARV are significantly associated with mother to child transmission of HIV [3, 24, 25]. More importantly, it has been shown that home delivery is one of the key challenges to effective uptake of eMTCT services [3], suggesting that HIV exposed children born at home are less likely to benefit from PMTCT interventions such as early- infant diagnosis and early initiation of ARV. Consistent with these previous observations our data reveal that late seroconversion is significantly associated with the late time of EID. Delayed initiation on ARV prophylaxis in our study setting may be attributed partly to late referral for EID since most infants were referred for early infant diagnosis from the ward and out-patient department suggesting that were delivered at home, and therefore missed early initiation on ARV prophylaxis.

Previously early postnatal HIV transmission was associated with ineffective nevirapine therapy [26]. Furthermore, infant antiretroviral initiation and adherence is further linked to maternal HAART uptake and adherence, in our study a greater percentage of mothers did not receive PMTCT intervention. This is attributed to the observed poor antenatal and post-natal service access and utilization since a high proportion of mothers delivered at home and failed to attend postnatal clinics. In our study, only 31.9% and 3.9% of women attended one and two postnatal visits respectively indicating that there is a loss to follow up during PMTCT continuum, which further explains delayed early EID uptake. This is consistent with the finding of another study on the PMTCT program in rural Malawi which revealed a progressive loss to follow up of up to 81% post-natally [27].

Postnatal visits are important for continued PMTCT intervention since some mothers' seroconvert post-natally putting their breastfeeding infants at cumulatively increased risk vertical transmission [26]. Low uptake of both antenatal and postnatal care in rural settings has been associated with late HIV infection [25, 28, 29]. Partner support is important for ongoing PMTCT service utilization post-natally. Ineffective access or utilization due to constrained support networks including partners and community have been reported elsewhere [26, 30]. It's worth noting that despite more than half of the women attending at least one antenatal visit, and having knowledge of their HIV status, a bigger number opted to deliver at home. This points to the need for healthcare workers educating mothers on the dangers of home delivery especially in HIV endemic areas, PMTCT services, strengthening of community follow-up and referral for all pregnant and post-natal mothers by linking them to the community health volunteers and community health assistants [31].

Social determinants such as maternal education and family sizes are important factors that influence both the health and risk of diseases [32]. Of note is that higher maternal education has been associated with a low prevalence of malaria [33] Similarly our results reveal that HIV exposed infants from mothers with secondary education were less likely to seroconvert late. Together these results suggest that maternal education can be the effective 'social vaccine' against several leading infectious causes of global childhood mortality [33, 34]. We

also observed that parity of 3-5 children increased the risk of late HIV seroconversion among the HIV exposed infants suggesting that mothers with many children may not effectively uptake PMTCT services. Family household sizes have been shown to significantly increase the risk of infectious diseases partly due to the inabilities of the families to provide prevention and treatment measures for all the children [35]. These observations suggest the need for integrating PMTCT service provision to the home visiting programs to take into consideration the particular needs of every household.

Our study reveals a high exclusive breastfeeding (89.6%), a low mixed (7.4%) and replacement, (3%) feeding among infants 0-6 months. Such a high rate of exclusive breastfeeding is uncommon in Kenya [36]. The Kenya demographic health survey 2008-2009 reported 32% exclusive breastfeeding for infants less than six months this however improved slightly to 42% with median breastfeeding duration of 3.3 months in the same survey reported in 2014/2015 [37]. High breastfeeding numbers, however, have been observed in Nigeria and Zambia that recorded 80% and 84% respectively [38], this may be attributed to the promotion of exclusive breastfeeding by the ministry of health. Our finding that mixed feeding was not common is not consistent with previous studies that have shown that mixed infant feeding is common among infants born to mothers from rural settings [25]. Although mixed feeding has been previously associated with HIV infection among HIV exposed infants in Ethiopia. This can be partly attributed to variations in the classification of breastfeeding options by health workers as per WHO definitions [3, 39]. Moreover, we employed the use of secondary data captured in the registers thus we had limited control which is often possible when progressive qualitative interviews of breastfeeding mothers are done, another possible explanation would be the stigma associated with replacement feeding in this age group in the study setting. Our bivariate analysis revealed that infants who were on mixed fed or on replacement feeding were more likely to seroconvert early but this was not statistically significant at multivariate analysis similar to recent findings from Uganda [3]. Hence there is need to a need to further strengthen HIV exposed infant feeding prevention strategies through health education especially among breastfeeding populations in the resource-limited set-ups [40, 41] while exploring ways of supporting exclusive replacement feeding.

V. STUDY LIMITATIONS

Our study had limitations related to missing data, completeness and accuracy of as is common when using routine service clinical data especially with a span of over 5 years. Furthermore, the unavailability of data on maternal viral load and information on adherence made it impossible for our study to account for these variables as predictors of mother to child transmission. The study is also unable to account for effects of changes in antenatal PMTCT intervention and regimen, as enrolment of some mothers into PMTCT were based on WHO staging and CD4 count while others enrolled regardless of these, we could not explore the reasons for high numbers of home deliveries which require further behavioral prospective studies. However ad hoc analysis and imputation of the missing data revealed no significant difference in characteristics at the end, we note that 89.6% of infants aged between 0-6 months were reported to be exclusively breastfeeding, this is attributed to the stigma associated with HIV positive mothers and a social desirability bias, since this was a self-report. The sampling method used for Homabay health facilities may make our results not to be generalizable; despite these limitations, our findings are still useful for policy and program managers for continued efforts to achieve virtual elimination of mother to child transmission.

VI. CONCLUSION

This study demonstrates that determinants of sero-conversion time in Homabay County were maternal secondary level of education which reduced the risk while parity of 3-5, and very late infant HIV diagnosis time (very late EID time) increased the risk of sero-conversion. In view of these findings, the study recommends the following: Increasing antenatal, post-natal service coverage, strengthening of data capture system both electronic and paper (registers) through proper linkage of Antenatal, HIV exposed infant follow-up, postnatal and comprehensive care records to bridge gaps on the missing data and for efficient referral for retention in care. The Ministry of health and partners should train and retrain more PMTCT service providers given the rapid changes in the PMTCT and HIV care guidelines and strengthen the community HIV care intervention programs. An evaluation of possible emerging antiretroviral drug resistance especially in high prevalence areas should be conducted.

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