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Research Article

Mother-To-Child HIV Transmission using Single, Dual and Triple ARV Prophylaxis Regimens and their Correlates in Western Kenya: Chart Review

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Background: It is estimated that 2.1 million individuals worldwide became newly infected with HIV in 2013, and this included 240,000 children (<15 years). Most of these children live in sub-Saharan Africa and were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.

Objective: This study sought to ascertain the different PMTCT approaches or regimens that mothers and infants receive, their Mother-To-Child Transmission of HIV (MTCT) rates and associated correlates in Western Kenya.

Methods: A retrospective cohort study using prospectively collected data in Ministry of Health HIV-Exposed Infant (HEI) register from 24 health facilities. The study population was HIV-positive mothers enrolled from January 2012 to June 2013. The main outcomes were infant HIV status at 6 weeks, 9 to <18 months and 18-24 months. The correlates were maternal haemoglobin levels, WHO staging, CD4 counts, duration between enrolment and delivery, duration between enrolment and ART initiation, TB status, place of delivery, mode of delivery, and infant feeding options at 6 weeks, 9 to <18 months and 18-24 months. Proportions were analyzed using Chi-square tests while associations between MTCT correlates and outcomes were established using logistic regression.

Results: 1,751 HIV mother-baby pairs were enrolled in the 24 health facilities: 78.1% received Highly Active Antiretroviral Therapy (HAART), 14.2% received Zidovudine (AZT), 1.7% received Single-dose Nevirapine (SdNVP), and 4.3% received no prophylaxis. MTCT rates were 5.5%, 7.4% and 5.6% at 6 weeks, 9 to <18 months and 18-24 months, respectively. MTCT rate at 18-24 months showed a significant difference (p<0.001) across PMTCT regimens. Women with CD4 cells between 350 to 500 cells/mm^3 were about twice as likely to have HIV-negative babies compared to those with CD4 cells count <350cells/mm^3. Women on TB treatment are less likely to have HIV-negative babies compared to those without TB. Exclusive breastfeeding at 6 weeks was associated with lower MTCT rates. Feeding option at 6 weeks is a strong predictor of HIV status (p<0.001) as compared to babies on exclusive breastfeeding (EBF).

Conclusion: Most of the mother-baby pairs received HAART. AZT depicted the lowest MTCT rate at 18-24 months. Higher CD4 counts, no TB signs, and EBF at 6 weeks were associated with lower MTCT rates at 18-24 months

Key words: Antiretroviral prophylaxis, Mother-To-Child Transmission of HIV rates.

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1. Introduction

The HIV/AIDS remains one of the key challenges in the 21st century with political, economic, public health, social and scientific consequences globally. HIV/AIDS cases have been reported in all regions of the world, but most people living with the disease reside in low- and middle-income countries, more so in sub-Sahara Africa that carries 60% of the world's disease burden despite having only 10% of the world's population(UNAIDS, 2009).

For the first time since the 1990s, the number of new HIV infections among children in the 21 Global Plan priority countries in sub-Saharan Africa dropped to under 200,000. This represents a 43% decline in the number of new HIV infections among children in these 21 countries since 2009, and providing reasons for optimism as the Global Plan pushes towards its 2015 goals of 90% reduction. However, between 2012 and 2013, the pace of progress in reducing new HIV infections among children across the priority countries slowed substantially. While a number of countries made impressive gains, others stagnated or lost ground (UNAIDS, 2014). Globally, 35 million people were living with HIV at the end of 2013 (WHO, 2014a). Of these, 3.2 million were children (<15 years old). According to WHO, an estimated 2.1 million individuals worldwide became newly infected with HIV in 2013, including over 240,000 children (<15 years). Most of these children live in sub-Saharan Africa and were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding (WHO, 2014b). There are 13 high burden countries which account for 75% of the estimated 1.5 million pregnant women living with HIV in 2007 in low- and middle-income countries and nearly 75% of all children living with HIV. All but one of these countries (India) are in sub-Saharan Africa, Kenya inclusive (UNAIDS, 2010).

Mother-to-child transmission (MTCT) occurs when an HIV-infected woman passes the virus to her baby at childbirth and through breastfeeding. Almost all infections in infants can be avoided by timely delivery of known, effective interventions to prevent mother-to-child transmission. About 90% of these MTCT infections occurred in Africa where AIDS is beginning to reverse decades of steady progress in child survival (UNAIDS, 2010), as access to services for preventing the MTCT of HIV has increased (UNAIDS, 2010).

Kenya's Ministry of Health (MoH), through National AIDS and STI Control Program (NASCOP), took several actions to expand and strengthen PMTCT interventions in the country over the years. In 1994, PMTCT services were initiated with establishment of pilot PMTCT sites in Nairobi, Karatina and Homa Bay. In 1996, the Kenya Obstetrical and Gynecological Society (KOGS) spearheaded the development of the first guidelines for PMTCT in the country. In 2000, a National Technical Working Group (TWG) on PMTCT was formed. The TWG, co-chaired by NASCOP and the Division of Reproductive Health, coordinates implementation and provides technical support to the National PMTCT Programme. By 2002, National guidelines for PMTCT had been prepared and distributed (MOH, 2004). As new PMTCT projects began, the TWG served as a forum to provide on-going review of guidelines, program implementation, update stakeholders and discuss challenges and upcoming activities. The TWG is also responsible for updating national guidelines for PMTCT. The goal of the National PMTCT Program is in line with the goal set out at the United Nations General Assembly Special Session on HIV/AIDS (UNGASS) in 2001 to reduce the proportion of infants infected with HIV by 20% by the year 2005 and 50% by 2010. This massive roll out of PMTCT services aims to meet the UNGASS target (DOC, 2001). In order to meet the stated PMTCT goals, the Kenya Ministry of Health adopted the global guidelines for prevention of MTCT transmission of HIV (MOH, 2005). In the wealthy countries, the rate of MTCT is less than 2% because of widespread access to anti-retroviral therapy (ART), planned caesarean sections (CS), the means to safe formula feed, and access to quality medical services (MOH, 2008). Consequently, modifications on the guidelines have been made to keep abreast as science reveals better ways of preventing MTCT of HIV. The revised 2008 PMTCT guidelines are part of the implementation instruments towards universal access to PMTCT services, and a response to the call to action towards HIV-free and AIDS-free generation (MOH, 2008).

Prevention of Mother-to-child Transmission of HIV (PMTCT) services in Western Kenya started in 2000 with the Provincial hospital being one of the original five PMCT pilot sites in the country. It has shown a steady growth from five PMTCT sites in 2003 to the current 271 PMTCT sites by 2013. This represents 88% (271/308) of the health facilities offering ANC services in Western Kenya. For the last four years, there have been concerted efforts within the Counties to increase access to the use of the more efficacious regimens as provided for in the national PMTCT guidelines. In the current study, the different PMTCT approaches or regimens that mothers and infants receive, their correlates and MTCT rates in Western Kenya were determined.

2. Methodology

2.1 Study design

This was a retrospective cohort study using prospectively collected data from 24 sampled health facilities providing PMTCT services according to the Ministry of Health/NASCOP guidelines in Vihiga, Kakamega, Bungoma and Busia Counties (formerly Western Province).

2.2 Study population

The study population was HIV-positive pregnant women who received PMTCT services during the study period (January 2012 to June 2013) and their HIV-exposed infants/babies who were at least 18-24 months of age from the 24 sampled health facilities.

2.3 Sampling and sample size

Multi-stage sampling technique was adopted for the health facilities. Stage one involved stratifying the health facilities by county (Vihiga, Bungoma, Busia and Kakamega counties). Stage two involved categorizing the health facilities by levels (county hospitals, sub-county hospitals, health centres and dispensaries). The

county hospitals that met the eligibility criteria were purposively sampled based on their big catchment areas and referral hospital status. Sub-county, health centres and dispensaries were randomly sampled. Due to missing data, all HIV-positive mother-baby pairs data from the sampled health facilities were extracted from the period covering January 2012 to June 2013 resulting in a total of 1751 mother-baby pairs. The MOH HEI registers were the primary data collection tool, and missing variables from the registers corroborated with data from the patient files in Maternal and Child Health (MCH) and Comprehensive Care Clinics (CCCs).

2.4 Eligibility criteria

The inclusion criteria was a) health facilities providing PMTCT and Early Infant Diagnosis as per the MOH protocol and guidelines b) health facilities who were willing to give informed consent to participate in the study c) health facilities that started providing PMTCT services from January 2012 d) mother-baby pairs that were enrolled in the sampled health facilities between January 2012 to June 2013.

2.5 Maternal and infant variables

Maternal (ARV prophylaxis regimens, maternal age, maternal weight, maternal haemoglobin levels, maternal CD4 counts, maternal age starting ART, duration between enrolment and ART initiation, duration between enrolment and date of delivery, maternal age at delivery, mode of delivery, place of delivery, maternal TB status and other maternal medical conditions) and infant (feeding options, babys' NVP prophylaxis. The key outcome variables were Babys' HIV status at 6 weeks, 9 to <18 months, 18-24 months) variables were collected.

2.6 Data analysis

Data collected was analysed using SPSS (Statistical Package for Social Sciences version 20). Descriptive statistics such as mean, median, standard deviation and range were used for continuous variables, whereas frequencies were used for categorical variables. The Chi-square tests were used to determine any associations between baby's HIV status at 6 weeks, 9 to <18 months and 18-24 months and categorical variables. Logistic regression was used to assess the association between maternal and infant characteristics and baby's HIV status at 6 weeks, 9 to < 18 months and 18-24 months. $p \leq 0.05$ were considered statistically significant.

2.7 Ethical considerations

This protocol was reviewed and approved by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (**P66/11/2012**). Confidentiality was assured throughout the study.

3. Results and Discussion

The MOH registers, patient files depicted missing information in varying degrees with variables such as haemoglobin levels, place of delivery, and mode of delivery having over 50% missing data while HIV status at 18 months was the best recorded at 1.5% missing data.

ARV prophylaxis regimen provided to HIV-positive pregnant women to reduce MTCT rates

Overall, most mothers 78.1% (n=1367) received HAART, 14.2% (n=249) received AZT, 1.7% (n=29) received NVP, 4.3% (n=76) received no prophylaxis and 1.7% (n=30) had not stated whether they received ARV prophylaxis or not (**Figure 1**). This demonstrated that HAART was the main ARV prophylaxis regimen in use and AZT and NVP are less commonly administered during the study period. The proportions of ARV prophylaxis regimens received across the counties were comparable (p=0.466).

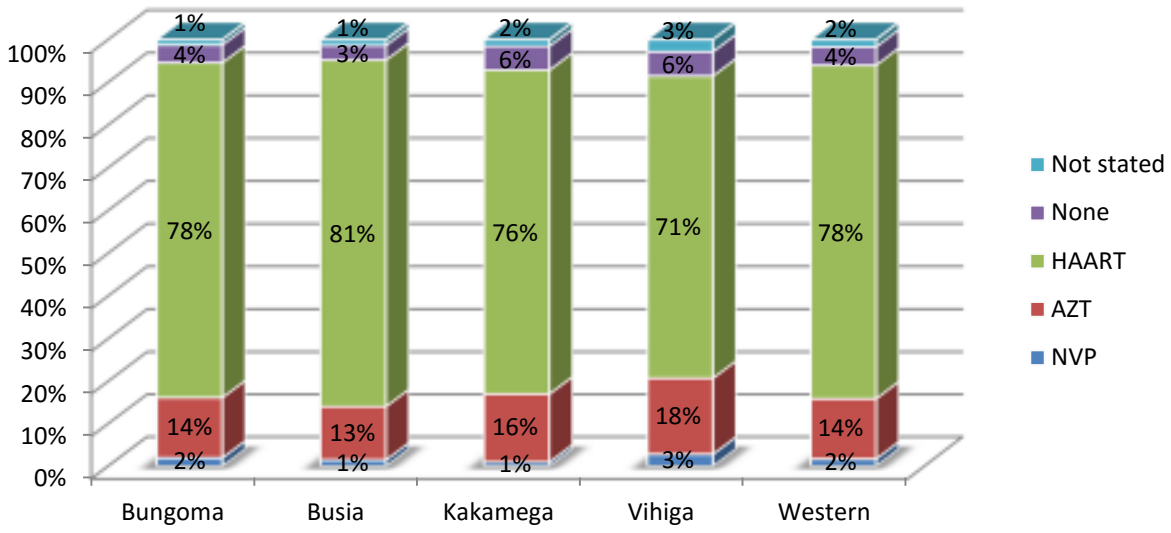

Figure 1: ARV prophylaxis regimens received disaggregated by county from January 2012 to June 2013

Table 1: HIV transmission rates at 6 weeks, 9 to <18 months and 18-24 months stratified by county, Jan 2012 to June 2013

County	HIV status at 6 weeks (*p*=0.961)			HIV status at 9 to <18 months (*p*=0.794)			HIV status at 18-24 months (*p*=0.900)		
	HIV-negative (n,%)	HIV-positive (n,%)	Not stated (n,%)	HIV-negative (n,%)	HIV-positive (n,%)	Not stated (n,%)	HIV-negative (n,%)	HIV-positive (n,%)	Not stated (n,%)
Bungoma (N=408)	375 (91.9%)	23 (5.6%)	10 (2.5%)	374 (91.7%)	28 (6.9%)	6 (1.5%)	383 (93.9%)	25 (6.1%)	-
Busia (N=817)	760 (93.0%)	42 (5.1%)	15 (1.8%)	750 (91.8%)	55 (6.7%)	12 (1.5%)	775 (94.9%)	42 (5.1%)	-
Kakamega (N=394)	363 (92.1%)	24 (6.1%)	7 (1.8%)	351 (89.1%)	35 (8.9%)	8 (2.0%)	371 (94.2%)	23 (5.8%)	-
Vihiga (N=106)	97 (91.5%)	6 (5.7%)	3 (2.8%)	96 (90.6%)	9 (8.5%)	1 (0.9%)	100 (94.3%)	6 (5.7%)	-
Total (N=1725)	1595 (92.5%)	95 (5.5%)	35 (2.0%)	1571 (91.1%)	127 (7.4%)	27 (1.6%)	1625 (94.4%)	96 (5.6%)	-

The HIV-negative and HIV-positive babies' were expressed as (n, %), i.e. absolute count (Frequency, n) and proportion (Percent, %). The statistical significance was determined using the Chi-square tests.

MTCT rates at 6 weeks, 9 to <18 months and 18-24 months and associated correlates

The study revealed the HIV transmission rates at 6 weeks (5.5%, 95% CI: 4.41%-6.59%), 9 to <18 months (7.4%, 95%CI: 6.15%-8.65%) and 18-24 months (5.6%, 95% CI: 4.51-6.69%). Furthermore, the HIV transmission rates at 6 weeks (*p*=0.961), 9 to <18 months (*p*=0.794) and 18-24 months (*p*=0.900) were comparable across counties (**Table 1**).

Statistical associations between various correlates for MTCT rates abstracted from MoH registers such as hemoglobin levels, WHO staging, CD4 cell counts, duration between enrollment and ART initiation, type of prophylaxis, NVP prophylaxis for the baby received, TB status, duration between enrolment and delivery, place of delivery, mode of delivery, feeding options at 6 weeks, feeding options at 9 to <18 months and feeding options at 18-24 months and Mother-to-child HIV transmission rates at 6 weeks, 9 to <18 months and 18-24 months were analyzed as shown in **Table 2** and **Annex 1** (Supplementary Information).

With regard to CD4 count, women with CD4 counts greater than 500 cells/mm^3 had the lowest HIV transmission rate at 18-24 months (3.7%), followed by those with CD4 counts between 350 to 500cells/mm3 (6.3%) while the ones with CD4 counts <350cells/mm^3 had the highest HIV transmission rates (7.3%) (**Table 2**). As such, higher CD4 cell counts amongst women were associated with low HIV transmission rates at 6 weeks (*p*=0.016), 9 to <18 months (*p*<0.0001) and 18-24 months (*p*=0.029).

The HIV transmission rate at 6 weeks, 9 to <18 months and 18-24 months varied with the type of ARV prophylaxis (**Table 2**) with AZT (3.0%) and HAART (5.4%) depicting the lowest HIV transmission rate at 6 weeks. Use of NVP was associated with highest HIV transmission rate of 7.1%. There were significant differences in transmission across the different ARV prophylaxes at 6 weeks (*p*=0.041).

Further analyses revealed that majority of babies received NVP prophylaxis, which was in turn associated with lower HIV transmission rates a 6 weeks (*p*=0.036), 9 to <18 months (*p*=0.061) and 18-24 months (*p*=0.330).

Women on TB treatment had the highest HIV transmission rates while those without had the least HIV transmission rates at 9 to <18 months (*p*=0.016) and 18-24 months (*p*=0.009). However, the HIV transmission rates were comparable at 6 weeks (*p*=0.334) between the two groups (**Table 2**). These observations imply that women having TB were likely to transmit HIV to their babies at 9 to <18 months and 18-24 months period.

Table 2 further shows the duration between enrolment and date of delivery and their effect on MTCT rates. Women who delivered within 6 months of enrolment had a lower HIV transmission rates at 6 weeks *(p*=0.001), 9 to <18 months (p<0.0001) and 18-24 months (p=0.001) as compared to those who delivered after 6 months.

Baby's' feeding options at 6 weeks, 9 to <18 months and 18-24 months and the MTCT rates were further determined. Exclusive breastfeeding options were associated with MTCT rates of 3.8% (6 weeks), 6.0% (9 to <18 months) and 3.8% (18-24 months). The feeding options was associated with the MTCT rates at 6 weeks (*p*<0.0001), 9 to <18 months (*p*=0.001), and 18-24 months (*p*<0.0001) (**Table 2**). These findings demonstrated that feeding options at 6 weeks is a strong predictor of MTCT rates at the selected time periods.

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Table 2: Statistical associations between the covariates and baby's' HIV Status at 6 weeks, 9 to <18 months and 18-24 months

	6 weeks				9 to <18 months				18-24 months			
Independent variables	**HIV-negative (n, %)**	**HIV-positive (n,%)**	χ^2	***p*-value**	**HIV-negative (n, %)**	**HIV-positive (n,%)**	χ^2	***p*-value**	**HIV-negative (n, %)**	**HIV-positive (n,%)**	χ^2	***p*-value**
CD4 count cells			8.321	**0.016**			19.131	**<0.0001**			7.094	**0.029**
<350 cells	431 (92.7%)	34 (7.3%)			418 (89.1%)	51 (10.9%)			443 (92.7%)	35 (7.3%)		
350 to 500 cells	295 (93.7%)	20 (6.3%)			292 (93.6%)	20 (6.4%)			299 (94.3%)	18 (5.7%)		
>500cells	731 (96.3%)	28 (3.7%)			732 (95.6%)	34 (4.4%)			743 (96.1%)	30 (3.9%)		
Not stated	138 (91.4%)	13 (8.6%)			129 (85.4%)	22 (14.6%)			144 (91.7%)	13 (8.3%)		
Type of prophylaxis received			8.273	**0.041**			7.601	0.055			3.425	0.331
NVP	26 (92.9%)	2 (7.1%)			23 (85.2%)	4 (14.8%)			26 (92.9%)	2 (7.1%)		
AZT	226 (97.0%)	7 (3.0%)			212 (90.2%)	23 (9.8%)			235 (96.7%)	8 (3.3%)		
HAART	1271 (94.6%)	72 (5.4%)			1262 (93.5%)	88 (6.5%)			1283 (94.6%)	73 (5.4%)		
None	60 (88.2%)	8 (11.8%)			60 (88.2%)	8 (11.8%)			67 (91.8%)	6 (8.2%)		
Not stated	12 (66.7%)	6 (33.3%)			14 (77.8%)	4 (22.2%)			18 (72.0%)	7 (28.0%)		
TB status of the patient			2.193	0.334			8.282	**0.016**			9.428	**0.009**
No signs	1429 (94.7%)	80 (5.3%)			1411 (93.0%)	107 (7.0%)			1457 (94.8%)	80 (5.2%)		
TB signs	61 (93.8%)	4 (6.2%)			61 (93.8%)	4 (6.2%)			61 (93.8%)	4 (6.2%)		
TB Treatment	4 (80%)	1 (20.0%)			3 (60.0%)	2 (40.0%)			4 (66.7%)	2 (33.3%)		
Not stated	101(91.0%)	10 (9.0%)			96 (87.3%)	14 (12.7%)			107 (91.5%)	10 (8.5%)		

ISSN 2303-9841

Independent variables	6 weeks				9 to <18 months				18-24 months			
	HIV-negative (n, %)	**HIV-positive (n,%)**	χ^2	***p*-value**	**HIV-negative (n, %)**	**HIV-positive (n,%)**	χ^2	***p*-value**	**HIV-negative (n, %)**	**HIV-positive (n,%)**	χ^2	***p*-value**
Duration between enrolment and delivery			14.002	**0.001**			18.818	**<0.0001**			14.622	**0.001**
<6months	1153 (96.0%)	48 (4.0%)			1135 (94.5%)	66 (5.5%)			1161 (96.1%)	47 (3.9%)		
6-24months	245 (90.7%)	25 (9.3%)			244 (88.7%)	31 (11.3%)			257 (90.8%)	26 (9.2%)		
24months	82 (92.1%)	7 (7.9%)			80 (86.0%)	13 (14.0%)			87 (92.6%)	7 (7.4%)		
Not stated	115 (88.5%)	15 (11.5%)			112 (86.8%)	17 (13.2%)			124 (88.6%)	16 (11.4%)		
Place of delivery			0.881	0.348			0.718	0.397			0.641	0.423
Feeding options at 6 weeks			34.748	**<0.0001**			13.983	**0.001**			31.520	**<0.0001**
EBF	1337 (96.2%)	53 (3.8%)			1305 (94.0%)	83 (6.0%)			1348 (96.2%)	53 (3.8%)		
ERF	16 (84.2%)	3 (15.8%)			16 (84.2%)	3 (15.8%)			16 (84.2%)	3 (15.8%)		
MF	129 (86.0%)	21 (14.0%)			130 (86.7%)	20 (13.3%)			131 (86.8%)	20 (13.2%)		
Not stated	113 (86.3%)	18 (13.7%)			120 (85.1%)	21 (14.9%)			134 (87.0%)	20 (13.0%)		

The number (n) and proportion (%) of HIV-negative and HIV-positive status at 6 weeks, 9 to <18 months and 18-24 months for different variables are shown. 'Not stated' = there was no documentation in the Ministry of Health registers. Statistical analysis was determined by χ^2 statistics and the p-value are also shown for each variable.

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Table 3: Logistic regression showing the associations between the covariates and baby's' HIV Status at 6 weeks, 9 to <18 months and 18-24 months

	6 weeks			9 to <18 months			18-24 months		
Independent variables	**Odds Ratio**	**95% CI for OR**	***p*-value**	**Odds Ratio**	**95% CI for OR**	***p*-value**	**Odds Ratio**	**95% CI for OR**	***p*-value**
CD4 count cells									
<350 cells	Ref			Ref			Ref		
350 to 500 cells	**2.059**	**1.232 - 3.444**	**0.006**	**2.627**	**1.674 - 4.121**	**<0.0001**	**1.957**	**1.185 - 3.231**	**0.009**
>500cells	1.770	0.982 - 3.192	0.058	1.475	0.835 - 2.604	0.181	1.491	0.819 - 2.716	0.192
Type of prophylaxis received									
NVP	0.577	0.115 - 2.905	0.505	1.304	0.358 - 4.752	0.687	0.859	0.163 - 4.532	0.858
AZT	**0.232**	**0.081 - 0.666**	**0.007**	0.814	0.346 - 1.911	0.636	0.380	0.127 - 1.134	0.083
HAART	**0.425**	**0.196 - 0.922**	**0.030**	0.523	0.242 - 1.128	0.098	0.635	0.267 - 1.513	0.306
None	Ref			Ref			Ref		
TB status of the patient									
No signs	Ref			Ref			Ref		
TB signs	0.224	0.025 - 2.027	0.183	**0.114**	**0.019 - 0.688**	**0.018**	**0.110**	**0.020 - 0.609**	**0.011**
TB Treatment	0.262	0.023 - 2.931	0.277	**0.098**	**0.013 - 0.768**	**0.027**	**0.131**	**0.018 - 0.946**	**0.044**
Duration between enrolment and delivery									
<6months	Ref			Ref			Ref		
6-24months	0.488	0.214 - 1.112	0.088	**0.358**	**0.189 - 0.676**	**0.002**	0.503	0.221 - 1.146	0.102
24months	1.195	0.498 - 2.866	0.689	0.782	0.390 - 1.567	0.488	1.257	0.527 - 2.999	0.606
Feeding options at 6 weeks									
EBF	Ref			Ref			Ref		
ERF	**0.244**	**0.142 - 0.416**	**<0.0001**	**0.413**	**0.246 - 0.696**	**0.001**	**0.258**	**0.149 - 0.444**	**<0.0001**
MF	1.152	0.309 - 4.297	0.833	1.219	0.326 - 4.562	0.769	1.228	0.328 - 4.597	0.760

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Independent variables	6 weeks			9 to <18 months			18-24 months		
	Odds Ratio	**95% CI for OR**	***p*-value**	**Odds Ratio**	**95% CI for OR**	***p*-value**	**Odds Ratio**	**95% CI for OR**	***p*-value**
Feeding options at 9 months									
MF				Ref			Ref		
NBF	-	-		1.166	0.734 - 1.853	0.514	**1.997**	**1.040 - 3.834**	**0.038**
RF	-	-		0.000	-	0.999	0.000	-	0.999

The significance value, Odds Ratio and 95% confidence intervals are also shown for independent variable taking certain reference categories for each variable. Home delivery for place of delivery, C-section for mode of delivery, Yes for baby NVP prophylaxis, WHO stage I for WHO staging, No TB signs for TB status, None for type of prophylaxis, EBF for feeding options at 6 weeks, MF for feeding options at 9 months and 18 months were considered as reference groups. Ref=Reference group.

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The associations between the correlates for MTCT rates such as hemoglobin levels, WHO stage, duration between enrollment and ART initiation, mode of delivery, place of delivery, feeding options at 9 to <18 months and feeding options at 18-24 months and MTCT rates at 6 weeks, 9 to <18 months and 18-24 months were determined and were comparable across groups (**Annex 1**, Supplementary Information).

Additional logistic regression analyses were carried out to determine the association between the correlates and MTCT rates (**Table 3** and **Annex 2**, Supplementary Information).

Relative to women with CD4 cells count less than 350 cells/mm^3, women with CD4 cells between 350 to 500 cells/mm^3 were about twice likely to have HIV-negative babies as opposed to those at 6 weeks (OR=2.059, 95% CI=1.232-3.444, p=0.006), 9 to <18 months (OR=2.627, 95% CI=1.674-4.121, p<0.0001) and 18-24 months (OR=1.957, 95% CI=1.185-3.231, p=0.009). However, the likelihood of having HIV-negative babies was comparable between those women with CD4 cells count greater than 500 cells/mm^3 and those with CD4 count less than 350 cells/mm^3 (**Table 3**).

Women with suspected TB signs and symptoms are less likely to have HIV-negative babies compared to those women who have no TB signs and symptoms at 9 to <18 months (OR=0.114, 95% CI=0.019-0.688, p=0.018) and 18-24 months (OR=0.110, 95% CI=0.020-0.609, p=0.011). In addition, women on TB treatment are less likely to have HIV-negative babies compared to those women who have no TB signs and symptoms at 9 to <18 months (OR=0.098, 95% CI=0.013-0.768, p=0.027) and 18-24 months (OR=0.131, 95% CI=0.018-0.946, p=0.044). These differences were statistically significant at these selected time points (**Table 3**).

Exclusive breastfeeding was associated with lower MTCT rates at 6 weeks (OR=0.244, 95% CI=0.142-0.416, p<0.0001), 9 to <18 months (OR=0.413, 95% CI= 0.246-0.696, p=0.001) and 18-24 months (OR=0.258, 95% CI=0.149-0.444, p<0.0001). Babies who are receiving exclusive replacement feeds at 6 weeks are less likely to be HIV-negative at 18-24 months as compared to babies are exclusively breastfed by 71% (p< 0.001) (**Table 3**).

The association between WHO stage, duration between enrollment and ART initiation, NVP prophylaxis for the baby received, of delivery, place of delivery, feeding options at 9 to <18 months and at 18-24 months 9 to <18 months and MTCT rates across the different times were comparable (p>0.05; **Annex 2**, Supplementary Information).

4. Discussion

PMTCT Guidelines in Kenya: 2012 - 2013

In 2012, Kenya published revised PMTCT guidelines based on WHO guidelines (2010) (MOH, 2012) which we used in the study area with a much greater focus on pharmaceutical prophylaxis than previous guidelines and which promote earlier initiation of therapy for all pregnant women. Women who are eligible to receive ART (CD4 cell count of 350 or below with WHO clinical stage of I or II, or WHO clinical stage III or IV, regardless of CD4 cell count) were to be started on highly active antiretroviral therapy (HAART) regardless of gestational age. Women not eligible for HAART would be started on combination antiretroviral (ARV) prophylaxis at 14 weeks or shortly thereafter and receive a combination of AZT, 3TC and NVP at the onset of labour (Option B). The Kenyan guidelines also include Option A (single dose nevirapine in labour) although option B was encouraged in settings with the capacity to monitor women receiving triple therapy (MOH, 2012). This could also be continued through the woman's life without interruption, known as option B-PLUS. According to the guidelines, at the first ANC visit, all HIV infected pregnant women should be given single dose nevirapine for themselves (to be taken at the onset of labour) and for the infants "to be administered soon after birth" (MOH, 2012).

ARV prophylaxis regimen provided to HIV-positive pregnant women to reduce MTCT rates

The current study revealed that 94% of mothers received some form of maternal prophylaxis with 78.1% receiving HAART, 14.2% receiving AZT and 1.7% receiving NVP. Only 4.3% received no form of ARV prophylaxis while 1.7% had not stated whether they received ARV prophylaxis or not. This contrasts with a cross-sectional study done in 2010 in South Africa that revealed that of all HIV-positive mothers, 30.5% received cART and 52.6% received AZT although 83.1% received some maternal ARV (Woldesenbet et al, 2015). Similarly an assessment done in KwaZulu-Natal, South Africa in 2008-2009, revealed that only 13.7% of HIV-positive pregnant women had started on maternal lifelong antiretroviral treatment and 67.2% had received maternal zidovudine and nevirapine meaning about 81% received some form of maternal ARV prophylaxis (Horwood et al, 2012). These variations in ARV regimens in use reflect the changing PMTCT guidelines as a result of new WHO guidance as WHO has been advocating for more efficacious regimens over the years. The study revealed a near universal uptake of ARV prophylaxis of 94% and this contrasts with the second Kenya AIDS Indicator Survey that was a nationally representative 2-stage cluster sample of households that showed 72.3% of HIV-positive pregnant women received antepartum antiretroviral prophylaxis (Sirengo et al, 2014). However, it closely mirrors a community-based cross-sectional study of PMTCT in Nyanza Province, Kenya done in 2011 that revealed that 82% were on PMTCT ARVs (Kohler et al, 2014). Increasing capacity building of Ministry of Health, increased donor support and changes in policy environment could be responsible for the increasing number of maternal ARVs being provided to HIV-positive pregnant women in Western Kenya.

MTCT rates at 6 weeks, 9 to <18 months and 18-24 months and associated correlates in Western Kenya

Most countries are making remarkable progress towards preventing mother-to-child transmission (PMTCT) of HIV, particularly in sub-Saharan Africa. But Mother-to-child transmission (MTCT) of HIV continues to occur in children during pregnancy, labour and delivery, or breastfeeding, at a time, when there are available effective interventions to curb the infection and better resourced countries have been able to bring the risk of children infected though MTCT to less than 2%. In sub-Saharan Africa, MTCT rates as high as 25%

have been reported (Jackson et al, 2003). Over 90% of HIV infections among children occur through mother-to-child transmission (UNICEF/UNAIDS/WHO, 2008). In the absence of any intervention, rates of MTCT of HIV can vary from 15% to 30%, without breastfeeding, and can reach as high as 30% to 45% with prolonged breastfeeding (De Cock et al, 2000).

The current study showed that HIV transmission rate at 18-24 months varied by ARV prophylaxis regimen received with AZT showing the lowest HIV transmission rate, followed by HAART and NVP at 3.3%, 5.4% and 7.1%, respectively. Mothers and their babies who never received any form of prophylaxis had 8.2% HIV transmission rates. This contrasts with HIVNET 012 study that showed an estimated risks of HIV-1 transmission in the Zidovudine and Nevirapine groups to be 25.8% and 15.7% by age 18 months, respectively (Jackson et al, 2003). It further contrasts with Kesho Bora study that revealed the cumulative rate of HIV transmission at 6 weeks was 3.3% in the triple antiretroviral group compared with 5.0% in the Zidovudine and single-dose nevirapine group (de Vincenzi, 2011). Study done in Nairobi, Kenya to evaluate the effectiveness of the HAART in PMTCT demonstrated that up to 90% of children were confirmed to be HIV-negative (Ngemu et al, 2014). However, other aspects of HAART such as adherence, costs, mothers' behavior during HAART may affect the overall efficacy of HAART in PMTCT. It also contrasts with a cohort study in the United States, which showed that the risk of MTCT was 10.4% among women receiving AZT monotherapy, 1.2% in women receiving triple-ARV regimens but is in agreement with 3.8% among those receiving dual ARV regimens and (Cooper et al, 2002). In Lusaka, the proportion of HIV PCR-positive samples was 12% (Sutcliffe et al, 2014). This, however, closely compares with the Kisumu Breastfeeding study in Kenya that showed HIV transmission rates at 6 weeks and 24 months were 4.2% and 7%, respectively (Thomas et al, 2011). The current study showed that the HIV transmission rate from Mother-to-child at 6 weeks and 18-24 months are similar at about 5.5% and 5.6%, respectively and this is in tandem with study done in Western Kenya that strongly suggested benefit of antiretroviral prophylaxis in reducing infant HIV infection but do not show a benefit at 18-months when compared to 6 weeks transmission rate (Nyandiko et al, 2010). Few studies have compared the programmatic effectiveness of the recommended strategies of ante-natal HAART and AZT for PMTCT. A study carried out in Botswana demonstrated that maternal HAART was associated with a substantial decrease in the rate of mother-to-child transmission as compared to Zidovudine in a programmatic setting (Dryden-Peterson et al, 2011). Further studies are needed to understand other limitations to the use of HAART in PMTCT of HIV in real life situations that could further explain why the MTCT rate for AZT seems to be lower than HAART in our study area. The focus for the PMTCT programming should be the quality of PMTCT services offered to realize the eMTCT targets by 2015 and beyond.

The CD4 counts is taken as a measure of the level of immunity and the lower the CD4 count the higher the immunosuppression and vice versa. According to the WHO guidelines, CD4 above 500cells/mm^3 is considered normal while CD4 between 350cells/mm^3 to 500cells/mm^3 is moderate immunosuppression and below 350cells/mm^3 is mild to severe immunosuppression. The current study revealed that lower CD4 cell count was associated with higher HIV transmission rate at 6 weeks, 9 to <18 months and 18-24 months. This study also found out that women with CD4 cells between 350 to 500 cells/mm3 are about twice likely to have HIV-negative babies as opposed to those women with CD4 cells count less than 350cells/mm3 (p=0.009). This corroborates with an intervention cohort study that depicted MTCT risk was significantly associated with maternal CD4-cell counts below 200 cells per mL (Bryson, 1996; Coovadia et al, 2007; Landesman et al, 1996). Therefore, early ANC attendance and HIV testing for women in reproductive age group should be strongly promoted.

In HIV-infected women, co-infections that target the placenta, genital tract have been shown to increase the risk for MTCT. Active co-infection stimulates the release of cytokines and inflammatory agents that enhance HIV replication and this weakens natural defenses to MTCT. Tuberculosis (TB) is a major cause of disease morbidity and mortality more so amongst HIV infected individuals. For women, the greatest burden of TB occurs during the reproductive years (ages 15-49 years). In this study, women with suspected TB signs and symptoms and on TB treatment are less likely to have HIV-negative babies compared to those women who have no TB signs and symptoms at 9 to <18 months and 18-24 months. Active TB infection is normally associated with lower CD counts amongst HIV infected individuals. Active TB infection increases HIV load and is associated with immunosuppression, which may explain the association between TB and MTCT (Day et al, 2004; Goletti et al, 1996; Pillay et al, 2004; Toossi et al, 2001; Zhang et al, 1995).

In Africa, more than 95% of infants are currently breastfed, but feeding practices are often inadequate: feeding water, and other liquids, to breastfed infants is a widespread practice. Nevertheless, prolonged breastfeeding is common, and the median duration of breastfeeding ranges between 16 and 28 months. Urbanization and mothers' education are the major factors that tend to shorten breastfeeding. However, recent trends show an increase in early initiation and in duration of breastfeeding as a result of promotion efforts deployed by WHO and UNICEF, local governments, and non-governmental organizations. To prevent MTCT of HIV, WHO recommends replacement feeding where feasible and safe. Otherwise, mothers are encouraged to practice exclusive breastfeeding for the first months of life followed by early and rapid weaning. Exclusive breastfeeding for a few months could carry a lower risk of death than replacement feeding. Infants of all mothers, whether HIV-positive or not, will benefit from improving the rate of exclusive breastfeeding (Dop, 2002).

In the current study, babys' who received exclusive breastfeeding at 6 weeks had a significantly low HIV transmission rate of 3.9% compared to those who received exclusive replacement feeding and mixed feeding each at about 15% (p<0.001) and it emerged as the strongest predictor of babies' HIV status at 18-24 months. This contrasts with an intervention cohort

study done in 2007 that showed 14.1% of exclusively breastfed infants were infected with HIV-1 by age of 6 weeks (Coovadia et al, 2007). It also contrasted with a cohort study done in Durban, South Africa in 1997 that found out that HIV transmission rate was 39% in those exclusively breastfed, 24% in those fed exclusively on formula and 32% in those receiving mixed feeding and that 50% of HIV-infected infants exclusively breastfed (Bobat et al, 1997). Similarly study done in KwaZulu Natal, South Africa revealed 14.1% of exclusively breastfed infants were infected with HIV-1 by age 6 weeks and 19.5% by 6 months (Coovadia et al, 2007).

Babies who are receiving exclusive replacement feeds at 6 weeks are less likely to be HIV-negative at 18-24 months as compared to babies that are exclusively breastfed by approximately 74% ($p< 0.001$). The first study to show such an association came from south Africa and found that infants who received both breast milk and other feeds were significantly more likely to be infected by 15 months of age (36%) than those who had been exclusively breastfed for the first three months (25%) or formula fed (19%) (Iliff et al, 2005). The study findings also compares favorably with a prospective cohort study done in Durban, South Africa that showed exclusive breastfeeding carried a significantly lower risk of HIV-1 transmission than mixed feeding (Coutsoudis et al, 1999). In addition, exclusive breastfeeding has been found to result in a three-to four-fold decrease in HIV transmission compared to non-exclusive breastfeeding in several large prospective studies South Africa (Coovadia et al, 2007; Coutsoudis et al, 2001), Zimbabwe (Iliff et al, 2005) and Ivory Coast (Becquet et al, 2008). Similarly, studies have shown that breastfed infants who also received solids ere significantly more likely to acquire infection than were exclusively breastfed children (p=0.018) (Coutsoudis et al, 2001). In Ethiopia, mixed infant feeding had been shown to increase the risk of mother- to- child transmission of HIV (Zelalem Berhan et al, 2014). Therefore this study corroborates earlier findings that have demonstrated exclusive breastfeeding within the first 6 months do reduce the risk of HIV transmission from Mother-to-child. Exclusive breastfeeding offers HIV-1-infected women in developing countries an affordable, culturally acceptable, and effective means of reducing mother-to-child transmission of HIV-1 while maintaining the overwhelming benefits of breastfeeding. Advocacy and campaigns for EBF needs to be sustained at all levels to ensure 100% uptake and coverage.

The study found out that for every one year duration between enrollment and delivery, the chances of the baby having an HIV-negative status at 18-24 months was approximately 1.5 times (p=0.001). This is in tandem with study that showed that starting ARV prophylaxis earlier in pregnancy is more effective to reduce infant HIV (Gaillard et al, 2004). Similarly, shorter duration of HIV treatment was associated with increased risk of mother-to-child transmission of HIV (Zelalem Berhan et al, 2014). So women should be encouraged to plan pregnancies and attend antenatal care sufficiently early, to diagnose and assess maternal HIV infection and be started on ARVs. Therefore, early ANC attendance and HIV testing of women and girls in the reproductive age should be encouraged and promoted by all stakeholders.

The greatest strength of this study is that it was conducted in the real world setting of Ministry of Health facilities in the four counties in Western Kenya. As a result, the findings of our study are more likely to reflect actual outcomes of MTCT rates within the public health facilities in Kenya and sub-Saharan African than do results from randomized clinical trials.

5. Conclusion

The results of this study are in agreement with some previous studies. The study reported MTCT rate varied at selected time points. Notable differences were reported with regard to the ARV prophylaxis regimen with dual therapy (AZT) recording the lowest MTCT rate at 18-24 months. Majority of the mother-baby pairs received HAART prophylaxis, followed by AZT. Very few were given NVP prophylaxis and fewer were not given any form of ARV prophylaxis. In the study, the HIV status at 18-24 months also showed variation with the feeding options. However, feeding option at 6 weeks was a key predictor of HIV status at 18-24 months. EBF had a low HIV positivity as compared with ERF and MF that had much higher HIV positivity. The study also found out that most babies with HIV-negative status at 18-24 months were EBF at 6 weeks as opposed to those who are HIV-positive status. Early treatment initiation was associated with HIV-negative status at 18-24 months.

Conflict of Interest Declaration

The authors declare no conflict of interest.

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