MOTHER-TO-CHILD TRANSMISSION OF HIV USING SINGLE, DUAL AND TRIPLE ANTIRETROVIRAL PROPHYLACTIC REGIMENS: CORRELATES AND TURNAROUND TIME IN VIHIGA, KAKAMEGA, BUNGOMA AND BUSIA COUNTIES, KENYA.

By

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DECLARATION

I declarethat this thesis is a presentation of my original work and has not been submitted or presented for an award of any degree in any University. No part of this thesis may be reproduced without prior written permission of the author and/or Maseno University.

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DEDICATION

To my loving and caring wife, Aynalem Zegeye Leliso

ABSTRACT

The World Health Organization report indicates that in 2013, about 35 million people worldwide lived with HIV and AIDS.HIV can be transmitted from mother to child during pregnancy, at childbirth and during breastfeeding. High rates of mother-to-child HIV transmission (MTCT) in developing countries continue to happen despite availability of efficacious interventions. Numerous studies have shown that socio-demographic, clinical and biological correlates and TAT are known to influence MTCT. Yet socio-demographic characteristics of the HIV positive mother-infant pair, the clinical and biological correlates, MTCT rates and the DBS-PCR turn-around-time (TAT) and the associated factors have not been ascertained in the local setting of Ministry of Health facilities in Kakamega, Bungoma, Vihiga and Busia counties, Kenya. The purpose of this study was to determine MTCT of HIV using single, dual and triple ARV prophylaxis regimens and their socio-demographic, clinical, biological correlates and to assess the DBS-PCR TAT and the underlying factors in the four counties. A retrospective cohort study using prospectively collected data in MOH HEI register from 24 health facilities was carried out. Between January 2012 and June 2013, 1751 HIV mother-baby pairs were enrolled in the 24 health facilities with missing data standing at an average of 18%.The study population comprised of HIV positive mother-baby pairs enrolled from January 2012 to June 2013. The outcome measures were infant HIV status at 6 weeks, 9 to <18 months and 18-24 months. Analysis was done using descriptive statistics, chi-square test, and logistic regression. Majority of mothers 79.3% were legally married, 5.4% were single, 5.4% were widowed, 3.5% divorced, 1.8% were cohabiting, 0.9% were separated. About 78.1% received HAART, 14.2% received AZT, 1.7% received NVP, 4.3% received no prophylaxis. The MTCT rates were 5.9%, 7.7% and 5.6% at 6 weeks, 9 to <18 months and 18 months respectively.HIV transmission rate at 18-24 months by ARV prophylaxis regimen received showed 7.1%, 3.3%, 5.4%, 8.2% for sdNVP, AZT, HAART and none respectively (p<0.001).EBF had 3.8% HIV positivity, ERF had 15.8% HIV positivity and MF had 13.2% HIV positivity (p<0.001*)*.Babies born to separated mothers had approximately 7 times likelihood of having HIV negative results at 18-24 months as compared to widowed women (OR=7.517, p=0.022).Babies who were exclusively breastfed at 6 weeks weremore likely to be HIV negative at 18-24 months by approximately 76% (p<0.001) as compared to babies who were exclusively breastfed on replacement feeds. The mean duration between collection and receiving specimens at Alupe KEMRI laboratory was 16.5days, between receiving and testing the specimens at the laboratory was 16.8days and between specimen collection and results received at the health facilities was 46.9days. Results showed most mothers were legally married. Widowed women wereless likely to have HIV negative babies at 18-24 months as opposed to separated women. Most of the mother-baby pairs received HAART prophylaxis, followed by AZT with 1.7%receiving NVP prophylaxis while4.3% didn't receive any form of ARV prophylaxis. AZT depicted the lowest MTCT rate at 18-24 months. Exclusive Breast Feeding (EBF)was associated with a low HIV positivity as compared with Exclusive Replacement Feeding (ERF) and Mixed Feeding (MF). Delays were noted in submitting the specimens to Alupe KEMRI laboratory due to batching and hubbing practices. HIV prevention efforts should focus on widowed women; EBF at 6 weeks be encouraged and specimen batching and hubbing be discouraged. The results of the study will inform PMTCT programming and policy formulation and county and national levels.

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ABBREVIATIONS AND ACRONYMS

ACTG	AIDS Clinical Trial Group
ANOVA	Analysis of Variance
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Clinic
ART	Anti-retroviral Therapy
ARVs	Anti-retroviral drugs (*also* Anteretrovirals)
AZT	Zidovudine
CDC	Centers for Disease Control and Prevention
CD4	Cluster of differentiation 4
CORPs	Community Owned Resource Persons
CTA	Call To Action
DASCO	DistrictHIV and AIDS and STI Coordinator
DBS	Dry Blood Spot
DMLTs	District Medical Laboratory Technologists
DHMT	District Health Medical Team
DNA	Deoxyribonucleic acid
DRC	Democratic Republic of Congo
DPT1	Diphtheria, Pertussis, Tetanus 1
EBF	Exclusive Breast Feeding
EID	Early Infant Diagnosis
FHI	Family Health International
FP	Family Planning
HAART	Highly active antiretroviral therapy

HCWs	Health Care Workers
HCT	HIV Counselling and Testing
HEI	HIV Exposed Infant
HIV	Human Immune Deficiency Virus
IEC	Information, Education and Communication
KAIS	Kenya AIDS Indicator Survey
KII	Key Informant Interview
KDHS	Kenya Demographic and Health Survey
KEMSA	Kenya Medical Supplies Agency
MCH	Maternal Child Health
MTCT	Mother to Child transmission of HIV
MTCTP	Mother to Child HIV transmission Prevention
MOH	Ministry of Health
NACC	National AIDS Control Council
NARESA	Network of AIDS Researchers in Eastern and Southern Africa
NASCOP	National AIDS and STI control Programme
NIAID	National Institute of Allergy and Infectious Diseases
NVP	Nevirapine
OIs	Opportunistic Infections
OVC	Orphans and Vulnerable Children
PARTO	Provincial Antiretroviral Officer
PATH	Program for Appropriate Technology in Health
PASCO	Provincial HIV and AIDS and STI Coordinator
PCR	Polymerase Chain Reaction

PCP	*Pneumocystis carinii* pneumonia
PMTCT	Prevention of Mother to Child Transmission of HIV
PEPFAR	The U.S. President's Emergency Plan For AIDS Relief
PLHIV	Persons Living with HIV
RH	Reproductive Health
RNA	Ribonucleic acid
RTI	Respiratory Tract Infection
sd-NVP	single dose Nevirapine
STI	Sexually Transmitted Infection
SPSS	Statistical Package for Social Sciences
TAT	Turn Around Time
TB	Tuberculosis
TWG	Technical Working Group
UNAIDS	Joint United Nations Programme on HIV and AIDS
UNGASS	United Nations General Assembly Special Sessionon HIV and AIDS
UNICEF	United Nations Children's Fund
US	United States of America
USAID	United States Agency for International Development
U5MR	Under 5 mortality rate
VCT	Voluntary Counselling and Testing
WHO	World Health Organization

DEFINITION OF TERMS

ARV: ARV is an abbreviation for anti-retroviral drugs. Antiretroviral drugs are medications for the treatment of infection by retroviruses, primarily HIV.

ARV prophylaxis: Isshort-term use of antiretroviral drugs to reduce HIV transmission from mother to infant.

Context*:* Is the circumstance that form the setting for an event, statement, or idea, and in terms of which it can be fully understood and assessed. It can also refer to the circumstances in which an event occurs; a setting [Free Dictionary (www.thefreedictionary.com/context, retrieved on 27th April 2011].

Early Infant Diagnosis (EID): Is the process of identifying HIV-infected infants under the age of 18 months using virology tests (DNA-PCR) methods to detect viral nucleic acids or proteins. This provides a critical opportunity in the early identification and strengthening of follow-up of HIV-exposed children, assures early access to ARV treatment for infected children, and aid evaluation of PMTCT programmes, and increase capacity to use laboratory technology in testing for HIV.

Mother-to-child transmission of HIV: HIV transmission from HIV-infected woman to her child which can occur during pregnancy, delivery or breastfeeding period.

MTCT rate: Proportion of children born to HIV positive women that tested positive for HIV at selected points in time.

PMTCT: Refers to interventions to prevent transmission of HIV from a mother living with HIV to her infant during pregnancy, labour and delivery, or during breastfeeding.

CHAPTER ONE
INTRODUCTION AND BACKGROUND
1.1Background information

The HIV and AIDS remains one of the key challenges in the 21st century with political, economic, public health, social and scientific consequences globally. HIV and 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). According to UNAIDS, there are 13 high burden countries which account for 75 percent of the estimated 1.5 million pregnant women living with HIV in 2007 in low and middle-income countries and nearly 75 per cent of all children living with HIV. All but one of these countries (India) are in sub-Saharan Africa, Kenya inclusive (UNAIDS, 2010). In 2009, around 400,000 children under 15 years became infected with HIV, mainly through mother-to-child transmission (MTCT). About 90% of these MTCT infections occurred in Africa where AIDS is beginning to reverse decades of steady progress in child survival (UNAIDS, 2010).

In Sub-Saharan Africa where HIV prevalence is highest, women are most affected with an average of 13 infected women for every 10 infected men. The high HIV prevalence in women of childbearing age threatens child survival and development globally as 640,000 children are infected with HIV mostly due to MTCT and 540,000 die of AIDS every year(Walker, Schwartlander, & Bryce, 2002). In many sub Saharan Africa countries including Kenya, this epidemic is reversing child survival gains of the past decade (Walker *et al.*, 2002). This is a worrying trend from a public health point of view.

According to Kenya AIDS Indicator Survey (KAIS) 2007, the HIV sero-prevalence in Kenya is 7.8% among adults aged 15-49 years, being higher in women (8.7%) than in men (5.6%)

(MOH, 2007b). With an HIV prevalence of 7.8%, the number of HIV - exposed babies is 114,101 and at least 45,640 HIV-positive babies are born, assuming a 40 % transmission(MOH, 2008).

In Kenya, the first case of HIV and AIDS was diagnosed in 1984 and by 2003 there were an estimated 2.3 million infected people with a prevalence of 10.2% among adults(MOH, 2004). Kenya's Ministry of Health (MoH), through NASCOP (National AIDS and STI Control Programme), 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 ongoing review of guidelines, program implementation, update stakeholders and discuss challenges and upcoming activities.The TWG is also responsible for updating national guidelines for PMTCT. These guidelines recommended routine opt-out HIV testing and counseling and administration at first contact of single dose Nevirapine to mother and baby. The goal of the National PMTCT Program was in line with the goal set out at the United Nations General Assembly Special Session on HIV and AIDS (UNGASS) in 2001 to reduce the proportion of infants infected with HIV by 20% by the year 2005 and 50% by 2010. In Kenya, the National PMTCT Programme plans for universal PMTCT coverage.This massive roll out of PMTCT services aimed 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).

HIV can be transmitted from a mother to her child during pregnancy, 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. Without treatment, around 15-30% of babies born to HIV positive women will become infected with HIV during pregnancy and delivery(De Cock *et al.,* 2000). A further 5-20% will become infected through breastfeeding (De Cock *et al.,* 2000).

The high rates of MTCT in developing countries, compared to much lower rates in richer countries, illustrate growing inequalities in global health. 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 safely 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).

The current PMTCT guidelines recommend use of more efficacious regimens—the dual and triple therapy.In the guidelines, pregnant women who are not eligible for ART should be started on ARV prophylaxis. They should be initiated on AZT (300 mg BD) from 14 weeks of pregnancy or as soon as possible thereafter. At the onset of labour, HIV-infected pregnant women receive AZT 600 mg PLUS 3TC 300 mg PLUS NVP 200 mg at once followed by

AZT (300 mg BD) and 3TC (150 mg BD) seven days post-delivery. Single dose NVP given at the beginning of labour has the ability to rapidly decrease intracellular and extracellular HIV viral levels and to act synergistically with AZT and 3TC. However, to reduce the risk of development of NVP resistance following sd-NVP, a 7-day post-partum regimen of AZT and 3TC is given to the mother after delivery. This is called OPTION A of ARV prophylaxis (MOH, 2011b).

However, in settings with the capacity to initiate and monitor triple therapy on HIV-infected pregnant women, triple ARV prophylaxis can be used, in a therapy regimen called OPTION B. Due to the risk of NVP-associated hepatic toxicity in women with a CD4+ count >250 cells/ mm3, it may be necessary to use LPV/r-based triple therapy(MOH, 2011b). Emerging evidence has shown increased morbidity and mortality in patients who interrupt ART hence women who are initiated on triple ARV prophylaxis (OPTION B) for PMTCT should continue with lifelong therapy irrespective of CD4+ count or WHO clinical stage or breastfeeding status. HIV-exposed infants of women on ART (for their own health or for PMTCT - option B**)** should receive 6 weeks of daily nevirapine irrespective of breastfeeding practices. Infants who are breastfeeding and whose mothers are not on ART should receive daily nevirapine until one week after complete cessation of breastfeeding. Infants who are not breastfeeding should receive 6 weeks of daily nevirapine (MOH, 2011b).

Significant programmatic experience and research evidence regarding HIV and infant feeding which have accumulated since WHO's recommendations on infant feeding in the context of HIV were last revised in 2006. In particular, evidence has been reported that antiretroviral (ARV) interventions to either HIV-infected mother or HIV-exposed infant can significantly reduce the risk of postnatal transmission of HIV through breastfeeding. This evidence has

major implications for how women living with HIV might feed their infants, and how health workers should counsel these mothers. Together, breastfeeding and ARV intervention have the potential to significantly improve infants' chances of surviving while remaining HIV uninfected. The benefits of breastfeeding can now be achieved by mothers living with HIV, with a very low risk of transmitting HIV to the infant when breastfeeding is combined with maternal or infant antiretroviral (ARV) interventions. This avoids the risks associated with formula feeding and attains the ultimate goal of "HIV-free survival" for more infants(WHO/UNICEF, 2010).

Where national authorities promote breastfeeding and ARVs, mothers known to be HIV-infected are now recommended to breastfeed their infants until at least 12 months of age. The recommendation that replacement feeding should not be used unless it is acceptable, feasible, affordable, sustainable and safe (AFASS) remains(WHO/UNICEF, 2010).

To determine the HIV status of children less than 18 months, virological tests such as DNA-PCR are recommended and are widely in use despite the limited availability of the laboratory services especially in developing countries such as sub-Saharan Africa.The Early Infant Diagnosis (EID) was born from the realization that children below 18 months may not benefit from HIV testing and yet they are at risk of getting the virus through their mothers(Ostfeld, 2009). Early Infant Diagnosis coverage is still unacceptably low, despite scale-up of laboratory capacity for virological testing and implementation of larger dried blood spot testing networks.Some of the challenges of EID include insufficient infrastructure, lack of access to EID for children born to women living with HIV and operational barriers such as turnaround time for results varies greatly and loss to follow up(Ostfeld, 2009).

Some countries have made great strides in providing access to early infant diagnosis of HIV. In 2007, 30 low- and middle-income countries used DBS filter paper to perform DNA PCR testing for HIV in infants, up from 17 countries in 2005 (UNICEF/UNAIDS/WHO, 2008). DBS has been used for transporting specimens to a centralized laboratory for HIV DNA testing in several countries in sub-Saharan Africa (Botswana, Côte d'Ivoire, Kenya, Rwanda, South Africa, Zambia and others).

Early Infant Diagnosis begun in Kenya in 2005, on a small scale in Nairobi and Busia, but has now expanded and covers the entire country. Currently, there are four testing laboratories that are based in different parts of the country: KEMRI HIV Research Laboratory in Nairobi, KEMRI-WRP CRC laboratory in Kericho, KEMRI-CDC Laboratory in Kisumu and KEMRI-ALUPE Laboratory in Busia. There is currently a coordinated plan to scale-up the testing in these laboratories and to increase the number of testing laboratories. Initially offered to symptomatic infants with known or suspected HIV exposure, the EID was expanded with the help of Ministry of Health (MOH), Clinton Foundation (CF) and PEPFAR. In May 2006, the MOH introduced a national EID algorithm recommending PCR testing in all HIV-exposed infants from 6 weeks with confirmatory antibody test at 18 months. The network of 4 laboratories provides DNA PCR testing (Roche Amplicor 1.5). Over 500 health care providers (HCP) from > 36 districts trained in DBS sample collection. Antenatal cards were used to identify HIV-exposed infants. DBS samples were shipped to network laboratories by courier services.

In collaboration with National AIDS and STD Control Programme (NASCOP), National Public Health Laboratories (NPHLS), The Walter Reed Project (WRP), The Clinton Foundation Health Access initiative (CHAI), Centers for Disease Control and Prevention

(CDC), International Centre for AIDS Care and Treatment Programs (ICAP), and Academic Model Providing Access to Healthcare (AMPATH), KEMRI has since 2006 worked on the study for EID of HIV in Kenya which is currently being coordinated by the Centre for Infection and Parasitic Diseases Control (CIPDCR) in Alupe-Busia.Since 2009, there have been deliberate efforts to scale-up EID in Western Kenya to ensure that all the PMTCT sites are offering the services as part of the routine laboratory support. This has seen improved access of the EID-DBS sites from the initial 2 sites (Kakamega Provincial Hospital and Busia District Hospital) to the current 300 by 2016.

Turnaround time (TAT) for results vary greatly. Slow TAT for PCR results is a major problem for retention, aggressive clinical progression and high HIV-related mortality in infants. In some countries, site level batching has significantly increased TAT and low rates of result return within 30 days. In cases where there is an additional step in the transport network between the site and the central lab (for example a hub site) TAT for EID result increased greatly. Even when results are returned within 30 days, many patients never receive their results, underscoring other challenges with counseling, patient follow up and data systems(Ostfeld, 2009).One challenge is that the type of laboratory which can support sophisticated PCR equipment is often only available at a referral point or center of excellence, although blood samples can be taken from more remote locations and brought into the central laboratory.

The context, resources and demands of PMTCT programmes differ greatly across regions and even across programmes within the same country. The greatest strength of this study is that it was conducted in the local setting of Ministry of Health facilities in the four counties in Western Kenya. As a result, the findings of the current study more likely reflect the actual

outcomes of MTCT rates within the public health facilities in Kenya and sub-Saharan African than do results from randomized clinical trials.

The objectives of this study were to describe the social and demographic characteristics of mother-infant pair and their association with MTCT, ascertain the different PMTCT approaches or regimens that mothers and infants receive, their MTCT rates and socio-demographic, clinical and biological associated correlates and determine the DBS-PCR TAT and associated factors in Vihiga, Bungoma, Kakamega and Busia counties, Kenya.

1.2Problem statement

Prevention of Mother-To-Child Transmission (PMTCT) of HIV is critical for most ministries of health in the world because Mother-to-child transmission of HIV accounts for over 90% of new pediatric HIV infections(UNAIDS, 2009) and therefore prevention of mother to child transmission of HIV is critical in averting the number of new infections in children. Social and demographic characteristics such as sex, maternal age, maternal weight, marital status have been shown to affect the MTCT rates.

Western Kenya has witnessed tremendous progress since 2001 and this has seen the scale-up of PMTCT sites from the initial 5 to the current 300 (90%) (DHS2, accessed in October 2015)and this means that Kenya has met the UN General Assembly Special Session on Drugs (UNGASS) target. Despite the rapid expansion of PMTCT programs, not all mothers are able to access PMTCT services leading to an increased infection of children born by these mothers. In addition, the exact MTCT rate with different PMTCT approaches in Kenya and western Kenya in particular had not been ascertained. Antiretroviral prophylaxis is a key PMTCT intervention and over the last decade, there has been progressive shift from the

initially WHO recommended sdNVP to more efficacious regimens. This shift also encourages initiation of ARV prophylaxis as early as the first trimester. The low proportion of women who make the 1st ANC visit during the 1st trimesterpresents a challenge for implementation of the more efficacious ARV PMTCT regimen that should be initiated for the HIV infected pregnant women starting from the end of the 2ndtrimester(Mutsotso *et al.,* 2009).

An essential first step in caring for HIV-infected children is accurate and early diagnosis of HIV. This requires scaling up of Early Infant Diagnosis (EID)as part of health systems strengthening interventions such as increasing laboratory capacity, provision of equipment, ensuring a reliable supply of reagents, the training of service providers and the establishment of networks that effectively link diagnosis with care.

In western Kenya, the scale-up of PMTCT services has served as bedrock for the scale-up of EID with all the PMTCT sites currently offering these services. Despite these successes, a number of challenges still exist. Forexample, inadequate infrastructure, shortage of human resource, lack of adequate training and stigma that could influence MTCT rates in Western Kenya. To date, there is inadequate dataon the context, the status of the ART prophylactic regimens in use and MTCT rates that would guide evidence-based PMTCT program implementation in Kenya. As such, the current study aimed at determining the social and demographic characteristics of mother-infant pairs, MTCT rates with single, dual (Option A) and triple ARV prophylaxis regimens (Option A, B and B+)and associated socio-demographic, clinical and biological correlates as well as the PCR-DBS TAT in Western Kenya.

1.3 Objectives

1.3.1 Broad objective

To determine the mother-to-child transmission of HIV using single, dual and triple antiretroviral prophylactic regimens, their correlates and turnaround time in Vihiga, Kakamega, Bungoma and Busia counties, Kenya.

1.3.2 Specific objectives

a) To examine the socio-demographic characteristics of HIV positive mother-infant pair in Vihiga, Kakamega, Bungoma and Busia counties in Kenya;
b) To determine the MTCT rates at selected time points for single, dual and triple ARV prophylaxis regimens and the associated socio-demographic, clinical and biological correlates in Vihiga, Kakamega, Bungoma and Busia counties in Kenya;
c) To determine the DBS-PCR turnaround time (TAT) and the underlying factors in Vihiga, Kakamega, Bungoma and Busia counties in Kenya.

1.3.3 Research questions

1. What are the socio-demographic characteristics of mother-child pair in Vihiga, Kakamega, Bungoma and Busia counties, Western Kenya?
2. What are the MTCT rates of single, dual and triple ARV prophylaxis regimens on MTCT rates in Vihiga, Kakamega, Bungoma and Busia counties, Western Kenya?
3. What are the DBS-PCR turnaround time and the associated factors in Vihiga, Kakamega, Bungoma and Busia counties, Western Kenya?

1.4Significance of the study

Most countries have made 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%. This study established the socio-demographic characteristics of the HIV positive mother-infant pairs in Vihiga, Bungoma, Kakamega and Busia counties in Kenya. It revealed that majority of the HIV positive women accessing PMTCT services are legally married and young adults aged between 25 to 49 years.

In sub-Saharan Africa, MTCT rates as high as 25% had been reported (Jackson *et al.*, 2003a). Prevention of mother to child transmission of HIV is one of the key interventions in reducing the number of new pediatric HIV infections. It also increased child health and survival, decreases the load on the health system and gives an opportunity to improve and expand health services and strengthen the existing health infrastructure. It is critical in keeping mothers alive and reduced the number of orphans. This study revealed near universal usage of ARV prophylactic regimen at 94% with majority receiving HAART prophylactic regimen. AZT and the single dose NVP is less commonly use in line with the Kenya national PMTCT guidelines. The study further demonstrated that AZT prophylactic regimen had the lowest MTCT rates at 3.3% with HAART prophylactic regimen recording an MTCT rate of 5.4%. While this contravenes numerous studies done that depicts HAART having the lowest MTCT rates and therefore more efficacious, further studies would be needed to understand why AZT still demonstrates a lower MTCT rate as compared to AZT. The study also demonstrated that

low CD4 count, signs of TB infection were associated with a higher likelihood of having HIV infected infant at 18-24 months. Exclusive breastfeeding at 6 weeks was the strongest predictor of infants HIV status at 18-24 months and should therefore be encouraged.

Initially, Early Infant Diagnosis (EID) had not been widely available but in the last 2 years efforts had been made to scale up the services to ensure all the PMTCT sites offer the services. It was believed that the timelier the rapid testing was performed, the more efficient and effective the treatment would be. The study revealed that the TAT was 47 days but there was county variation with Vihiga County recording lower TAT of 33 days. The reasons for the high TAT is due to specimen batching and hubbing at the peripheral and central health facilities respectively. Vihiga County tended to have less batching and less hubbing of DBS specimens at the health facilities.The results of this study would support PMTCT program design in Western Kenya and also be useful in informing the national PMTCT policy implementation.

CHAPTERTWO
LITERATURE REVIEW

2.1 Socio-demographic characteristics of HIV positive mother-infant pairs

Over 33.4 million people are living with HIV and AIDS worldwide, and about two-thirds or 22.4 million of PLHIV live in sub-Saharan Africa(UNAIDS, 2004; 2009). HIV and AIDS mainly affects people of reproductive age and increasingly affects women, who now account for 57% of new infections in sub-Saharan Africa, where women are 30% more likely to be living with HIV and AIDS than men, and young women aged 15-24 are nearly four times more likely to be infected than their male counterparts(UNAIDS, 2004; 2009). As the period from infection to the development of AIDS and subsequent death is much shorter for children than adults, 20-25% of infected children die before the age of 2 and 60-70% die before 5(UNAIDS, 2004; 2009).

Children constitute 14 percent (370,000 of 2.7 million) of new global HIV and AIDS infections 14 percent (270,000 of 2.0 million) of HIV and AIDS deaths annually, 6 percent (2.0 million of 33.0 million) of the persons living with HIV. Over 90% of HIV infections among children occur through mother-to-child transmission(UNAIDS/WHO/UNICEF, 2008).

In Sub-Saharan Africa where HIV prevalence is highest, women are most affected with an average of 13 infected women for every 10 infected men. This difference is even more marked among young people (15-24 years) with three out of four people living with HIV being female(UNAIDS, 2006).HIV and AIDS transmission from mother to child in Kenya is one of the biggest health and development challenges in Kenya(MOH, 2007a). According to Kenya AIDS Indicator Survey (KAIS) 2007, the HIV sero-prevalence in Kenya is 7.8%

among adults aged 15-49 years, being higher in women (8.7%) than in men (5.6%)(MOH, 2007a).

Numerous studies have demonstrated associations between social and demographic factors such as marital status, level of education, gender, maternal weight, maternal age, baby's birth weight and the prevalence of HIV (Barongo *et al.*, 1992; Dunkle *et al.*, 2008; Farquhar *et al.*, 2011; Hira *et al.*, 1990; Manyahi *et al.*, 2015; Matovu, 2010; Melku, Kebede, & Addis, 2015; Taha *et al.*, 2005; Yahya-Malima, Olsen, Matee, & Fylkesnes, 2006). However, no known study from the literature search has been done to demonstrate the social and demographic characteristics of HIV positive pregnant women in western Kenya.This study sought to determine the socio-demographic characteristics of mother-baby pairs in Kakamega, Vihiga, Busia and Bungoma counties.

2.2 Mother-to-Child Transmission of HIV (MTCT) rates at selected time points for dual and triple ARV prophylaxis regimens and the associated factors

Mother to child transmission of HIV can occur during pregnancy, delivery and breastfeeding. 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). Transmission during the peri-partum period accounts for one- to two-thirds of the overall transmission rate, depending on whether breastfeeding occurs or not, and the peri-partum and breastfeeding period has thus become the focus for efforts to prevent MTCT.

2.2.1Mother-to-Child Transmission (MTCT) of HIV rates

Prevention of mother to child transmission of HIV (PMTCT) is supposed to reduce MTCT rate to single digit figures. The transmission of HIV from an infected mother to her child can be reduced to 2 % or less by intensive interventions that include combination potent anti-retrovirals, obstetrical interventions including elective caesarean section at 38 weeks and complete avoidance of breastfeeding (Cooper *et al.,* 2002; Dorenbaum *et al.,* 2002; ECS, 2001; Mofenson & Munderi, 2002). ARV prophylaxis alone, administered in the period around a vaginal delivery, reduces by between 30% and 50% the rate of peri-partum transmission(Cooper *et al.*, 2002).

In resource-constrained settings, elective cesarean section is seldom available and safe, and refraining from breastfeeding is often not feasible or acceptable. Also, even where peri-partum ARV prophylaxis is used, infants remain at substantial risk of acquiring infection in the breastfeeding period (Philippe, 2006). Furthermore, preventive ARV interventions have not yet been implemented on the scale required (Dabis & Ekpini, 2002).

2.2.2 Rates of Mother-to-Child Transmission of HIV of different PMTCT regimens

Mother to child transmission of HIV (MTCT) is highly preventable and the incidence has fallen over 95% in the United States - from over 2,000 to less than 100 each year (Barnhart, October 2007). Breastfeeding through 6 months leads to about 10% extra transmission (from 20% to 30%), while breastfeeding through 18-24 months leads to about 17.5% extra transmission (from 20% to 37.5%), compared to no breastfeeding. In PMTCT programmes,

breastfeeding was proposed to be as short as possible, around 6 months. Hence that will still lead to about 10% transmission (De Cock *et al.,* 2000).

Studies on MTCT and PMTCT in developing countries depict varied MTCT rates with different ARV prophylactic regimens with different breastfeeding options. A recent review of PMTCT rates for various infant feeding options and PMTCT regimens has been summarized in the 2004 WHO document "Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants". The impact on overall MTCT rates is less due to the continued transmission risk in the post-natal period during breastfeeding. There are different transmission rates at 18-24 months for breastfeeding populations, at 6 months or later for non-breastfeeding populations.

In Mozambique, a study revealed that a combination of AZT, lamivudine, and Nevirapine taken from week 28 of pregnancy and up to one month after delivery resulted in significantly reduced HIV levels in breast milk as compared to the HIV levels found in the breast milk of women who were not treated prophylactically (Giuliano *et al.*, 2007). However, in Botswana in 2010, a randomized trial in which one arm received one of two triple drug regimens (Abacavir/Zidovudine/Lamivudine and or Lopinavir/Ritonavir/Combivir) and the control arm received dual prophylaxis of Nevirapine/Combivir showed that HIV transmission did not differ significantly among the groups (Shapiro *et al.,* 2010).

2.2.3 PMTCT Guidelines in Kenya: 2013

The context, resources and demands of PMTCT programmes differ greatly across regions and even across programmes within the same country. In 2012, Kenya published revised PMTCT guidelines based on WHO guidelines (2010) (MOH, 2012). This guideline was in use in the

study area during the study period. Based on the four-pronged approach promoted by the WHO, it focused on primary prevention of HIV infection in women, prevention of unintended pregnancies, reducing transmission during pregnancy, labor and breastfeeding and providing support to HIV-positive women and their families. The revised guidelines have a much greater focus on pharmaceutical prophylaxis than previous guidelines and 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. The Kenyan guidelines include Option A (single dose nevirapine in labour) although option B (more efficacious regimens) (MOH, 2012)was encouraged in settings with the capacity to monitor women receiving triple therapy. This could also be continued through the woman's life without interruption, known as option B PLUS. Infants would receive nevirapine six weeks following birth if the mother was on HAART before pregnancy or is not breastfeeding. If the mother was breastfeeding, the infant would receive nevirapine from birth to one week following the last exposure to breast milk. The guidelines also instructed that, 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). These revised guidelines adhered closely to the best evidence for PMTCT as captured in the WHO guidelines and could contribute to the elimination of mother-to-child transmission by 2015, if implemented across the country. Barriers to

implementation, however, could lead to inconsistent implementation and reduce the guidelines impact.

2.2.4 Anti-retroviral drugs in the prevention of Mother-to-Child Transmission of HIV

2.2.4.1 ARV mono-therapy for PMTCT

Human Immunodeficiency Virus (HIV) infection can be averted through the use of anti-retroviral drugs (Soucat & Knippenberg, 1999). Anti-retrovirals work mainly through two mechanisms (i) Reducing the viral load in the mother (a lesser quantity of virus goes to the infant) and (ii) Preventing the virus from "fixating" itself in the child ("post-exposure prophylaxis"). In 1994, a landmark study conducted by the Pediatric AIDS Clinical Trial Group protocol 076, demonstrated that AZT, given to HIV-infected women during pregnancy, delivery and post-natally to both mother and infant in a population with minimal or no prior antiretroviral therapy reduced the risk of MTCT by two-thirds, from 25 percent to 8 percent. At the time this study was carried out, ARVs were extremely expensive and therefore completely out of reach for developing countries where the majority of HIV infected women live. Therefore, trials were designed to evaluate shorter duration of AZT in Thailand among a non-breastfeeding population and later in West Africa in a breastfeeding population. The Thailand study demonstrated Zidovudine initiated at 34-36 weeks of pregnancy and given through to delivery reduced mother to child HIV transmission by half among non-breastfeeding HIV infected women. In this study, MTCT transmission was 9.4% on Zidovudine and 18.9% on placebo and efficacy was 50.1 % (Shaffer *et al.,* 1999). Since then many other protocols have been evaluated and shown to have varying efficacy in breastfeeding populations (Dabis *et al.,* 1999; Jackson *et al.,* 2003a; Wiktor *et al.,* 1999).

In Ditrame study carried out in Cote d'Ivoire and Burkina Faso among breastfeeding HIV infected women with Zidovudine given from 34-36 weeks to delivery, probability of HIV infection in the infant at 6 months was 18.0% in the Zidovudine group and 27.5% in the placebo group. The regimen led to a 38% reduction in early vertical transmission of HIV-1 infection despite breastfeeding (Dabis *et al.,* 1999). A similar study done without postpartum dose was aimed at assessing the safety and efficacy of short course perinatal oral Zidovudine among HIV-1 positive breastfeeding women in Abidjan showed that the estimated risk of HIV-1 transmission in the placebo and Zidovudine groups were 21.7% and 12.2% at 4 weeks and 24.9% and 15.7% at 3 months respectively and that the efficacy of Zidovudine was 44% at age 4 weeks and 37% at 3 months (Wiktor *et al.,* 1999).

In a randomized clinical trial to evaluate the efficacy of two short course antiretroviral drug regimens for prevention of HIV transmission from infected mothers to their babies found single dose Nevirapine (sdNVP) given to the mother at the onset of labor and to the infant within 72 hours of life reduced the risk of perinatal HIV transmission among breastfeeding women in Uganda by 47% at 14-16 weeks and by 41% at 18 months compared to a short intrapartum/neonatal regimen of AZT(Jackson *et al.,* 2003b). A longer period of follow of HIVNET 012 study showed that estimated risks of HIV-1 transmission in the Zidovudine and Nevirapine groups were 25.8% and 15.7% by age 18 months, respectively. Nevirapine was associated with a 41% reduction in relative risk transmission through to age 18 months (Jackson *et al.,* 2003a). The simplicity and affordability of the sdNVP enabled African governments for the first time to begin to integrate PMTCT into the health care settings. The new PMTCT guidelines recommends use of more efficacious regimens, which isa departure from use of these single dose regimen for ARV prophylaxis (MOH, 2012).

2.2.4.2 Dual ARV therapy for PMTCT

In general, combination regimens are more efficacious than single-drug regimens. A meta-analysis of individual recordsof data from several African MTCT-prevention trials indicated that the combination of AZT and 3TC from 36 weeks of pregnancy had greater efficacy in preventing MTCT than ARV monotherapy with either AZT from 36 weeks of pregnancy or Sd-NVP (Valeriane, 2005). Studies in high-income countries also indicate that a combination of ARV drugs is more efficacious than single-drug regimens (Mandelbrot *et al.,* 2001). In a cohort study in the United States, the risk of MTCT was 10.4% among women receiving AZT monotherapy, 3.8% among those receiving dual ARV regimens and 1.2% in women receiving triple-ARV regimens (Cooper *et al.,* 2002).

2.2.4.3 CD4 driven ARV therapy for PMTCT

The previous consensus was that women meeting eligibility criteria should receive HAART with ZDV +sdNVP plus Combivir tail for women not needing treatment and sdNVP and 1 week ZDV for babies and recommended extended infant ARV prophylaxis for those that are breastfeeding (IAS, Cape town, 2009). A new concept that might address MTCT in HIV-infected women with moderate to high CD4-cell counts is a triple antiretroviral prophylaxis during pregnancy and breastfeeding (Becquet *et al.,* 2009).New data from the Kesho Bora multicenter randomized trial in Kenya, Botswana and South Africa compares a triple antiretroviral prophylaxis strategy before and after birth with standard short-course antiretroviral regimen in HIV-infected women who are not eligible for ART for their own health. A 43% risk reduction of MTCT was shown at 12 months in the triple antiretroviral group compared with the standard short-course antiretroviral group, whereas the number of laboratory and clinical serious adverse events was similar in both groups. It also showed that starting ARV prophylaxis earlier in pregnancy is more effective to reduce infant HIV

(Gaillard *et al.,* 2004). So, women should be encouraged to plan pregnancies and attend antenatal care sufficiently early, to diagnose and assess maternal HIV infection and start ARVs treatment regimen.

From the foregoing, it is clear that even though the mother to child transmission rates has been carried out extensively in these previous studies, these had been based on randomized controlled clinical trials and none has been conducted in the local setting of Ministry of Health facilities in Western Kenya. Similarly, no study has been done to demonstrate superiority of the HIV transmission rates for single, dual and triple ARV prophylactic regimens in Western Kenya.

2.2.5 Breast milk transmission of HIV

Given the need to minimize the risk of HIV transmission to infants while at the same time not increasing their risk of other causes of morbidity and mortality, WHO/UNICEF/UNAIDS HIV and infant feeding guidelines for decision-makers recommendations state that "when replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of lifeand should then be discontinued as soon as feasible. The recommendations further state that "when HIV-infected mothers choose not to breastfeed from birth or stop breastfeeding later, they should be provided with specific guidance and support for at least the first two years of the child's life to ensure adequate replacement feeding" (WHO/UNICEF/UNAIDS, 2003).

In sub-Saharan Africa, where breastfeeding is critical forinfant survival, postnatal transmission of human immunodeficiencyvirus type 1 (HIV-1) occurs in up to 16% of

untreated infantswhen breast-feeding continues into the second year of life (Wilfert & Fowler, 2007).The main mode of postnatal mother to child HIV transmission is breastfeeding (MOH, 2007b). Breastfed babies continue to acquire new infections as long as they are breastfed. Breastfeeding contributes 10-15% of HIV infections due to MTCT and therefore significantly reduces the efficacy of ARV prophylaxis in PMTCT(De Cock *et al.*, 2000). Breastfeeding through 6 months leads to approximately 10% extra transmission while breastfeeding through 18-24 months leads to approximately 17.5% extra transmission compared to no breastfeeding (De Cock *et al.*, 2000). The estimated annual risk of late postnatal transmission of HIV after 2.5 months of age was 3.2 cases per 100 breastfed children born to HIV infected women (95% CI: 3.1-3.8) in data collected before the use of ARV (Leroy *et al.*, 2002). Although effective interventions have been shown to reducein utero and intrapartum transmission of HIV-1 in resource-limitedcountries, breast-feeding attenuates the efficacy of such methods (Leroy *et al.*, 2002).Thus, a major concern in developing countries is HIV-1 transmissionthrough breast milk (John-Stewart *et al.*, 2004).

Babies are at risk of breast milk transmission of HIV, as long as they continue breastfeeding. Risk of MTCT transmission of HIV is 15-30% without breastfeeding, 25-35% with breastfeeding shortened to 6 months and 30-45% for women breastfeeding for a median of 18-24 months (Gantt *et al.*, 2007). In Kenya, the frequency of breast milk transmissionof HIV-1 was 16.2% in the randomized clinical trial, and themajority of infections occurred early during breastfeeding.The use of breast milk substitutes prevented 44% of infant infectionsand was associated with significantly improved HIV-1–freesurvival in a highly selected population of ARV naïve women (Nduati *et al.*, 2000). Another study estimated annual risk of late postnatal transmission of HIV after 2.5 months of age was 3.2 cases per

100 breastfed children born to HIV infected women (CI:3.1-3.8) in data collected before the use of ARV (Leroy *et al.,* 2002). Among women recently infected with HIV, the risk of transmission through breastfeeding is nearly twice as high as for women infected before or during pregnancy, because of high viral load shortly after initial infection (WHO/UNICEF/UNAIDS, 2003).

In evaluating the efficacy of a maternal triple-drug antiretroviral regimen or infant Nevirapine prophylaxis for 28 weeks during breast-feeding to reduce postnatal transmission of human immunodeficiency virus type 1 (HIV-1) in Southern Botswana, a randomized clinical trial was done with two arms of treatment: either maternal triple drug prophylaxis or standard of care treatment. The findings suggested that the use of HAART in women from early in the third trimester of pregnancy through 6 months of breast-feeding is an effective strategy for preventing mother-to-child transmission while allowing for the benefits of breast-feeding (Chasela *et al.,* 2010). In Mozambique, a prospective observational cohort study of HIV-1 exposed infants of mothers depicted that late postnatal transmission of HIV-1 is significantly decreased by maternal use of HAART with high infant survival rates up to 12 months of age (Marazzi *et al.,* 2009).

In Cape Town, South Africa, PEARL study was conducted by collecting cord blood samples from 43 delivery centers in Cameroon, Côte d'Ivoire, South Africa, and Zambia, where all sites used NVP for prophylaxis, either alone or in combination with other drugs. Of nearly 30,000 cord blood samples collected, 12 percent were HIV positive. Among positive cases, complete charts were available for just over 3,000 cases; of those, roughly half of mother/baby pairs received both mother and infant Nevirapine. The study also showed

service-related failures occurred at every step of the PMTCT cascade including NVP not being dispensed, mothers not taking NVP, and infants not being dosed. Even in sites where PMTCT is available, less than 50% of HIV-exposed infants received sd-NVP prophylaxis (Ekouevi *et al.*, 2012).

In the Eastern Cape and Free State of South Africa, a study showed high HIV incidence during pregnancy and concluded that HIV retesting should be offered in pregnancy in order to promote PMTCT and to identify women living with HIV whose antibody levels were low at first testing (Moodley, Esterhuizen, Pather, Chetty, & Ngaleka, 2009).

Mixed breastfeeding during the first months post-delivery is a common cultural practice in Western Kenya and no study has been done in the Kenya to determine the impact of this practice in the mother to child HIV transmission in an observational or operation research. This is one of the key correlates that the study seeks to determine its effect of pediatric HIV transmission.

The Kesho Bora Randomized Controlled Clinical Trial study conducted in Burkina Faso and Kenya, randomized 824 pregnant women living with HIV and with CD4 counts of 200 to 500 to receive either triple ARV prophylaxis or short-ARV prophylaxis. Over three-quarters of infants in both groups were breastfed. Infants in both groups were treated with single-dose Nevirapine. At 12 months, the cumulative HIV infection rates among infants born to women receiving triple-ARV and short-ARV were 5.6% and 9.3%, respectively (de Vincenzi, 2011).

In Kenya, the frequency of breast milk transmissionof HIV-1 was 16.2% in the randomized clinical trial, and themajority of infections occurred early during breastfeeding.The use of

breast milk substitutes prevented 44% of infant infectionsand was associated with significantly improved HIV-1–freesurvival (Nduati *et al.,* 2000). The risk of transmission through breastfeeding among women recently infected with HIV is nearly twice as high as for women infected before or during pregnancy, because of high viral load shortly after initial infection (WHO/UNICEF/UNAIDS, 2003).

Complete avoidance of breastfeeding is efficacious in preventing MTCT of HIV, but this intervention has significant associated morbidity (e.g. diarrhoea morbidity). If breastfeeding is initiated, two interventions: 1) exclusive breastfeeding during the first few months of life; and 2) extended antiretroviral prophylaxis to the infant (Nevirapine alone, or Nevirapine with Zidovudine) are efficacious in preventing transmission (Horvath *et al.,* 2009). Extended prophylaxis with Nevirapine or with Nevirapineand Zidovudine for the first 14 weeks of life significantlyreduced postnatal HIV-1 infection in 9-month-old infants (Kumwenda *et al.,* 2008).

2.2.6 Risk factors during pregnancy

Early *in utero* HIV infection is rare, and is thought to be more common towards the end of pregnancy. Major factors that have been associated with increased transmission include a high maternal virus load, decreased CD4+ count, lack of HIV neutralizing antibody, advanced clinical disease, primary infection, first-born twins, and obstetric factors including chorio-amnionitis, mode of delivery and more than four hours of ruptured membranes before delivery (Bryson, 1996; Landesman *et al.*, 1996) Progressively, greater disturbances of vaginal flora increase HIV acquisition during pregnancy (Taha *et al.,* 1998). Placental

disruption by for example, chorio-amnionitis, or cigarette smoking and illicit drug use, has been associated with increased HIV transmission risk (Newell, 1998).

To determine the effects of plasma and genital immunodeficiency virus type 1 (HIV-1) on perinatal HIV-1 transmission, a nested case-control study was conducted within a randomized clinical trial of breast-feeding and formula feeding among HIV-1seropositive mothers in Nairobi, Kenya. Analyses showed that, maternal viral RNA levels >43,000 copies/mL (cohort median) were associated with a 4-fold increase in risk of HIV transmission. Maternal cervical HIV-1 DNA, vaginal HIV-1 DNA, and cervical or vaginal ulcers were significantly associated with infant infection, independent of plasma virus load (John *et al.,* 2001). Similarly, in a multicenter retrospective cohort study done in four cities in Sao Paulo State, Brazil, to evaluate the effect of maternal, obstetric, neonatal and post-natal factors on the risk of vertical transmission of HIV-1 supported the importance of severity of maternal HIV-1 disease in the risk of vertical transmission of HIV-1(Tess, Rodrigues, Newell, Dunn, & Lago, 1998).

2.2.7 Risk factors during delivery

Transmission during labor and delivery could occur via direct contact of the fetus/infant with infectious maternal blood and genital secretions during passage through the birth canal, through ascending infection from the vagina or cervix to the fetal membranes and amniotic fluid, and through absorption in the fetal-neonatal digestive tract(Nielsen *et al.,* 1996). Long labor and prolonged membrane rupture may increase the risk of transmission, although this has not been found in all studies. InFrench peri-natal cohort, hemorrhage during labor and the presence of bloody amniotic fluid substantially increased the risk of vertical transmission(Mandelbrot *et al.*, 1998).

In 1999, a study conducted in Mombasa, Kenya aimed at examining the correlation between the presence of HIV-1 in maternal cervico-vaginal secretions and in the infant's oro-pharyngal secretions at birth, andMTCT revealed that infant exposure to HIV-1 in the birth canal and the presence of HIV-infected cells in the infant's oro-pharyngal cavity are independently associated with intrapartum and early postpartum MTCT(Gaillard *et al.,* 2000).

A prospective clinical trial done in a governmental hospital in Mombasa, Kenya to evaluate the effect of vaginal lavage with diluted chlorhexidine onMTCT revealed that vaginal lavage with diluted chlorhexidine during delivery did not show a global effect on MTCT. However, the data suggest that lavage before the membranes are ruptured might be associated with a reduction of MTCT, especially with higher concentrations of chlorhexidine(Gaillard *et al.,* 2001).

Women and infants'transmission in prospective and observational studies demonstrated that the risk of transmission of HIV-1 from mother to infant increases when the fetal membranes rupture more than four hours before delivery(Landesman *et al*., 1996). Similarly, in a multicenter retrospective cohort study done in four cities in Sao Paulo State, Brazil to evaluate the effect of maternal, obstetric, neonatal and post-natal factors on the risk of vertical transmission of HIV-1 indicated that MTCT transmission can be reduced by avoiding amniocentesis(Tess *et al.,* 1998).

A systemic review to assess the efficacy of elective cesarean section showed that elective cesarean section is an efficacious intervention for the prevention of MTCT among HIV-1-infected women not taking ARVs or taking only Zidovudine(Read & Newell, 2005). However, the risk of MTCT of HIV-1 according to mode of delivery among HIV-1-infected

women with low viral loads (low either because the woman's HIV-1 disease is not advanced, or because her HIV-1 disease is well-controlled with ARVs) is unclear(Read & Newell, 2005).

2.2.8 Risk factors in the postnatal period

Breast milk can transmit HIV at any time during lactation; therefore, the rate of HIV infection in breastfed infants is cumulative and increases with duration of breastfeeding. A meta-analysis estimated that the cumulative probability of late postnatal transmission between 4 weeks and 18months of age was 9 infections per 100 child years of breastfeeding, and that the risk of transmission was constant throughout breastfeeding. In this meta-analysis, approximately 42% of all HIV infections in infants were attributable to breastfeeding(Coutsoudis *et al.,* 2004).

Despite a burgeoning literature on the possible mechanisms for the transmission of HIV through breastfeeding a recent review of the subject concluded that the exact mechanism is still unknown(Kourtis *et al*., 2007). Possible portals of virus entry include M cells in the tonsils or overlying the intestinal lymphoid Peyer's patches, direct infection of the enterocyte or possibly direct passage through disruptions in mucosa or between immature mucosa junctions. The roles of cell-free and cell associated virus in transmission and the association between virus levels in plasma and in milk have not been reliably quantified(Kourtis *et al.*, 2007).Epidemiological study has identified a number of both maternal and infant factors known to increase the risk of HIV transmission through breast milk. The maternal factors include high plasma viral load, low CD4 count, breast pathology (including mastitis and abscesses), mode of infant feeding and prolonged duration of breastfeeding (more than 6 months)(Kourtis *et al.,* 2007).

A nested case-control study was conducted within a randomized clinical trial of breast-feeding and formula feeding among HIV-1seropositive mothers in Nairobi, Kenya to determine the effects of breast milk human immunodeficiency virus type 1 (HIV-1) and breast infections on perinatal HIV-1 transmission. The study revealed that breast-feeding, mastitis were associated with increased transmission overall, while mastitis and breast abscess were associated with late transmission (occurring >2 months postpartum) (John *et al.,* 2001).

Breastfeeding is important for the health of children and survival of young infants. Unfortunately, breastfeeding contributes significantly to MTCT of HIV especially in the absence of ARV treatment or prophylaxis. High viral loads of HIV in breast milk are particularly important. In South Africa and Malawi, women with a detectable RNA viral load in their milk at any time during the first six months postpartum were more likely to transmit HIV than were women who did not have detectable virus in their milk(Semba *et al.,* 1999). In West Africa, the rate of late postnatal transmission increased 2.6 times for every log 10 increase in plasma RHA viral load measured in late pregnancy(Leroy *et al.,* 2003).

A study done in Malawi demonstrated that mastitis and breast milk HIV-1 load may increase the risk of vertical transmission of HIV-1 through breast-feeding(Semba *et al.,* 1999). However, another study done in Zimbabwe in 2005 revealed that HIV-1 DNA loads in breast milk were not increased during mastitis. Neither milk cell counts nor electrolyte concentrations were useful predictors of milk HIV-1 RNA or DNA loads for individual women(Gantt *et al.,* 2007).

Infant factors known to increase the risk of transmission through breastfeeding include damage to the mucous membranes (e.g. by oral thrush), damage to the intestinal mucosa by cow's milk or allergic reactions to complementary foodswhich may affect intestinal permeability(Kourtis *et al.,* 2007).

The 2008 Kenya Ministry of Health Guidelines captures risk factors for MTCT (Table 2.1).

Table 2.1: Summary of risk factors for Mother-To-Child transmission of HIV(MOH, 2008)

	Strong evidence	**Limited evidence**
Viral	High viral load	Viral resistance(theoretical possibility) Viral genotype and phenotype.
Maternal	Immune deficiency(low CD4 count), HIV infection acquired during pregnancy or breastfeeding period	Vitamin A deficiency, anemia, sexually transmitted diseases, chorio-amnionitis, frequent unprotected sexual intercourse, multiple sexual partners, smoking, injecting drug abuse.
Obstetric	Vaginal delivery(compared to elective caesarean section), rupture of the membranes for more than 4 hours	Invasive or traumatic procedures: instrumental deliveries, amniocentesis, episiotomy, external cephalic version(ECV),etc., intrapartum hemorrhage.
Fetal/infant	Prematurity	Lesions of skin and/or mucous membranes.
Breastfeeding	Duration of breastfeeding, mixed feeding, breast disease(mastitis/cracked nipples)	Oral thrush (baby).

Replacement feeding is the only way to completely avoid post-natal HIV transmission; however, this is not an affordable, feasible, acceptable, sustainable or safe option for many HIV-infected women in developing countries(WHO/UNICEF, 2010). Weighted against the low (<1% per month) but ongoing risk of transmission through breast milk, breastfeeding substantially reduces the risk of infant mortality from other infectious diseases and malnutrition-by 4-6 fold in the first 6 months and close to 2 fold in the second six months of life(Bhutta *et al.,* 2008).

More recently 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), Zambia (Kuhn, 2007) and Ivory Coast (Becquet *et al.,* 2008). 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%)(Coutsoudis *et al.,* 2001). A similar finding was reported from the ZVITAMBO trail in Zimbabwe in 2005(Iliff *et al.,* 2005). In this study amongst 2060 HIV positive mothers with infants who were HIV-Polymerase Chain Reaction negative at 6 weeks, the rates of postnatal HIV transmission were 5.1, 6.7 and 10.5 per 100 child years of exclusive, predominant and mixed breastfeeding respectively. Most recently the Vertical Transmission (VT) study in KwaZulu Natal, South Africa, assessed transmission rates at 6 and 22 weeks depending on the feeding mode. A 1372 mother-infant pairs were followed: 82% of mothers initiated exclusive breast-feeding (EBF) while women with CD4+ count <200 were most likely to use replacement feeding from birth. By 3 months two thirds of the

mothers were reported to still be exclusively breastfeeding and 40% were EBF at 6 months. Replacement feeding (RF) was associated with 2-3-fold increase risk of mortality during the first 3 months compared to EBF; and mixed feeding including solids was associated with11-fold increased risk of infant mortality compared to EBF. Women with CD4+ counts <200 had the highest risk of transmission, even with EBF, and of infant mortality(Coovadia *et al.,* 2007).

From the foregoing, it is clear that clinical and biological correlates have been ascertained in controlled research settings but none has been conducted in the local setting of Ministry of Health facilities more so in the four counties in Western Kenya given that no local literature exists on the same.The study sought to ascertain the clinical and biological correlates of MTCT rates in Western Kenya.

2.3Dry Blood Spot-Polymerase Chain Reaction (DBS-PCR) turnaround time (TAT) for Early Infant Diagnosis

2.3.1 Early Infant Diagnosis

The primary goal of early infant diagnosis is to identify the HIV-infected child early prior to the development of clinical disease during the first months of life and not to exclude HIV infection(Pahwa *et al.,* 2008). A number of different testing strategies for early infant diagnosis have been investigated, including surrogate markers, such as hypergammaglobulinemia, IgA HIV antibodies (since this antibody subtype is not transferred across the placenta but is produced by the infant), qualitative p24 antigen assays, determination of reverse transcriptase activity, and HIV viral culture (previously the gold standard assay). Assays currently favored for early infant definitive diagnosis include nucleic acid testing using polymerase chain reaction (PCR) assays (both qualitatively [DNA and RNA] and quantitatively [RNA]), and p24 antigen quantitation. More recent experimental approaches have included investigation of CD4/CD8 ratios for distinguishing HIV-infected

from HIV-uninfected infants at an early age following exposure to HIV(Pahwa *et al.*, 2008; Swaminathan, Gangadevi, & Perumal, 2007).Data contributed from multiple perinatal studies, primarily in the US and Europe, with formula fed populations showed that DNA PCR for infant diagnosis has a sensitivity of 96-98% at 4-6 weeks of age(Dunn *et al.*, 1995).

Early definitive diagnosis of HIV infection in infants is critical to ensuring that HIV-infected infants receive appropriate and timely care and treatment. For this reason, the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the Centers for Disease Control and Prevention (CDC) have recommended that countries provide access to early virological testing for HIV-exposed infants(Stevens *et al.*, 2008; WHO, 2007a, 2007b). The use of the Perkin Elmer heat-denatured p24 antigen quantitation assay, designed by Schüpbach and colleagues, has been extensively evaluated as a tool for infant diagnosis and monitoring in several countries across different subtypes. The assay's sensitivity in different subtypes has been determined to be in the range of 97.7% to 100%, with specificities similarly being between 97% and 100%(Table 2.2).

Table 2.2: Summary of Performance of Ultrasensitive Heat-Denatured p24 Antigen Quantitation Assay for Early Infant Diagnosis of HIV

Region	Prevalent Subtype*	Sensitivity and Specificity
Tanzania(Lyamuya *et al.*, 1996)	A, D	99% sensitivity, 100% specificity
Uganda (Mulago) (Elyanu, 2007)	A, D	94% sensitivity, 98% specificity overall (compared with Roche DNA PCR)
Switzerland and United States(Nadal *et al.*, 1999)	B	97% – 98% sensitivity, 98% – 99% specificity
South Africa(Sherman, Stevens, & Stevens, 2004)	C	97.7% sensitivity, 100% specificity at 6 weeks
Zimbabwe(Zijenah *et al.*, 2005)	C	96.7% sensitivity, 96.1% specificity
Thailand and Cambodia(Nouhin, Nguyen, Reynes, & Henin, 2004; Sutthent *et al.*, 2003)	E	97% – 98% sensitivity, 97% – 99% specificity
Vietnam (Annette, 2007)	E, recombinant AE	100% sensitivity, 100% specificity

*subtype nomenclature provides us with an important tool that enables us to monitor the spread of human immunodeficiency virus type 1 (HIV -1), and the creation of an international HIV genetic sequence database has facilitated better classification of globally circulating viral strains. Phylogenetic analyses of the *env* and *gag* genes of HIV-1 indicate that there are three distinct groups (M, N and O) of the virus circulating worldwide. Within the major group M, there are currently nine defined subtypes, or clades (A to D, F to H, J and K)(Cornelissen, van Den Burg, Zorgdrager, & Goudsmit, 2000).

The general conclusion from published data is that the HIV-1 p24 antigen in blood is sensitive enough for early diagnosis of HIV infection in infants and young children across different subtypes, but only if the ultrasensitive HIV p24 antigen assay described earlier is used. In addition, it should be noted that this assay cannot be widely recommended until the consistent supply of kits can be guaranteed(Stevens *et al.,* 2008; WHO, 2007a).Nucleic acid–based testing strategies have become the approach of choice in many centers around the world. Qualitative DNA-based assays have been evaluated quite extensively, with the commercial Roche HIV DNA PCR version 1.5 having the most published data to date. Earlier assays, such as the Roche HIV DNA PCR version 1.0, were found to have reduced sensitivities for HIV non-subtype-B viruses(Haas, Geiss, & Bohler, 1996; Obaro, Losikoff, Harwell, & Pugatch, 2005); thus, careful evaluation across subtypes is essential. Various studies have demonstrated that the sensitivity of DNA PCR is less than 40% within the first 48 hours after birth, though sensitivity improves to more than 90% by 2 to 4 weeks of age(Bremer *et al.,* 1996; Dunn *et al.,* 1995). This increase in sensitivity should apply to all group M subtypes detected by the current Roche version 1.5 assay(Ampliprep, 2003). The performance of the commercially available Roche HIV DNA PCR version 1.5 assay has been evaluated in several laboratories across a variety of different subtypes, with sensitivities and specificities ranging from 96% to 100% and from 94% to 100%, respectively(Fischer *et al.,* 2004; Lyamuya, Olausson-Hansson, Albert, Mhalu, & Biberfeld, 2000; Sherman *et al.,* 2005; Zijenah *et al.,* 1999).

A CDC-sponsored meeting held in Uganda in 2005 presented the collective experience with the assay from several different African countriesshared data demonstrating the overall

positive performance of the DNA PCR version 1.5 assay across different settings and HIV subtypes(Stevens *et al.*, 2008).

2.3.2 Dry blood spot-Polymerase Chain Reaction (DBS-PCR) turnaround time and associated factors

Among the technologies available for diagnosis of HIV in infants, PCR on DNA in blood is the most widely used and is generally considered to be the standard method. Recent studies have also demonstrated evidence that real-time PCR for HIV RNA provides a reliable and suitable alternative. HIV DNA PCR is a qualitative test (that is, it gives a yes/no diagnosis for HIV infection)(Sherman *et al.*, 2005).

Turnaround time (TAT) is the total time between specimen collection, submission, processing and dispatch of the results for patient use.Turnaround time is one of the most noticeable signs of laboratory service and is often used as a key performance indicator of laboratory performance. It is useful as a source of benchmarking laboratory performance and as measure for continuous quality improvement. It is associated with clinical outcomes and therefore need to improve approaches to TAT. A 90% completion time (sample registration to result reporting) of <60 minutes for common laboratory tests is suggested as an initial goal for acceptable TAT(Hawkins, 2007).Clinicians desire a rapid, reliable and efficient service delivered at low cost(Neuberger & Peters, 1996). Of these characteristics, timeliness is perhaps the most important to the clinician, who may be prepared to sacrifice analytical quality for faster turnaround time(Watts, 1995). Over 80% of laboratories receive complaints about TAT, yet there is little agreement among clinicians on what constitutes acceptable TAT(Valenstein, 1989).

Across Africa, implementation of early infant diagnosis has been met with challenges, one of which is the long turnaround time of the PCR results that results in delay in initiating infants and children under 18 months on ARV treatment. In Côte d'Ivoire, the average test turnaround time from sample collection to results sent to the clinic was 33 days with a range of 8 to 58 days(Kouakou *et al.,* 2008).However, in Rwanda the test turnaround time between blood draw and test result back on site had a median of 17 days with a range of 9 to 54 days(Finkbeiner, 2006). In Swaziland the mean time from test to result pick-up was 63 days(Chouraya, Kieffer, Lukhele, & Madhi, 2008).In 2008, an evaluation of an Early Infant Diagnosis Program using DNA Polymerase Chain Reaction (PCR), on Dried Blood Spot (DBS) in Nigeria to demonstrate the feasibility of early infant diagnosis program in Nigeria using DBS DNA PCR by assessing DBS collection success, average turnaround time for return of results showed a median turnaround time of 3 to 4 weeks(Abutu *et al.,* 2008).

In some parts of Kenya, though the ideal turn-around time of two weeks between sample collection and delivery of results has not yet been reached, there is an improvement from an average of four weeks to three(PIK, 2007).Factors shown to correlate with shorter total TATs were rural locations,a lower sample collection to staff ratio,intensive care unit specimens,plasma for potassium measurements,the practice of delivering each specimen as it is collected,pneumatic tube delivery system,direct delivery route and continuous versus batch testing. Computerization and transport system also affects the TAT(Di Luca *et al.*, 1995). However,faster TAT does not necessarily improve patient outcome.

A study sought to identify barriers to follow-up of HIV-exposed infants in rural Zambézia Kenya and Mozambique, showed three of four HIV-infected women in rural Mozambique

did not bring their children for early infant HIV diagnosis and the median age at first test was 5 months. The predictors of follow up for early infant diagnosis were larger household size, independent maternal source of income, greater distance from the hospital and maternal receipt of antiretroviral therapy (Cook *et al.*, 2011).

The review of various literature illustrates few studies have been done on TAT for DBS-PCR in Kenya and none has been carried out in Western Kenya despite concerted efforts to scale up the EID. This study therefore sought to ascertain the turnaround time for DBS-PCR and its associated factors in Western Kenya since the introduction of the DBS-PCR testing in KEMRI Alupe.

2.4 Conceptual framework

Figure 1.1 shows the underling and proximate determinants of the mother-to-child transmission of HIV (this reflects the independent variables) and the health outcome (this reflects the dependent variable).

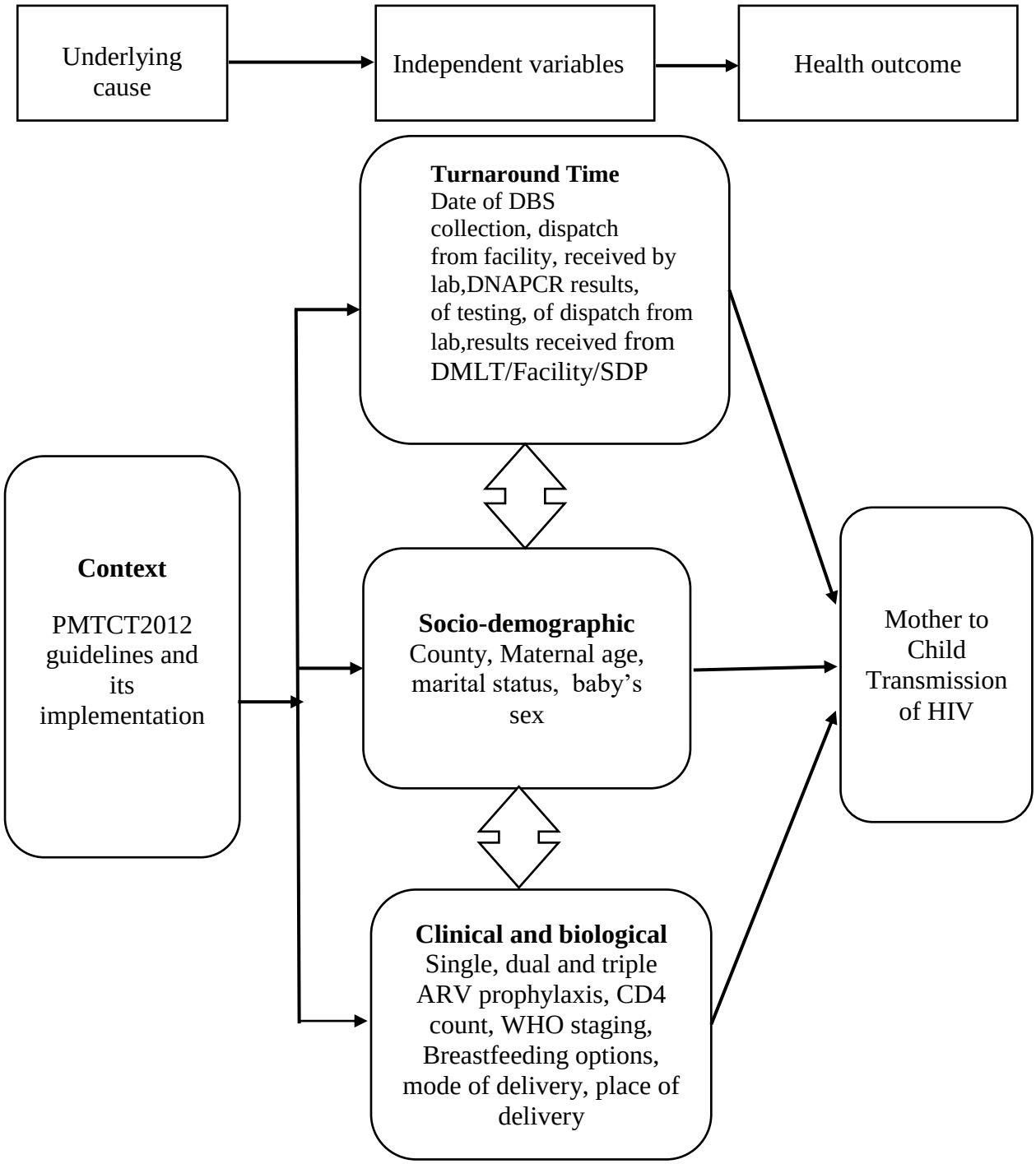

Figure 1.1: The Conceptual framework on factors affecting the Mother-To-Child HIV Transmission rate

CHAPTER THREE
MATERIALS AND METHODS

3.1The study site

Western Kenya, bordering Uganda, is one of Kenya's seven administrative units outside Nairobi. It is west of the Eastern Rift Valley and is inhabited mainly by the Luhyacommunity. Quakerism is widely practiced here. Kenya's second highest mountain, Mount Elgon is located in Bungoma District. The Kakamega Forest rainforest is part of the area. The Western Kenya capital is the town of Kakamega. The total population was of 4.3 million inhabitants within an area of 8,361 km² according to the 2010 Kenya Population and Housing Census. It comprises of four counties: Kakamega, Bungoma, Vihiga and Busia. HIV prevalence among adults aged 15 to 64 years stands at 5.6% nationally and 4.7% in Western Kenya comprising the four counties. HIV prevalence was higher among women (6.9%) than among men (4.4%). HIV prevalence among children aged 18 months to 14 years was 0.9% (MOH, 2007a).

Western Kenya has diverse physical features, from the hills of northern Bungoma district to the plains bordering Lake Victoria in Busia District. The highest point in Western Kenya is the peak of Mount Elgon, while the lowest point is the town of Busia on the water at Lake Victoria (Appendix 1).

The climate is mainly tropical, with variations due to altitude. Kakamega District is mainly hot and wet most of the year, while Bungoma District is colder but just as wet. Busia District is the warmest, while the hilly Vihiga District is the coldest. The entire Kenya experiences very heavy rainfall all year round, with the long rains in the earlier months of the year.

3.2The study population

The study was carried out in health facilities providing PMTCT and early infant diagnosis according to the Ministry of Health/NASCOP guidelines in Vihiga, Kakamega, Bungoma and Busia Counties (formerly former Western Kenya). The study population included HIV-positive pregnant women who received PMTCT services during the study period (January 2012 to June 2013) and their babies who were at least 18-24 months of age.The women of child bearing age were of particular interest since they are the ones eligible for the enrolment in the study. They provided the index cases for the retrospective cohort study.

Table 3.1 shows the type and number of health facilities in Western Kenya and this will form the sampling frame for the study.

Table 3.1: Number and type of health facilities in Bungoma, Vihiga, Kakamega, Busia counties, Kenya(MOH, 2011a)

		GOK	**FBO**	**NGO**	**Private**	**Total**
Hospital (Includes Prov. And Sub-District Hosp) Centre	No. of hospitals	27	8	0	1	36
Health Centre	No. of health center's	67	16	0	1	84
Nursing /Maternity home	No.of nursing homes	4	2	0	8	14
Dispensary	No. of dispensaries	181	31	8	13	233
Clinic		9	1	5	92	107

Legend: The number of health facilities was stratified by government of Kenya (GOK), Faith Based Organization (FBO), Non-Governmental Organizations and Private health facilities. These were: GOK=291; FBO=60; NGO=13, Private=113.

3.3 The study design

A retrospective cohort study using prospectively collected data in Ministry of Health (MOH) HIV-Exposed Infant (HEI) and the NASCOP EID database. A retrospective cohort study design is a longitudinal study that studies a cohort of individuals that share a common exposure factor to determine its influence on the development of a disease or outcome. A total of 24 health facilities were sampled (representing 20% of 124 health facilities that met the eligibility criteria) from Vihiga, Bungoma, Kakamega and Busia Counties, Kenya.

3.4The study variables

3.4.1 Dependent variables

Mother to child HIV transmission rates.

3.4.2 Independent variables

3.4.2.1 Maternal variables

*Socio-demographic variables:*County, maternal age, marital status.

*Clinical and biological variables:*Type of prophylaxis regimen received, CD4 count, WHO staging, breastfeeding options, mode of delivery, place of delivery (Home, facility).

3.4.2.2 Infant variables

The infant variables were infant sex and NVP prophylaxis received.

TAT variables: Date of DBS collection, date of dispatch from facility, date received by KEMRI lab, DNA PCR results, date of testing, date of dispatch from KEMRI lab, date results received from DMLT/Facility/SDP.

3.5Sample size determination and sampling procedures

3.5.1 Sample of HIV-positive pregnant women and their babies

The most crucial outcome variable of the study wasHIV transmission rate at MTCT at 18-24months. The sample size was calculated based on the formula (Fishers, 1998)

$$n = (Z^2 p\ q) \div d^2$$

Where:

n = Sample size

Z = Standard deviation at required confidence level (1.96 at 95% confidence level)

p = eMTCT rate (0.20)(De Cock *et al.*, 2000)

q = 1-p

d = the level of statistical precision (0.05).

The calculation:

$\mathbf{n} = (1.96)^2\,(0.20)\,(0.80)/0.05^2 = 246$ mother-baby pairs

The study took3 repeated measurements at 6 weeks, 9-18 months and at 18-24months from the eligible respondents.

The study was to enroll a minimum of 246subjects and to take care of the design effect and lost to follow up the unadjusted sample size was multiplied by 1.2 and adjusted 40% further respectively (Table 3.2).

Table 3.2: Sample size stratification

ARV Prophylaxis Regimen	Unadjusted sample size	Adjusted for design effect of 1.2	Minimum sample size (including 40% upward adjustment for missing records)
Dual and Triple therapy-AZT/NVP	246	300	420

In sample size calculation, several factors were taken into consideration. Twenty-four health facilities were sampled and data abstracted from the MOH HEI registers and missing data from the registers were corroborated with data from patient files in MCHs and CCCs to attain the minimum sample size of 420 mother-baby pairs for the study after factoring in the design effect and missing data values. NASCOP EID Database was used to extract the DBS-PCR study variables covering the study period from January 2012 and June 2013.The minimum sample size for the study was 420 mother-baby pairs disaggregated. A total of 1751 mother-baby pairs data were abstracted from twenty-four health facilities across the Kakamega, Vihiga, Busia and Bungoma counties against a minimum sample size of 420 mother-baby pairs. These were distributedas follows: Bungoma county- 414 (23.6%); Busia County- 828 (47.3%); Kakamega county–401(22.9%) and Vihiga County- 108 (6.2%). These were further stratified by the level of health facility (see Appendix 2).

For the DBS-PCR TAT, the study was also carried out in the 24 health facilities targeting HIV-exposed babies whose blood specimens were collected and transported to Alupe KEMRI Reference Laboratory during the study period (January 2012 to June 2013). Due to missing data, all HIV-exposed babies whose blood specimens were collected for PCR testing from the sampled health facilities were enrolled and their data abstracted from prospectively collected data from the MOH Laboratory registers. As a result, 2,789 HIV-exposed babies' laboratory records were abstracted.

3.5.2Sampling procedures and recruitment of study participants

Multi-stage sampling procedure was used as follows:

3.5.2.1 Sampling of health facilities

A multi-stage sampling method was used to select study sites. Western Kenya is administratively divided into four counties: Kakamega County, Vihiga County, Bungoma County, and Busia County.About 20% of eligible 124 health facilities were sampled (representing 24 health facilities). These were sampled as follows:

a) Four County Referral Hospitals were purposively sampled – for Kakamega, Vihiga, Busia and Bungoma counties;
b) The remaining 20 health facilities were then proportionately allocated to the four counties and health facilities using population proportionate to size (PPS) and based on the PMTCT (+) annual workload – ratio of 5:3:8:8(representing Kakamega, Vihiga, Busia and Bungoma counties, respectively). Dispensaries were omitted since they were not eligible. As a result, county referral hospitals, sub-county referral hospitals and health centers were sampled;
c) Mother-baby pairs data were consecutively enrolled from 1stJanuary 2012 to 30thJune 2013 for the study as per the eligibility criteria.

Within each county, the health facilities were further stratified as Level 5, Level 4 and Level 3 and the numbers of health facilities to be sampled for each stratum were determined by PPS using annual ANC attendance for the health facilities. The sampled health facilities were then visited by the research assistants in advance to introduce the study to the officers in charge of the health facility and with their permission met the health care providers of PMTCT services and arranged the logistics for data collection. Consent for participation was obtained from the respondents (see Appendix 3).

3.5.2.2 Sampling of HIV positive pregnant women and their iinfants'

From the sampled health facilities, the research assistants abstracted data from the HIV Exposed Infant (HEI) register. Patients filesat maternal and child health (MCH) and comprehensive care clinic (CCC) were used to obtain missing information from the registers. Mother-baby pairs that were enrolled from 1st January 2012 to 30th June 2013 were consecutively enrolled for the study. For the TAT, the NASCOP Early Infant Database was accessed for the same health facilities and their January 2012 to June 2013 registers extracted as per the variables under study.

3.6Inclusion and exclusion criteria

3.6.1 Inclusion criteria

a) Health facilities providing PMTCT and Early Infant Diagnosis as per the MOH protocol and guidelines;
b) Health facilities that were willing to give informed consent to participate in the study;
c) Health facilities that started providing PMTCT services from 1stJanuary 2012;
d) Health facilities that had mother-baby pairs that were enrolled in the sampled health facilities from January 2012 to June 2013 with some attaining at least 18 months.

3.6.2 Exclusion criteria

a) Health facilities not providing PMTCT and Early Infant Diagnosis services as per the MoH protocol and guidelines;
b) Unwillingness to give informed consent to participate in the study;
c) Health facilities that were not providing PMTCT services by 1st January 2012.
d) Health facilities that had mother-baby pairs that were enrolled in the sampled health facilities from January 2012 to June 2013 with none attaining at least 18 months.

3.7Data collection tools techniques and procedures

3.7.1 Data collection tools

Quantitative data were collected using Initial forms – sheet A (see Appendix 4), Abstraction forms – sheet B (Appendix 5) and Laboratory abstraction forms – sheet C (see Appendix 6). Qualitative data was collected using key informant interview guide targeting the health facility's laboratory-in-charges, Alupe KEMRI laboratory-in-charge, sub-county laboratory technologists and county laboratory technologists KII guides (see Appendix 7).

3.7.2 Data collection techniques and procedures

At the sampled health facilities data were abstracted from the period covering January 2012 to June 2013. These were extracted primarily from the MOH HEI register (MOH 408)[1]and patient files but due to the missing data, the research assistants had to extract the missing data from the MOH ANC/PMTCT registers (MOH 333)[2]as well.An initial form – sheet Awas used for line listing all the mother-babies pair at the sampled health facilities. The mother and infant names, CCC/HEI number, baby's HIV status at 6 weeks, 9 to <18 months and 18-24 months were captured from the PMTCT MoH registers. Only mother-baby pairs that had a

[1]MOH 408 is Kenya Ministry of Health (MOH) HIV Exposed Infant Register.
[2]MOH 333 is Kenya Ministry of Health (MOH) ANC/PMTCT Register.

baby with a positive HIV results at 18-24 months were enrolled in the Initial form-sheet A (Appendix 4). Once the initial form is completely filled for a particular sampled health facility, the research assistants would then use the details in the sheet A to locate mother-baby pairs from the MoH HEI registers. Abstraction form - sheet B was used to enter the social and demographic characteristics, maternal variables, infant variables and baby's HIV status at 6 weeks, 9 to <18 months and 18 – 24 months as captured in Appendix 5.The data collection was limited to the variables collected in MOH HEI register as the primary data collection tool. The mothers CCC unique number and the baby's HEI numbers were used as unique identifiers.

For the TAT, NASCOP EID database was used and the specific TAT variables extracted for the period covering January 2012 to June 2013 for the sampled health facilities. The primary variables abstracted from the NASCOP EID database were facility name, county, district, patient ID, date collected, date received, date tested, date updated, date dispatched and date received at the health facility. These were then used to compute secondary variables that included i) T1,Duration Between Collection and receiving in Days ii) T2,Duration between Received and Tested in Days iii) T3,Duration between received and updated in days iv) T4,Duration between received and dispatched v) T5,Duration between collected and received vi) T6,Duration between dispatched and received. Laboratory abstraction form – Sheet C (see Appendix 6) was used for this purpose.

The research assistants reviewed all the Initial forms – sheet A, Abstraction forms – sheet B and the Laboratory abstraction form – sheet C for each sampled health facility for completeness and accuracy. The completed forms werecollected, collated for each sampled

health facility and submitted to the principal investigator at the end of every week via G4S courier services.The principal investigator conducted weekly random field checks of the completed forms for completeness and accuracy and adherence to study protocol.Quality assurance was maintained throughout the process of data abstraction.

The potential errors and biases were minimized by:

i. Training research assistants so as to make sure that they understood the variables;
ii. Pre-testing of the data abstraction forms and any ambiguity corrected before the actual collection of data;
iii. The filled Initial forms- Sheet A and Abstraction forms – Sheet B was reviewed on a regular basis for completeness and to made sure that the entry was accurate;
iv. Using multivariate methods- using logistic regression the possible confounding factors such as CD4 count, type of ARV prophylaxes and feeding options were controlled for;
v. The trained research assistants were able to check every 10^{th} entry made. This was part of the quality control checks at the field level

The key informant interviews were conducted after preliminary analysis of the quantitative data. The preliminary key findings of the quantitative data analysis were used to formulate questions for the key informant interviews with county and sub-county laboratory officers, Laboratory-in charges, MCH/PMTCT coordinators. As a result, 9 key informant interviews with laboratory in-charges at the health facilities, sub-county and county health management teams across the four counties were conducted (see Appendix 7: Key Informant Guide)

The study schema shows the sampling and data collection process (Figure 3.1).

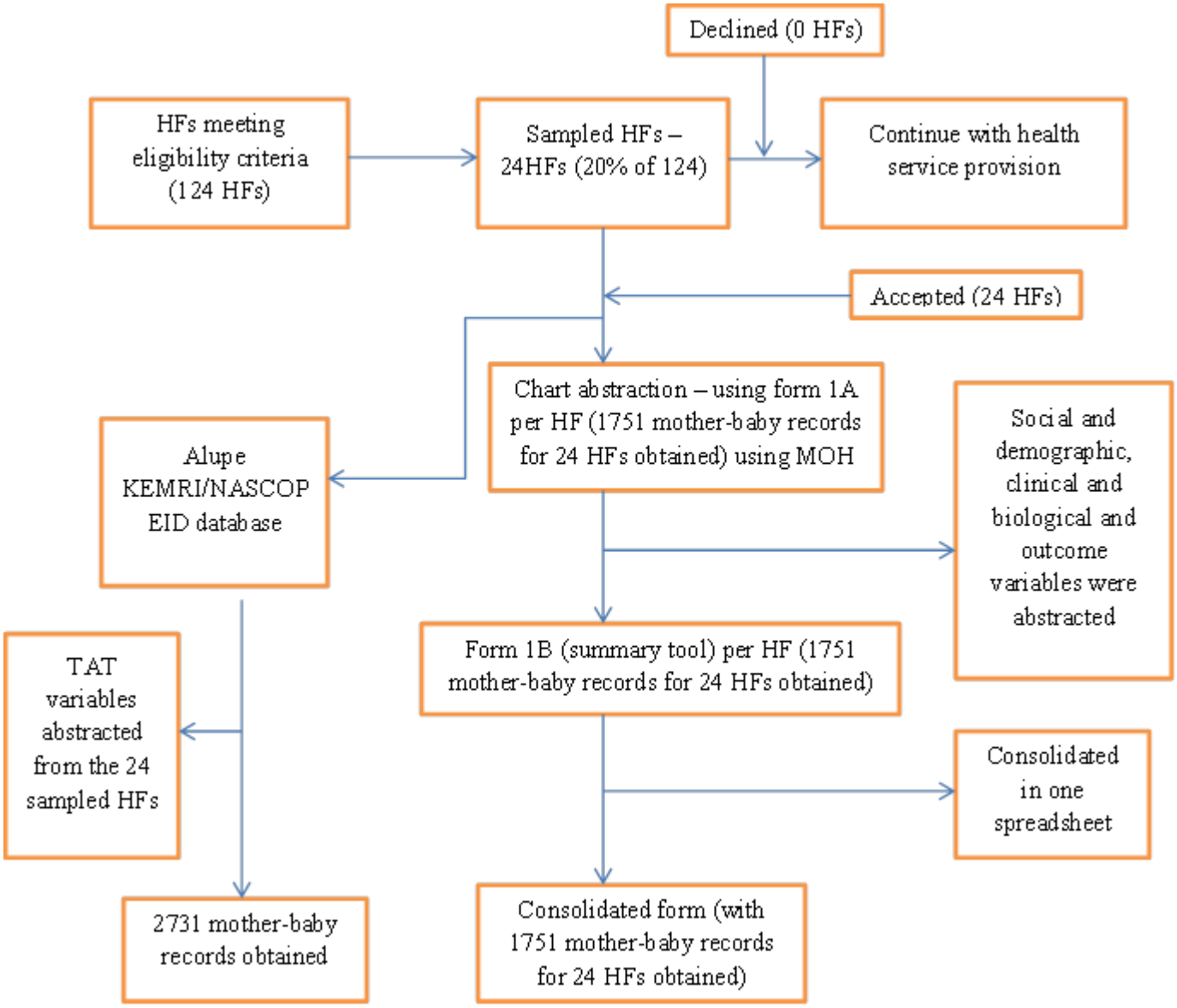

Figure 3.1: Study schema

3.7.2.1 Recruitment and training of research teams

Research assistants underwent one week training on study procedures and protection of human participants. The training covered information on the study, obtained informed consent, autonomy of participants and handling of data collection tools to assure confidentiality. Human participants training covered the principles of beneficence, autonomy and justice in research with reference to this study. The study protocol and measures for quality control and quality assurance during the data collection process was also covered.

The study sites were covered by four research teams each representing one of the counties. Each team comprised of two research assistants who were health records and information officers who were conversant with the MOH HIV data collection tools. They were trained and experienced in conducting research. In each team, they were allocated a number of health facilities for data collection. The research assistants were in each sampled health facility for one to two days collecting the data depending on the workload and accessibility of the records.

3.8Data processing and analyses and presentation

Data collected was analyzed using SPSS (Statistical Package for Social Sciences version 20.0).Measures of central locations, frequencies and measures of variability such as range, standard deviation, standard errorswere used for analysis. Pearson's chi-square tests, logistic regression, Analysis of Variance methods of inferential statistical analyses were used.The key predictors of HIV status at 18-24 months were determined using logistic regression. One-way analysis of variance was used to compare the two groups (HIV positive and HIV negative subjects at selected time points). The selected time points were in tandem with MOH guidelines for DBS-PCR testing for HIV-exposed children 18 months and below. These time points were 6 weeks, 9 months and 18 - 24 months and were captured in MOH 408 (MOH HEI Register).

The key informant interviews data obtained through audio recordings were transcribed and were subjected to qualitative analyses techniques. The data was largely analyzed using a comprehensive thematic matrix to facilitate identification of common patterns and trends arising from the narratives. To generate a detailed matrix, KII transcripts were scrutinized

separately for text element and key word coding and developed coding template. Following coding, an initial data presentation matrix was generated and organized overarching themes.Data presentation was done graphically using bar diagrams and tables.

3.9Ethical considerations

To assure confidentiality, KII was conducted in a room or an area that assured audio and visual privacy. The research assistants were trained on human participants and provided with lockable boxes where they stored completed Initial forms – Sheet A, Abstraction forms – Sheet B and Laboratory abstraction forms – Sheet C. The forms were then transported to the principal investigator using G4S couriers. In Nairobi, data were entered into password protected data bases and the filled in data collection tools stored in a locked cabinet.

Written informed consent was received from the County Health Directors of the four counties, from the sampled health facilities and Alupe KEMRI Laboratory. They were clearly informed that they have the right to refuse participation or withdraw from the survey at any point. This protocol was reviewed and approved by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (P66/11/2012) (Appendix 9: KNH/UoN Ethical Review Approval).

CHAPTER FOUR
RESULTS

The MOH registers, patient files depicted missing information in varying degrees from facility to facility and from variable to variable with a mean of 18%. Variables such as haemoglobin levels, place of delivery and mode of delivery had over 50% missing data that were either not asked or documented by health care workers while HIV status at 18 months was the best documented at 1.5% missing data (see Appendix 8).

4.1 Socio-demographic characteristics of HIV-positive mother-infant pairin Vihiga, Kakamega, Bungoma and Busia counties Kenya

The MOH registers which were the primary source documents for this study had six social and demographic variables: marital status, maternal age, maternal weight, baby's sex, baby's birth weight and county. Regarding the marital status, 15/1751 (0.9%) separated, 31/1751 (1.8%) cohabiting, 62/1751 (3.5%) divorced, 94/1751 (5.4%) widowed, 95/1751 (5.4%) single, 1389/1751(79.3%) were legally married and 65/1751 (3.7%) were not stated. There were variations in marital status across the four counties of Western Kenya (Table 4.1). These differences by county were statistically significant (p<0.001) with Kakamega County having proportionately less legally married women at 69% (n=272) compared to the three other counties. This means majority of HIV positive pregnant women were legally married at enrollment to PMTCT.

The overall mean maternal age of enrollment was 29.8882years (SD 5.89476). The mean maternal age at enrollment was 29.8532yearsfor HIV positive women who had HIV negative babies at 18-24 months period and 31.0607years for HIV positive women who had HIV positive babies at 18-24 months period. These differences were not statistically significant (p<0.058). When grouped into age categories, the maternal age at enrollment was as follows: 1.1% (n=20/1751) were <18 years old, 19.7% (n=345/1751) were between 18 and 24 years

old, 74.8% (n=1309/1751) were aged between 25 and 49 years, 0.3%(5/1751) were greater than 50 years old and 4.1%(72/1751) did not state their ages. These when further stratified by county as shown in Table 4.1 demonstrated comparability across the four counties (p=0.329). This study demonstrated that majority of the HIV positive pregnant women were aged between 24 - 49 years and those women who had HIV positive babies at 18-24 months period were more mature at enrollment to PMTCT than those who tended to have HIV negative babies at the same time period.

Since it has been shown that baby's sex affects acquisition of HIV at birth, we assessed the distribution of the sample based on baby's sex. Overall 49.2% (n=861) of the babies born were females, 42.9% (n=751) were males and 7.9% (n=139) had no stated sex. Table 4.1 shows the differences in baby's sex by county and these differences were statistically different (p<0.001) since Vihiga County had more females while Kakamega County had less males compared to the other counties. This demonstrated that there are more females than male sex at birth amongst HIV positive pregnant women and this was comparable with the normal population demographics.

Table 4.1: Marital status, Sex of the baby and age at enrolment in MCH/PMTCT services by Counties, Jan 2012 to June 2013

	Marital Status[a] $p<0.001$[a1]							**Sex of the Baby[b] $p<0.001$[b1]**			**Maternal Age at enrolment in MCH/PMTCT services[c] $p=0.329$[c1]**				
Counties	Cohabiting	Divorced	Legally Married	Separ-ated	Single	Widowed	Not stated	Female	Male	Not stated	<18 years	18-25 years	>25-49 years	>49 years	Not stated
Bungoma (N=408)	3.7% (n=15)	3.2% (n=13)	79.9% (n=326)	0.7% (n=3)	6.4% (n=26)	5.6% (n=23)	0.5% (n=2)	50.7% (n=207)	43.9% (n=179)	5.4% (n=22)	2.2% (n=9)	23.8% (n=97)	72.5% (n=296)	0.2% (n=1)	1.2% (n=5)
Busia (N=817)	1.1% (n=9)	4.3% (n=35)	83.2% (n=680)	0.7% (n=6)	5.8% (n=47)	4.8% (n=39)	0.1% (n=1)	51.2% (n=418)	44.6% (n=364)	4.3% (n=35)	0.7% (n=6)	20% (n=163)	78.9% (n=645)	0.2% (n=2)	0.1% (n=1)
Kakamega (N=394)	1.8% (n=7)	2.5% (n=10)	69% (n=272)	1% (n=4)	4.6% (n=18)	5.8% (n=23)	15.2% (n=60)	42.6% (n=168)	39.8% (n=157)	17.5% (n=69)	1.3% (n=5)	14.5% (n=57)	68% (n=268)	0.5% (n=2)	15.7% (n=62)
Vihiga (N=106)	0% (n=0)	3.8% (n=4)	83.0% (n=88)	1.9% (n=2)	3.8% (n=4)	7.5% (n=8)	0% (n=0)	53.8% (n=57)	42.5% (n=45)	3.8% (n=4)	0% (n=0)	17.9% (n=19)	80.2% (n=85)	0% (n=0)	1.9% (n=2)

Legend: *[a]The number (n) and proportion (%) of different marital status are shown across the four counties. Not stated means there was no documentation of the marital status in the Ministry of Health register; [a1]Statistical analysis as determined by χ^2 statistics. [b]Legend: The number (n) and proportion (%) of females and males shown across the four counties. Not stated means there was no documentation of the sex of the baby in the Ministry of Health registers; [b1]Statistical analysis as determined by χ^2 statistics; [c]The number (n) and proportion (%) of different age brackets are shown across the four counties. Not stated means there was no documentation of the ages in the Ministry of Health registers; [c1]Statistical analysis as determined by χ^2 statistics.*

The study also assessed the maternal weights at enrolment. The mean maternal weight was 58.469kgs (SD±10.067). Using the adult females' normal physiological weight as 60.0kg, the maternal weights were then stratified by the physiological weights ≤60.0kg and >60.0kg. Mothers weighing ≤60kg were 57.9% (1014/1751) and those weighing >60kg were 33.3% (583/1751) and 8.8% (154/1751) had not stated their weight (Table 4.2). This demonstrated that majority of HIV positive women were less than or equal to 60.0kg body weights at enrolmentto PMTCT.

Studies have demonstrated that baby's birth weights affect HIV transmission rates from mother to infant. Low birth weights are considered <2.0kg and overweight >3.50kg. This criterion was used to stratify the baby's birth weights. Approximately 3.5% (62/1751) of the babies had birth weights <2.0kg, 44.2% (774/1751) had birth weights between 2.0kgs and 3.50kgs while19.1% (334/1751) had birth weights >3.50kgs and 33.2% (581/1751) had their birth weights not stated (Table 4.2). This showed that a significant proportion of babies born of HIV positive women weighed between 2.0-3.5kg though this is not conclusive given about a third of the babies' weights were not documented in the MoH registers.

Table 4.2: Maternal birth weights and baby's birth weights, January 2012- June 2013

Independent variables	Frequency, (%,n)	HIV status at 18-24 months	
		Negative (n, %)	Positive (n, %)
Maternal body weight			
≤60.0kg	57.9% (1014/1751)	938 (94.2%)	59 (5.8%)
>60.0kg	33.3% (583/1751)	551 (95.5%)	26 (4.5%)
Not stated	8.8% (154/1751)	140 (92.1%)	12 (7.9%)
Birth weight of the baby			
<2.0kg	3.5% (62/1751)	58 (93.5%)	4 (6.5%)
2.0-3.5kg	44.2% (774/1751)	738 (96.1%)	30(3.9%)
>3.5kg	19.1% (334/1751)	314 (94.3%)	19(5.7%)
Not stated	33.2% (581/1751)	519 (92.2%)	43 (7.7%)

Legend: *The table shows maternal and baby's birth weights variables abstracted from the Ministry of Health registers. The number (n) and proportion (%) of HIV positive pregnant women and then stratified by the HIV status of their babies at 18-24 monthsare shown. Not stated means there was no documentation in the Ministry of Health registers.*

4.2 MTCT rates at selected time points for dual and triple ARV prophylaxis regimens and the associated factors in Vihiga, Kakamega, Bungoma and Busia counties, Kenya

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

Overall, the study revealed that most HIV positive pregnant women 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 4.1). 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).

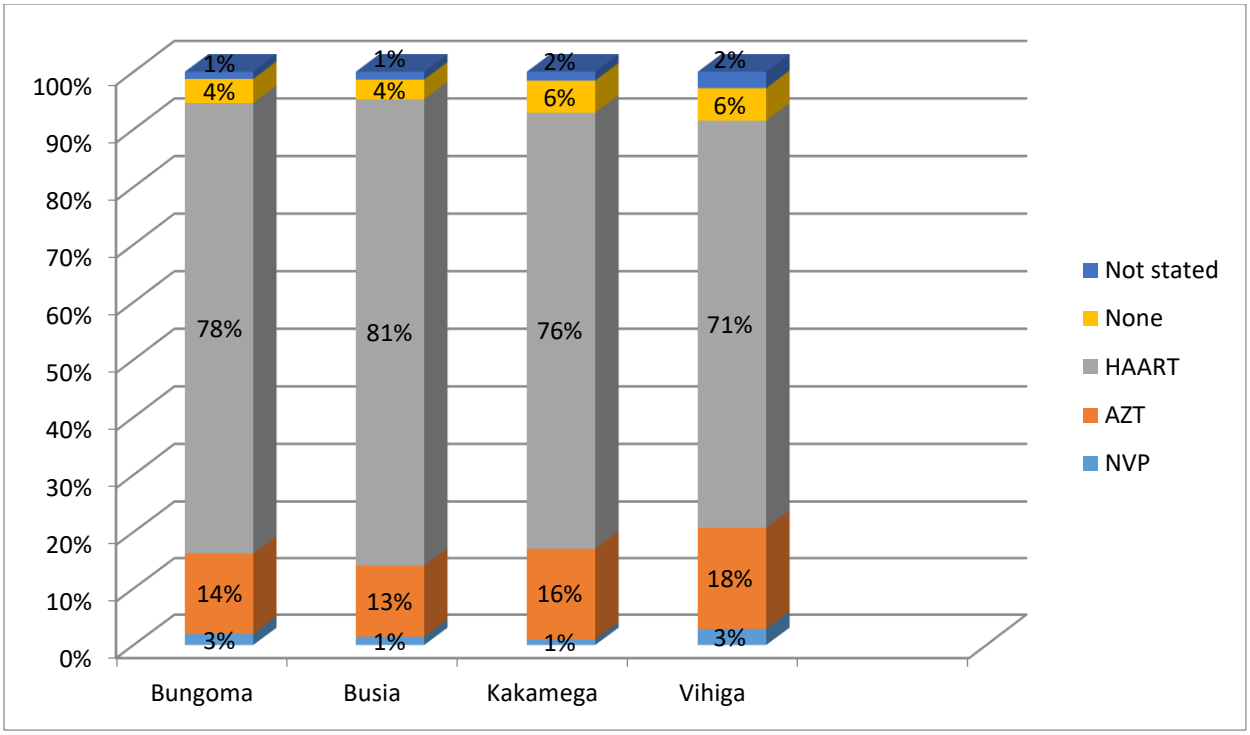

Figure 4.1: ARV prophylaxis regimens received disaggregated by County between Jan 2012 to June 2013

Figure legend:*This figure depicts the ARV prophylaxis regimens received (NVP, AZT, HAART, None) and those whose regimens status was not stated/documented. These were stratified by counties and expressed in stacked bar graphs as %.The proportions across counties were comparable (p=0.466).*

4.2.2 MTCT rates at 6 weeks, 9 to <18 months and 18-24 months and associated correlates in Vihiga, Kakamega, Bungoma and Busia counties, Western Kenya

Overall, 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%) between January 2012 to June 2013. Furthermore, 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 4.3). When disaggregated by County Busia was 5.1% (n=817), Kakamega was 5.8% (n=394), Vihiga was 5.7% (n=106) and Bungoma was 6.1% (n=408) at 18-24 months

period. However, these county level differences were not statistically different (p=0.900) (Table 4.3).

Table 4.3: HIV transmission rates at 6 weeks, 9 to <18 months and 18-24 months stratified by county, Jan 2012 to June 2013

	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)		
County	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%)	0%
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%)	0%
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%)	0%
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%)	0%
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%)	0%

Table Legend:*HIV transmission rates were presented at 6 weeks, 9 to <18 months and 18-24 months, stratified by county. The HIV-negative and HIV-positive babies were expressed as (n, %). These were presented in absolute count (n) and in proportions (Percent, %).The statistical significance was determined using Pearson'sChi-square test.This was done by cross-tabulating the counties against the HIV status at 6 weeks, 9 to <18 months and 18 -24 months.*

In addition, HIV transmission rate at 18-24 months varied with ARV prophylaxes regimen received. HIV positive pregnant women who received sdNVP prophylaxis had the highest HIV transmission rate at 7.1% (n=28), women who received AZT prophylaxis had the lowest HIV transmission rate at 3.3% (n=243), women who received HAART prophylaxis had HIV transmission rate of 5.4% (n=1356), while HIV pregnant women who received no prophylaxis had an HIV transmission rate of 8.2% (n=73). These differences in HIV transmission rates were comparable (p=0.331) (Figure 4.2). This demonstrated that use of ARV prophylaxes reduced

MTCT rates and that AZT (with 3.3% MTCT rate) and HAART (with 5.4% MTCT rate) had the lowest HIV transmission rates at 18-24 months.

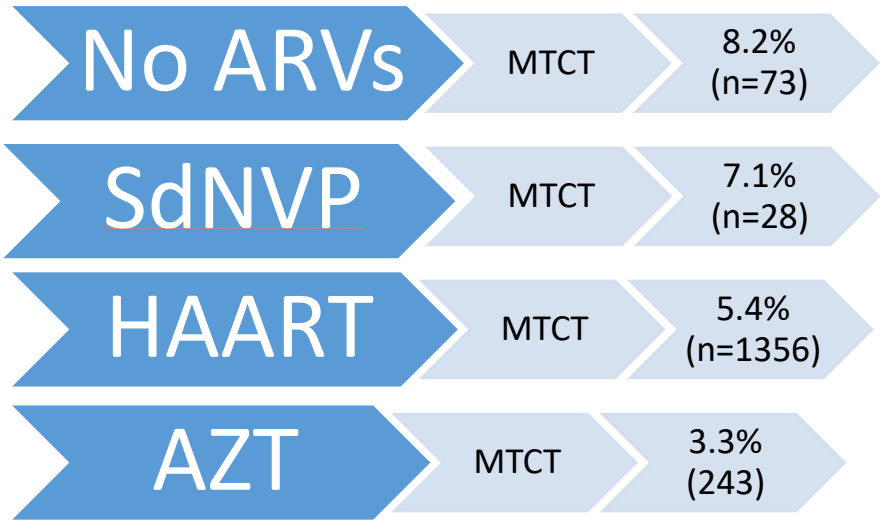

Figure 4.2:MTCT rate at 18-24 months with ARV prophylaxes regimen received.

Figure legend: *This figure shows the MTCT rates at 18-24 months varied with different ARV prophylaxes regimen received. Use of AZT was associated with the lowest MTCT rate while no ARVs used was associated with highest MTCT rates (p=0.331). The statistical significance was determined using Chi-square test. The data was pooled from all the four counties.*

4.2.3 Socio-demographic correlates in Vihiga, Kakamega, Bungoma and Busia counties, Kenya

Analyses looked at the distribution of baby's HIV sero-status in the context of maternal age, maternal weight and baby's birth weight. The overall mean maternal age at enrollment was 29.888 years (SD 5.895). The mean maternal age at enrollment was comparable between those whose children were HIV-negative (29.853 years) and HIV-positive (31.061 years) at 18-24 months (p=0.058) (Table 4.4). Likewise, the overall mean maternal weight was 58.469kg (SD 10.067). The mean maternal weight at enrollment was comparable between those whose children

were HIV-negative (58.559kg) and HIV-positive (57.251kg) at 18-24 months (p=0.248) (Table 4.4). Finally, the overall mean birth weight for the babies was 3.258kg (SD 0.644). The meanbaby's birth weight at enrollment was comparable between those who were HIV-negative (3.255kg) and HIV-positive (3.321kg) (p=0.470) (Table 4.4). These results collectively demonstrated that maternal age, maternal weight and babies' birth weight are not associated with baby's HIV status at 18-24 months in this population.

Table 4.4: Association between maternal age and weight, baby's birth weight and baby's HIV sero-status at 18-24 months

Variable		HIV Negative	HIV Positive
Maternal Age	Median age in years	29.615	30.810
	Mean age in years	29.853	31.061
	95% CI	95% CI: 29.560,30.146	95% CI: 29.847,32.274
	SD	5.905	5.828
	Range	48.510	30.130
	Interquartile range	8.430	5.810
	p-value	*p*=0.058	
Maternal weight	Median weight in Kgs	57.000	56.500
	Mean weight in Kgs	58.559	57.251
	95% CI	58.046,59.072	55.072,59.431
	SD	10.090	10.044
	Range	99.800	53.000
	Interquartile range	12.000	13.770
	p-value	*p*=0.248	
Birth weight	Median weight in Kgs	3.000	3.000
	Mean weight in Kgs	3.255	3.321
	95% CI	3.218,3.293	3.117,3.524
	SD	0.640	0.739
	Range	7.000	3.400
	Interquartile range	0.800	1.000
	p-value	*p*=0.470	

Table Legend: *the median, mean, 95% Confidence Interval, range and interquartile range were calculated for maternal age, maternal weight and baby's birth weight and comparison made between HIV positive and HIV negative babies at 18-24 months. The statistical significance was determined using t-test.*

In order to determine MTCT rate in children aged 18-24 months, the proportion of HIV positive babies at 18-24 months in HIV exposed babies was evaluated. The MTCT rate at 18-24 months showed variations with marital status (*p*=0.003). The MTCT rate was highest amongst women in separated 4/15(26.7%), single 10/95(10.5%), cohabiting 3/31(9.7%) and widowed 6/93 (6.5%) relationships and lowest amongst divorced 2/60(3.2%) and legally married 67/1366(4.9%) women (Table 4.5). This demonstrated that MTCT rate is highest amongst separated, single, widowed and cohabiting women and lowest amongst the legally married HIV positive pregnant women.

In order to test the associations between the social and demographic characteristics and HIV status at 18-24 months, bivariable analyses between baby's HIV status at 18-24 months and county, maternal age, marital status, maternal body weight, sex of the baby and bays' birth weight was carried out. The results demonstrated that marital status and baby's HIV status at 18-24 months was statistically significant association (p=0.003) (Table 4.5). Logistic regression was done to ascertain the strength of association. Babies born to mothers separated had approximately 7 times likelihood of having HIV negative results at 18-24 months as compared to widowed women (OR=7.517, 95% CI: 1.344 – 42.031, p=0.022)(Table 4.5). However, there were no associations between the maternal weight and baby's HIV status at 18-24 months (p=0.263), maternal age and baby's HIV status at 18-24 months (p=0.174) and baby's sex and baby's HIV status at 18-24 months (p=0.341) after controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 counts (Table 4.5). These findings demonstrate that there is a significant statistical association between marital status and baby's HIV status at 18-24 months with HIV positive pregnant women who are widowed more likely to have higher MTCT rates as compared to separated women. However, it showed no statistical association between maternal age, maternal weight, baby's sex, babies' birth weight and baby's HIV status at 18-24 months.

Table 4.5: Associations between the social and demographic characteristics and baby's HIV status at 18-24 months

Independent variables	**HIV status at 18-24 months**		χ^2	***p*-value**	**Odds Ratio**	**95% CI for OR**		***p*-value**
	Negative (n, %)	Positive (n, %)				Lower	upper	
County								0.592
Vihiga County (N=106)	94.3% (100)	5.8% (6)			Ref			
Bungoma County (N=408)	93.9% (383)	6.1% (25)	0.583	0.900	1.649	0.468	5.808	1.649
Kakamega County (N=394)	94.2% (371)	5.8% (6)			1.494	0.441	5.066	0.519
Busia County (N=817)	94.9%(775)	5.1% (42)			0.995	0.258	3.839	0.994
Maternal Age at enrollment								0.031
>49years	5(100%)	0 (0%)			Ref			
<18 years	18(90%)	2(10%)	5.258	0.262	n/a	n/a	n/a	n/a
18years <25 years	325(96.7%)	11(3.3%)			n/a	n/a	n/a	n/a
25 years-49years	1216 (94%)	78 (6%)			n/a	n/a	n/a	n/a
Not stated	65 (92.9%)	5(7.1%)						
Marital status								0.138
Widowed	87 (93.5%)	6 (6.5%)			Ref			
Co-habiting	28 (90.3%)	3 (9.7%)			2.061	0.371	11.447	0.409
Divorced	60 (96.8%)	2 (3.2%)	**20.147**	**0.003**	1.072	0.169	6.816	0.941
Legally married	1299(95.1%)	67 (4.9%)			1.249	0.375	4.164	0.717
Separated	11 (73.3%)	4 (26.7%)			**7.517**	**1.344**	**42.031**	**0.022**
Single	85 (89.5%)	10 (10.5%)			1.774	0.399	7.878	0.451
Not stated	59 (93.7%)	4 (6.3%)						
Maternal body weight			1.254	0.263				

Independent variables	HIV status at 18-24 months		χ^2	*p*-value	Odds Ratio	95% CI for OR		*p*-value
≤60kg	938 (94.2%)	59 (5.8%)			Ref			
>60kg	551 (95.5%)	26 (4.5%)			1.167	0.680	2.001	0.576
Not stated	140 (92.1%)	12 (7.9%)						
Sex of the baby								
Female	811 (95.4%)	39 (4.6%)			Ref			
Male	703 (94.4%)	42 (5.6%)	0.907	0.341	0.915	0.550	1.523	0.734
Not stated	115 (88.5%)	15 (11.5%)						
Birth weight of the baby								
<2kg	58 (93.5%)	4 (6.5%)			Ref			
2-3.5kg	738 (96.1%)	30(3.9%)	2.270	0.321	1.529	0.478	4.889	0.474
>3.5kg	314 (94.3%)	19(5.7%)			0.597	0.311	1.146	0.121
Not stated	519 (92.2%)	43 (7.7%)						

Table Legend: *The table shows the independent categorical variables abstracted from the Ministry of Health registers with regard to the social and demographic characteristics for the mother-baby pairs. The number (n) and proportion (%) of HIV negative and HIV positive status at 18-24 months for different variables are shown. Not stated means there was no documentation in the Ministry of Health registers. The Pearson'schi-square statistics and the P-value are also shown for each variable. The table also shows the results of the logistic regression analysis. The significance value, Odds Ratio and 95% confidence intervals are also shown for independent variable taking certain reference categories for each variable after controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 count. Statistical analysis was determined by χ^2 statistics. County referral hospitals for the level of health facilities, Vihiga county for the County, >49years for maternal age, Widowed women for the marital status,≤ 60kg for maternal weight, females for sex of the baby and <2kg for baby's birth weight were considered as reference groups. Ref=Reference group.*

4.2.4 Clinicaland biological correlates

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 (Table 4.6).

With regard to CD4+ count, women with CD4+ counts greater than 500cells/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%). As such, higher CD4+ cell counts amongst women were statistically 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) (Table 4.6). This therefore demonstrated that HIV positive pregnant women with lower CD4+ counts on enrollment had a significantly higher risk of transmitting HIV to their babies as compared to those women with higher CD4+ counts on enrollment.

The HIV transmission rates at 6 weeks, 9 to <18 months and 18-24 months varied with the type of ARV prophylaxis with AZT and HAART prophylaxes depicting the lowest HIV transmission rates of 3.0% and 5.4% at 6 weeks, respectively. Use of NVP was associated with highest HIV

transmission rate of 7.1%. These differences in HIV transmission rates were statistically significant across the different ARV prophylaxes at 6 weeks (p=0.041) but not at 9-18 months and 18-24 months period(Table 4.6). This illustrated that AZT and HAART prophylaxes are associated with lower MTCT rates as compared to NVP at 6 weeks postpartum.

Further analyses revealed that majority of babies received infant NVP prophylaxis (94.7%), which was in turn associated statistically with lower HIV transmission rates at 6 week. Though this was marginally significant (p=0.036) but not 9 to <18 months (p=0.061) and 18-24 months (p=0.330)(Table 4.6). While there was a near universal use of infant NVP, this was associated with lower MTCT rate at 6 weeks period and not 9-18months and 18-24 months period.

HIV positive pregnant women on TB treatment had the highest HIV transmission rates while those with no TB signs had the least HIV transmission rates. These were statistically significantat 9 to <18 months (p=0.016) and 18-24 months (p=0.009). However, the HIV transmission rates were comparable at 6 weeks between those on TB treatment, with TB signs and no TB signs (p=0.334). 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 4.6). This showed that HIV positive pregnant women on TB treatment had a higher MTCT rates at 9 to <18 months and 18-24 months.

The study demonstrated that the duration between enrolment and date of delivery and their associationwith MTCT rates. Women who delivered within 6 months of enrolment had a lower

HIV transmission rates and these were statistically significant at 6 weeks (p=0.001), 9 to <18 months (p<0.0001) and 18-24 months (p=0.001) as compared to those whose duration between enrollment and date of delivery was greater than 6 months(Table 4.6). This showed that the shorter the duration between enrollment and date of delivery, the lower the MTCT rates at the selected time points.

The study further determined the statistical association between the baby's feeding options at 6 weeks, 9 to <18 months and 18-24 months and the MTCT rates. 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) and these were statistically significant at selected time periods (p<0.0001) (Table 4.6). These findings demonstrated that exclusive breastfeeding at 6 weeks is a strong predictor of MTCT rates at the selected time periods with exclusive breastfeeding showing the lowest MTCT rates.

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 ascertained and were statistically comparable across groups (Table 4.6). This demonstrated that these variables had association with MTCT rates at the selected time points.

Table 4.6: Statistical associations between the covariates and babys' 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**
Hemoglobin levels												
<7mmHg	25 (92.6%)	2 (7.4%)			25 (92.6%)	2 (7.4%)			25 (92.6%)	2 (7.4%)		
7-10mmHg	84 (90.3%)	9 (9.7%)	2.840	0.242	83 (87.4%)	12 (12.6%)	5.541	0.063	87 (90.6%)	9 (9.4%)	2.687	0.261
>10mmHg	421 (94.8%)	23 (5.2%)			420 (94.2%)	26 (5.8%)			427 (94.9%)	23 (5.1%)		
Not stated	1065 (94.6%)	61(5.4%)			1043 (92.3%)	87(7.7%)			1090 (94.6%)	62 (5.4%)		
WHO staging												
I	738 (94.0%)	47 (6.0%)			735 (92.5%)	60 (7.5%)			754 (94.1%)	47 (5.9%)		
II	450 (95.5%)	21 (4.5%)	3.228	0.358	449 (95.7%)	20 (4.3%)	6.140	0.105	461 (95.6%)	21 (4.4%)	3.719	0.293
III	224 (93.3%)	16 (6.7%)			222 (92.1%)	19 (7.9%)			227 (93.0%)	17 (7.0%)		
IV	22 (100.0%)	0 (0.0%)			21 (95.5%)	1 (4.5%)			22 (100.0%)	0 (0.0%)		
Not stated	-	-			-	-			-			
CD4 count cells												
<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%)	8.321	**0.016**	292 (93.6%)	20 (6.4%)	19.131	**<0.0001**	299 (94.3%)	18 (5.7%)	7.094	**0.029**
>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%)		

	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**
Duration between enrolment and ART initiation												
<6months	193 (92.8%)	15 (7.2%)			191 (92.7%)	15 (7.3%)	0.370	0.831	194 (92.8%)	15 (7.2%)	4.597	0.100
6-12months	522 (96.1%)	21 (3.9%)			511 (93.9%)	33 (6.1%)			532 (96.4%)	20 (3.6%)		
>12months	581 (94.6%)	33 (5.4%)	3.742	0.154	578 (93.5%)	40 (6.5%)			586 (94.5%)	34 (5.5%)		
Not stated	299 (92.0%)	26 (8.0%)			291(88.2%)	39 (11.8%)			317 (92.2%)	27 (7.8%)		
Type of prophylaxis received												
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%)	8.273	**0.041**	1262 (93.5%)	88 (6.5%)	7.601	0.055	1283 (94.6%)	73 (5.4%)	3.425	0.331
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%)		
NVP prophylaxis for the baby received												
Yes	1514 (94.7%)	84 (5.3%)			1487 (92.8%)	116 (7.2%)			1536 (94.8%)	85 (5.2%)		
No	24 (85.7%)	4 (14.3%)	4.382	**0.036**	26 (83.9%)	5 (16.1%)	3.507	0.061	30 (90.9%)	3 (9.1%)	0.950	0.330
Not stated	57 (89.1%)	7 (10.9%)			1571(92.5%)	127 (7.5%)			63 (88.7%)	8 (11.3%)		
TB status of the patient			2.193	0.334			8.282	**0.016**			9.428	**0.009**

	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**
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%)		
Duration between enrolment and delivery												
<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%)	14.002	**0.001**	244 (88.7%)	31 (11.3%)	18.818	**<0.0001**	257 (90.8%)	26 (9.2%)	14.622	**0.001**
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												
Home	211 (95.9%)	9 (4.1%)			205 (94.5%)	12 (5.5%)			217 (96.0%)	9 (4.0%)		
Facility	525 (97.2%)	15 (2.8%)	0.881	0.348	513 (92.8%)	40 (7.2%)	0.718	0.397	541 (97.1%)	16 (2.9%)	0.641	0.423
Not stated	859 (92.4%)	71 (7.6%)			853 (91.9%)	75 (8.1%)			871 (92.5%)	71 (7.5%)		
Mode of delivery												
C-section	47 (100.0%)	0 (0.0%)	1.682	0.195	43 (91.5%)	4 (8.5%)	0.164	0.685	48 (100.0%)	0 (0.0%)	1.731	0.188
Spontaneous	753 (96.5%)	27 (3.5%)			736 (93.0%)	55 (7.0%)			775	28		

	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**
Vaginal									(96.5%)	(3.5%)		
Not stated	795 (92.1%)	68 (7.9%)			1571 (92.5%)	127 (7.5%)			806 (92.2%)	68 (7.8%)		
Feeding options at 6 weeks												
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%)	34.748	**<0.0001**	16 (84.2%)	3 (15.8%)	13.983	**0.001**	16 (84.2%)	3 (15.8%)	31.520	**<0.0001**
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%)		
Feeding options at 9 months												
MF	n/a	n/a			1077 (92.9%)	82 (7.1%)			1105 (94.8%)	61 (5.2%)		
NBF	n/a	n/a			4 (100.0%)	0 (0.0%)	0.720	0.698	4 (100.0%)	0 (0.0%)	4.688	0.096
RF	n/a	n/a			383 (93.9%)	25 (6.1%)			398 (97.3%)	11 (2.7%)		
Not stated	n/a	n/a			107 (84.3%)	20 (15.7%)			22 (83.6%)	24 (16.4%)		
Feeding options at 18 months												
MF	n/a	n/a			n/a	n/a			134 (93.7%)	9 (6.3%)		
RF	n/a	n/a			n/a	n/a			916 (95.7%)	41 (4.3%)	1.158	0.282
Not stated	n/a	n/a			n/a	n/a			579 (92.6%)	46 (7.4%)		

Table Legend: *The table shows the independent categorical variables abstracted from the Ministry of Health registers with regard to the social and demographic characteristics for the mother-baby pairs. 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 means there was no documentation in the Ministry of Health registers. EBF = exclusive breastfeeding, ERF = exclusive replacement feeding and MF = mixed feeding. Statistical analysis was determined byPearson's* χ^2 *statistics and the p-value are also shown for each variable.*

Additional logistic regression analyses were carried out to determine the strength of association between the correlates and MTCT rates (Table 4.7).

Relative to HIV positive pregnant 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}at 6 weeks (p=0.058), 9-18months (p=0.181) and 18-24 months (p=0.192) (Table 4.7). This demonstrates that HIV positive pregnant women with CD4+ counts between 350 to 500 cells/mm^3 had a higher MTCT rates at the selected time points.

HIV positive pregnant 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 were also 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 4.7). This means that HIV positive pregnant women with suspected or confirmed TB have a higher MTCT rates.

Exclusive breastfeeding was significantly 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, 9 to <18 months and 18-24 months are less likely to be HIV-negative by about 76% as compared to babies are exclusively breastfed ($p<$ 0.001) (Table 4.7). This revealed that exclusive breastfeeding was a strong predictor of having HIV negative babies at the selected time points.

The association between WHO stage, duration between enrollment and ART initiation, NVP prophylaxis for the baby received, mode 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 ($p>0.05$; Table 4.7). This means that these independent variables have no association with MTCT rates at the selected time points in this study.

Table 4.7: Logistic regression showing the associations between the covariates and babys' 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**
		Lower limit	Upper limit			Lower limit	Upper limit			Lower limit	Upper limit	
Hemoglobin levels												
<7mmHg	1.464	0.327	6.564	0.618	1.292	0.290	5.756	0.737	1.485	0.331	6.657	0.605
7-10mmHg	1.961	0.876	4.388	0.101	**2.335**	**1.133**	**4.814**	**0.022**	1.921	0.859	4.293	0.112
>10mmHg	Ref				Ref				Ref			
WHO staging												
I	Ref								Ref			
II	102878877.1	0.000		0.998	1.714	0.227	12.965	0.602	100701246.5	0.000		0.998
III	75386138.86	0.000		0.998	0.935	0.120	7.306	0.949	73591338.79	0.000		0.998
IV	115386947.2	0.000		0.998	1.797	0.229	14.102	0.577	120984963.7	0.000		0.998
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
Duration between enrolment and ART initiation												
<6months	Ref				Ref				Ref			
6-12months	1.368	0.728	2.574	0.331	1.135	0.613	2.100	0.687	1.333	0.711	2.499	0.371
>12months	0.708	0.405	1.240	0.227	0.933	0.580	1.502	0.776	0.648	0.368	1.140	0.132
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			
NVP prophylaxis for the baby received												
Yes	Ref				Ref				Ref			
No	3.004	1.019	8.855	0.046	2.465	0.929	6.539	0.070	1.807	0.541	6.040	0.337

	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**
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
Place of delivery												
Home	Ref				Ref				Ref			
Facility	1.493	0.643	3.464	0.351	0.751	0.386	1.460	0.398	1.402	0.610	3.222	0.426
Mode of delivery												
C-section	Ref				Ref				Ref			
Spontaneous Vaginal	0.000	0.000	-	0.998	1.245	0.431	3.595	0.686	0.000	0.000		0.998
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
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	0.000		0.999	0.000	0.000	-	0.999
Feeding options at 18 months												
MF	-	-	-		-	-	-		Ref			
RF	-	-	-		-	-	-		1.501	0.713	3.157	0.285

Legend: The table shows the results of the logistic regression analysis. 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.EBF = exclusive breastfeeding, ERF = exclusive replacement feeding and MF =mixed feeding.

4.3 Dry Blood Spot –Polymerase Chain Reaction (DBS-PCR) Turnaround Time (TAT) and the associated factors In Vihiga, Bungoma, Kakamega and Busia Counties, Kenya

The study revealed the mean duration between specimen collection at the health facilities and results received at the health facilities was 46.9020days with Vihiga having the least mean duration at 33.6625days and Kakamega having the longest duration at 51.7025days with a range of 6 days to 487 days. These county level differences were statistically significant (p=0.001) (Table 4.8). Further analyses showed the mean duration between specimen collection at the health facilities and receiving specimens at Alupe KEMRI laboratory was 16.4553 with variations across the four counties with a range of 1day to 131 days. Vihiga County had the least mean duration at 13.0108days while Busia County had the longest duration at 18. 9853days (p= 0.001) (Table 4.8). The key informant interviews (KIIs) conducted revealed batching and hubbing to be common in Bungoma, Kakamega and Busia Counties as opposed to Vihiga County that tended to send theirlaboratory specimens directly to Alupe KEMRI Reference Laboratory through the G4S courier services that were contracted by the USAID APHIAPlus Project. In addition, most of the peripheral and remote health facilities tended to have lower caseload and would take up to three weeks to get two DBS specimens (USAID APHIAPlus Project set two specimens as the minimum for laboratory networking) from HIV exposed infants and this significantly delayed the submission of the specimens to the nearest referral hospitals who then submit the specimens to Alupe KEMRI reference laboratory through the G4S courier services.

A Key Informant Interview with a laboratory in-charge in a health center in Kakamega County noted… *"…We have to batch our specimens to at least 2 specimens before we submit to Kakamega PGH otherwise we would not be entitled to transport reimbursement by APHIAPlus Project…."*

A KII with one of the Bungoma County DBS sample hubbing was a key practice and *…" …we advise facilities to bring their DBS specimens to Bungoma District Hospital so that we can verify that the specimens are of good quality and standards before submitting to Alupe KEMRI Reference Laboratory via G4S courier services to reduce sample rejection rates which is a problem…"*

KII with laboratory personnel noted that *"…pooling of samples by far away facilities is a challenge..".* This sentiment was shared by laboratory technicians at Alupe KEMRI Reference laboratory, one of whom noted that health facilities that prefer hubbing delays samples to be shipped to Alupe KEMRI Reference Laboratory. KII revealed that hubbing is a common phenomenon that is employed to help ensure poor quality DBS specimens are not submitted to Alupe KEMRI laboratory and would reduce the overall TAT since health facilities are advised to collect fresh specimens.

The study further revealed that the mean duration between receiving the specimens from the health facilities and testing the specimens was 16.8045days with a minimum of 1day and a maximum of 90days. These were comparable across the counties (p=0.085) (Table 4.8).

The study showed that the mean duration between receiving the specimens from health facilities and updating the results of the processed specimens was 18.5380 with a minimum of 1 day and a maximum of 90 days. These were comparable across counties (p=0.111). Moreover, the mean duration between receiving specimens from the health facilities and dispatching the results to the health facilities was 25.5954days with a range of 1day to 270days. Vihiga County had the least time at 22.8889days while Kakamega County had 27.2793days. These county level variations were statistically significant (p=0.002) (Table 4.8).

It also showed that the mean duration between the dispatch of the PCR results from Alupe KEMRI to results being received at the health facilities was 10.3039days with a minimum of 1 day and a maximum of 186days. These were comparable across the four counties (p=0.104) (Table 4.8).

Table 4.8: DBS-PCR Turn-around Time in Bungoma, Busia, Kakamega and Vihiga counties

Duration Between Collection and receiving in Days									**p-value**
	N	Mean	Std. Deviation	Std. Error of the mean	95% Confidence Interval for Mean		Min	Max	**<0.001**
					Lower Bound	Upper Bound			
Bungoma	600	17.0883	15.89743	0.64901	15.8137	18.3629	1.00	104.00	
Busia	340	18.9853	12.28267	0.66612	17.6750	20.2955	1.00	81.00	
Kakamega	1208	17.0199	14.90593	0.42887	16.1785	17.8613	1.00	131.00	
Vihiga	558	13.0108	10.51509	0.44514	12.1364	13.8851	2.00	81.00	
Total	2706	16.4553	14.15148	0.27204	15.9219	16.9887	1.00	131.00	
Duration between Received and Tested in Days									
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max	0.085
					Lower Bound	Upper Bound			
Bungoma	608	17.6299	16.28382	0.66040	16.3330	18.9269	1.00	90.00	
Busia	350	15.7429	12.93613	0.69147	14.3829	17.1028	1.00	66.00	
Kakamega	1237	17.1633	15.68116	0.44585	16.2886	18.0380	1.00	88.00	
Vihiga	567	15.7919	14.61759	0.61388	14.5861	16.9977	1.00	90.00	
Total	2762	16.8045	15.29354	0.29100	16.2339	17.3751	1.00	90.00	
Duration between received and updated in days									
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max	0.111
					Lower Bound	Upper Bound			
Bungoma	608	19.4030	16.54709	0.67107	18.0851	20.7209	1.00	91.00	
Busia	350	17.4257	13.23337	0.70735	16.0345	18.8169	1.00	69.00	
Kakamega	1239	18.8370	15.89869	0.45167	17.9508	19.7231	1.00	89.00	
Vihiga	567	17.6437	14.83788	0.62313	16.4198	18.8677	1.00	91.00	
Total	2764	18.5380	15.52914	0.29538	17.9588	19.1172	1.00	91.00	
Duration between received and dispatched to health facility in days									
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max	**0.002**
					Lower Bound	Upper Bound			
Bungoma	608	25.4638	18.31048	0.74259	24.0055	26.9222	1.00	91.00	
Busia	342	24.2164	17.78397	0.96165	22.3249	26.1079	1.00	71.00	
Kakamega	1239	27.2793	28.28258	0.80350	25.7029	28.8556	1.00	270.00	

Vihiga	567	22.8889	19.03642	0.79945	21.3186	24.4591	2.00	91.00	
Total	2756	25.5954	23.45075	0.44670	24.7195	26.4713	1.00	270.00	
Duration between collected from the health facility and received at the health facility in days									
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max	**0.001**
					Lower Bound	Upper Bound			
Bungoma	61	38.1475	16.93895	2.16881	33.8093	42.4858	7.00	75.00	
Busia	33	47.7576	21.75292	3.78670	40.0443	55.4708	18.00	101.00	
Kakamega	326	51.7025	47.32916	2.62132	46.5456	56.8594	11.00	487.00	
Vihiga	80	33.6625	15.24479	1.70442	30.2699	37.0551	6.00	82.00	
Total	500	46.9020	40.16420	1.79620	43.3730	50.4310	6.00	487.00	
Duration between dispatched and received at the health facility									
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max	0.104
					Lower Bound	Upper Bound			
Bungoma	40	5.7500	5.53196	0.87468	3.9808	7.5192	1.00	24.00	
Busia	29	6.9655	6.89970	1.28124	4.3410	9.5900	1.00	18.00	
Kakamega	300	11.7967	22.22284	1.28304	9.2717	14.3216	1.00	186.00	
Vihiga	72	7.9583	9.25452	1.09066	5.7836	10.1330	1.00	34.00	
Total	441	10.3039	18.97889	0.90376	8.5276	12.0801	1.00	186.00	

Table Legend: *This table shows the descriptive characteristics of six key turnaround variables that were abstracted from the registers and shows the mean, standard deviation, standard error, 95% confidence interval, min (minimum) and max (maximum) days and the p-values. This was done using one-way ANOVA.*

CHAPTER FIVE
DISCUSSION

5.1 The socio-demographic characteristics of HIV-positive mother-infant pair in Vihiga, Kakamega, Bungoma and Busia counties, Kenya

The MOH HEI register had six social and demographic characteristics being recorded on a routine basis namely marital status, maternal age, maternal weight, baby sex, baby birth weight and county. The study revealed approximately 79% of women were legally married, 5% single, 5% widowed, 3% divorced, 2% cohabiting and 1% were separated. These findings were in agreement with a study done at a rural tertiary care hospital in Maharashtra state of India that showed that 70.53% were married and living with their spouse, 4% unmarried, 2.5% divorced and 2% separated (Adejuyigbe, Fasubaa, & Onayade, 2004). High number of married persons having HIV and AIDS was also reported amongst attendees in voluntary counseling and testing centers of a medical college hospital in coastal Karnataka in 2012 and among HIV-positive women in 2014 enrolled in HIV care and support service in Amhara region, Ethiopia (Berhan, Gedefaw, Tesfa, Assefa, & Tafere, 2014; Jayarama, Shaliny Shenoy, Unnikrishnan, John Ramapuram, & Manjula Rao, 2008). The study findings also corroborated with findings that showed that most new HIV infections in sub-Saharan Africa now occur in married and cohabiting couples (Berhan et al., 2014). Consistent with previous studies carried out elsewhere in Kenya, majority (78.5%) of women HIV-positive were married(du Plessis *et al.,* 2014). However, Kenya Demographic Health Survey for 2014 showed that of the HIV positive women, 55% were married, 5.1% cohabiting/living together, and 3.7% widowed(KNBS, MOH, NACC, KEMRI, & NCPD, 2014). By showing that married women are the majority, it tied in with the general Kenyan population where nearly 2 out of 3 Kenyans aged 15-64 are married or cohabitating (NASCOP & MOH, July 2008). The study findings was also in tandem with results

of population-based data from Demographic and Health Surveys (DHS) on heterosexual behavior in Zambia in 2001-02 and in Rwanda in 2005 that revealed that most heterosexual HIV transmission takes place within marriage or cohabitation (Dunkle *et al.,* 2008). This goes on to demonstrate that married women represent the bulk of the HIV-infected population amongst the HIV-infected women attending ANC Western region of Kenya. Focusing on HIV prevention and control efforts to this population will be critical in reversing the trend of pediatric HIV and AIDS and also aid in controlling the HIV and AIDS related morbidity and mortality.

However, the findings of this study were inconsistent with others reported in Mwanza region, Tanzania that demonstrated that HIV infection was associated with being separated or widowed (Barongo *et al.,* 1992). The study was also at variance with Surveillance of HIV infections among antenatal clinic attendees in Tanzania-2003/2004 that showed HIV prevalence to be higher among single women (9.7%) than married women (8.6%) (Swai *et al.,* 2006). It contradicted a study done in Mainland Tanzania in 2011 that showed marital status had no statistically significant association with HIV infection (Manyahi *et al.,* 2015). These contrasting results may reflect the epidemiological shift of the HIV epidemic pattern in Sub-Saharan Africa region from affecting mostly singles, separated, divorced and widowed women to now predominantly affecting married women/couples who now seem to be at a higher risk of HIV acquisition and transmission.

The study revealed that the mean maternal age was 29.888 years, slightly older than most of the studies reported in the region. This finding contrasted with those done in Nigeria which showed

that HIV-positive mothers were young (Adejuyigbe *et al.*, 2004) and in Zambia where the mean age was 26.200 years (Hira *et al.,* 1990)but compares with a study done in Western Kenya that showed the average age of women in PMTCT program was 29.400 years(Dunkle *et al.,* 2008). The study also revealed that approximately 75% of women were aged between 25 and 49 years of age, the standard sexually active and productive age group. This compares favorably with findings from a study done at a rural tertiary care hospital in Maharashtra state of India in which it was demonstrated that 84.77% females were in the age group of 20-39 years (Joge *et al.,* 2012)and in Mwanza Region, Tanzania that showed that mostly women aged 15-34 years were HIV infected (Barongo *et al.,* 1992). Collectively, the findings are a pointer that the bulk of HIV infected women are young adults and they constitute the majority of HIV infected women in Western Kenya. Evidence-based interventions targeting this age-group needs to be designed and implemented in an effort to control the HIV epidemic and eliminate Mother-To-Child HIV Transmission..

The relationship between the baby's sex and the risk of HIV acquisition from a HIV-infected mother has not been clearly documented. This study showed that 50% of the babies born were females and 43% were males giving a male to female ratio of 0.86:1. This contrasted with study done in 2012 in Nigeria among HIV positive children that showed 52.7% males and 47.3% females giving a male to female ratio of 1:0.9(Omolola, Christiana, & Ade, 2012). However, these findings may not be conclusive due to ascertainment bias when recording the sex of the baby in the MOH HEI registers and the fact that the missing data was about 7% for the entry on sex of the baby in the registers compromising the findings and conclusions on infant sex.

The study further revealed that approximately 44% of babies weighed between 2.0 - 3.5kgs at birth. This is not surprising given that a previous study done in Nigeria in 2012 among HIV positive children showed that 40% of children's populations under the study weighed between 2.5 and 2.9kg at birth(Omolola *et al.*, 2012).

5.2 MTCT rates at selected time points for dual and triple ARV prophylaxis regimens and the socio-demographic, clinical and biological correlates in Vihiga, Kakamega, Bungoma and Busia counties, Kenya

5.2.2 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). The majority of the maternal prophylaxis received was HAART and the least was sdNVP. 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 compares with the second Kenya AIDS Indicator Survey that showed 72.3% of HIV-positive pregnant women received antepartum antiretroviral prophylaxis (Sirengo *et al.,* 2014). It also closely mirrors a community-based cross-sectional study of PMTCT in Nyanza Kenya, 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 Kakamega, Vihiga, Busia and Bungoma counties, Kenya.

5.2.3 MTCT rates at 6 weeks, 9 to <18 months and 18-24 months for ARV prophylaxes

Most countries are making remarkable progress towards preventing mother-to-child transmission (PMTCT) of HIV, particularly in sub-Saharan Africa. However, 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.,* 2003a). 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, 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, 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). However, it 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.,* 2003b). It alsocontrasts 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). 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). The study also contrasted with a study carried out in Botswana that 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). This could be due to the fact that other aspects of HAART such as adherence, costs, mothers' behavior during HAART may affect the overall effectiveness of HAART in PMTCT. Delays in HAART initiation and poor adherence and compliance to HAART medications could also be contributing factors. 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). This observation seems to have been due to the fact that more efficacious regimens have a durable effect in viral suppression and this suppression is sustained throughout the duration of treatment and therefore baby's HIV sero-conversion once a prophylaxis has been initiated is very low(Nyandiko *et al.*, 2010). Further studies are needed to understand other limitations to the use of HAART in PMTCT of HIV in Ministry of Health settings that could further explain why the MTCT rate for AZT seems to be lower than HAART in our study area. This will be critical in re-programming the PMTCT in these counties and in similar settings in resource-limited countries. The focus for the PMTCT programming should be the quality of PMTCT services offered to realize the eMTCT targets.

5.2.4 Socio-demographic correlates for MTCT rates

The MTCT rates at 18-24 months were highest amongst women in separated (26.7%), single (10.5%) and cohabiting (9.7%), widowed (6.5%) relationships and lowest amongst divorced (3.2%) and legally married (4.9%) women. However, this conflicts with a closely related study carried out in Nigeria that showed that HIV prevalence of divorced women were more than double those currently married/cohabiting with a sexual partner; and more than three times those that were never married (Adebayo, Olukolade, Idogho, Anyanti, & Ankomah, 2013). The high MTCT rate amongst separated and single mothers observed in the current study could be due to lack of a regular partner and a possibility of ending up having multiple partners. HIV prevalence

in the widowed women may have been due to death of their spouses from advanced HIV disease. The associated poor socio-economic status of separated, single and widowed mothers further increases their vulnerability to sexual advances and reduces their condom negotiating abilities.

The study further showed that there was a significant association between marital status and baby's HIV status at 18-24 months and that the baby is likely to be HIV positive if the mother was widowed. This probably could be due to the fact that becoming widowed is strongly associated with HIV positive status in this part of the country and HIV positive widowed women are likely to have had their spouses' die of HIV and AIDS, an indication of advanced HIV and AIDS. I hold the view that HIV among majority of widows is a result of infections acquired while in marital unions rather than as widows. This finding also concurs with my understanding that, in Western Kenya, the practices of widow cleansing and widow inheritance are common and viewed by many as contributing to the rapid spread of HIV. Widow inheritance is associated with apparent risk for HIV and STI acquisition and transmission since the wife inheritors do not use safer sex practices and the widows tend to have multiple partners for economic support. The social neglect, cultural and sexual malpractices and high poverty levels could be contributing to their likelihood to have HIV positive baby at 18-24 months due to social, cultural and economic barriers. However, the study findings contradict a prospective study in which there was no significant differences between the HIV infected and non-infected infants and mother's marital status among infants of sero-positive mothers (Nair *et al.,* 1993). Qualitative studies is therefore needed to create a better understanding of the social, cultural and economic patterns and characteristics of the different marital relationships and further determine what could be the key

determinants of the mother to child HIV transmission for different marital status beyond the known biological risk factors and whether these substantiate the quantitative results.

The study also revealed that there is no association between maternal age and baby's HIV status at 18-24 months ($p>0.05$) and this agreed with reviewed clinical records of 1088 mother-infant pairs within the Tingathe program in Lilongwe, Malawi that showed no association between HIV transmission and maternal age ($p=0.164$) (Kim *et al.,* 2013). It also concurred with a prospective study that depicted no significant difference between the HIV infected and non-infected infants with the same mean maternal age (Kim *et al.,* 2013). Though not necessarily a comparable study, it contradicted studies done in Tanzania in 2003/2004 and 2011 and in Gondar, Northwest Ethiopia that revealed that the risk for HIV infection was significantly higher among women aged 25-34 years (Manyahi *et al.*, 2015; Melku *et al*., 2015; NASCOP & MOH, July 2008). The findings also contrasts other observations in rural Northern Tanzania that revealed that the highest HIV prevalence was among women aged between 15-19 years (Yahya-Malima *et al.*, 2006). However, the study findings agreed with a prospective study in European countries that showed that maternal age were not a factor in risk of transmission (Newell, Dunn, Peckham, Semprini, & Pardi, 1996). It therefore seems that maternal age may not be a key predictor of the baby's HIV status at 18-24 months despite the fact that majority of the HIV-infected women are young adults.

The study also showed that the baby's sex had no association with baby's HIV status at 18-24 months consistent with earlier reports (Newell *et al.,* 1996).However, this differed with other observations that revealed significantly more girls (12.6%) than boys (6.3%) were infected with

HIV and at 6 to 8 weeks more girls acquired HIV (10.0%), compared with boys (7.4%) (Melku *et al.,* 2015). In Kenya, a study demonstrated that female sex are associated with HIV-1-specific CD8+ T-cell responses in HIV-1-exposed and that female infants were also more likely to have positive ELISPOT assays than male infants ($p = 0.046$) (Farquhar *et al.,* 2011). Taken together, these data demonstrate that there could be a likelihood link between baby's female sex and risk of HIV acquisition but more studies need to be done to determine the association between baby's sex and HIV status at 18-24 months born to HIV infected women in an African context.

Studies have provided inconsistent results for the association between maternal HIV infection and LBW/PTD.For example, some studies suggested that maternal HIV infectioncould increase the risk of LBW and PTD (Ellis, Williams, Graves, & Lindsay, 2002; Temmerman *et al.,* 1994)but others reported no significant association between them(Awoleke, 2012; Bucceri *et al.,* 1997; Patil *et al*., 2011). This study demonstrated that baby's birth weight had no association with baby's HIV status at 18-24 months. This contradicted findings from a prospective study in Europe in which it was shown that low birth weight had the strongest association with vertical transmission of HIV (Newell *et al.,* 1996). HIV-infected women were at higher risk of having a low birth weight infant or a preterm delivery infant as compared to HIV uninfected women. Such associations did not change significantly over time or were not significantly affected by the usage of antiretroviral drugs(Xiao *et al*., 2015).There is a possibility that maternal HIV infection has severe effects on pregnancy outcomes. It is known that HIV-infected women are more likely to encounter adverse pregnancy outcomes, such as low birth weight and preterm delivery(Xiao *et al*., 2015). Given that there was a huge missing data for birth weight (about 33%) and the fact that the different health facilities were using different weighing scales, more studies still needs to

be done to ascertain if an association exists between the birth weights and the baby's HIV status at 18-24 months.

5.2.5 Clinical and biological correlatesfor MTCT rates

The CD4+counts are 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). The lower the CD4+, the high the immunosuppression and this shows advanced HIV disease. Mothers with advanced HIV disease have a high serum viral load and therefore more likely to transmit HIV to the baby. To reduce the viral load, HIV–infected mothers need to seek early diagnosis and treatment for HIV which therefore calls for early ANC attendance and HIV testing for women in reproductive age group.

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, Nakata, Weiden, & Rom, 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 mother-to-child transmission of HIV, WHO recommends replacement feeding if it is 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). Studies on

MTCT and PMTCT in developing countries depict varied MTCT rates with different ARV prophylactic regimens with different breastfeeding options.

In the current study, babies' 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, Moodley, Coutsoudis, & Coovadia, 1997). Similarly, a 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). This is because breastfeeding carries so much protection against other nutritional and infectious diseases which then facilitates HIV acquisition and transmission from mother to child. Exclusive breastfeeding, coupled with antiretroviral drug therapy for both significantly reduces the MTCT rate(Coovadia *et al*., 2007). Combining breastfeeding with other food increases the MTCT rate due to likelihood of infections that erodes the gut mucosa and increases the MTCT rates(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 ($p< 0.001$). 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). This 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, Pillay, Spooner, Kuhn, & Coovadia, 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(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. Exclusive breastfeeding together with near universal use of efficacious regimens namely HAART and AZT contributes to the low MTCT rates. Mixed feeding and exclusive

replacement feeding does not confer the nutritional values associated with exclusive 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(Berhan *et al.*, 2014). Early diagnosis and treatment is always associated with good prognosis. In this case, women who seek early HIV diagnosis and treatment and are enrolled early during their pregnancy are more likely to receive the PMTCT interventions early and this is likely to result in lower MTCT rate. Birth preparedness and birth plans are key and should be encouraged to allow mothers to plan pregnancies and attend antenatal care sufficiently early and receive early HIV diagnosis and treatment including ARVs initiation.

5.3. To assess the DBS-PCR turnaround time (TAT) and the associated factors in Vihiga, Kakamega, Bungoma and Busia counties, Kenya

The primary goal of early infant diagnosis is to identify the HIV-infected child early prior to the development of clinical disease during the first months of life and not to exclude HIV infection. Faster TAT is universally seen as desirable. It is believed that the timelier the rapid testing is performed, the more efficient and effective the treatment will be.TAT is the total time between specimen collection, submission, processing and dispatch of the results for patient use.

Turnaround time is one of the key performance indicator of laboratory performance. It is associated with clinical outcomes and therefore need to improve approaches to TAT.

Across Africa, implementation of early infant diagnosis has been met with challenges, one of which is the long turnaround time of the PCR results that results in delay in initiating infants and children under 18 months on ARV treatment. The study showed mean TAT from specimen collection to results being received at the health facility as 47 days with a range of 6 days to 487days and with variations across the four counties. This contrasts with study done in Côte d'Ivoire, where the average test turnaround time from sample collection to results sent to the clinic was 33 days with a range of 8 to 58 days (Kouakou *et al.,* 2008). In Rwanda, the test turnaround time between blood draw and test result back on site had a median of 17 days with a range of 9 to 54 days (Finkbeiner, 2006). In 2008, an evaluation of an Early Infant Diagnosis Program using DNA Polymerase Chain Reaction (PCR), on Dried Blood Spot (DBS) in Nigeria to demonstrated an average turnaround time for return of 3 to 4 weeks (Abutu *et al*., 2008)(Abutu *et al.,* 2008). However, in Swaziland the mean time from test to result pick-up was longer at 63 days (Brad *etal.*, 2013; Chouraya *et al*., 2008). A study done in Western Kenya at Kapsabet District Hospital in 2013 showed the average number of weeks from sample collection to return of the PCR result as 4.08weeks(Brad *et al.*, 2013). This shows that the TAT is long and could be due to delays at pre-analytical, analytical and post-analytical phases. A lot still need to be done to reduce the TAT time that ultimately determines the ART initiation amongst the HIV-infected children.

This study revealed the mean duration between specimen collection at the health facilities and receiving specimens at Alupe KEMRI laboratory was 16.4553days with variations across the four counties with a range of 1 day to 131 days. Vihiga County had the least mean duration at 13.0108days while Busia County had the longest duration at 18. 9853days. This compares with median time between sample collection and arrival at the central laboratory in Lusaka, which was 17 days (Sutcliffe, van Dijk, Hamangaba, Mayani, & Moss, 2014). However, this contrasts with mean sample turn-around time from collection at site to laboratory of 1.38 days in Namibia, 5.25 days in Cambodia, and 12.6 days in Uganda over the life of the program (Chatterjee *et al.*, 2011). This demonstrates that there are significant delays at pre-analytical phases due to specimen hubbing at the central health facilities before specimens are transported to Alupe KEMRI Laboratory. The continuous batching of specimens by the peripheral health facilities also contributed to pre-analytical delays since peripheral health facilities will only get transport reimbursements if they do submit at least two specimens per trip.

The study showed the mean duration between receiving the specimens from the health facilities and testing the specimens was 16.8045days with a range of 1 day to 90days. This contrasts with TAT determined in Lusaka that showed the time between specimen arrivals at the central laboratory to testing was 6 days (Sutcliffe *et al.*, 2014). In most of the sampled facilities, health facility registers did not routinely document the date that the result arrived back at sites and therefore the total TAT from sample collection to result arrival at site could not be measured for most of the specimens. The study mean TAT of 46 days contrasts with TAT for processing within laboratories averaged 9 days in Namibia, and 3.33 weeks in Uganda but compares with 18

days in Cambodia, over the life of the program. Similarly in all countries health facility registers did not systematically document the date that the result arrived back at sites and therefore the total TAT from sample collection to result arrival at site could not be measured (Chatterjee *et al.,* 2011).TAT from sample collection to result return decreased from 49 to under 14 days(Kiyaga *et al.,* 2015). The analytical phase is long and this could be due to lack of adequate and skilled staff to do DBS-PCR testing coupled with the high workload at Alupe KEMRI Laboratory, given that it is the only laboratory in the region with the capacity to conduct DBS-PCR. In addition, the laboratory staff from the satellite health facilities may not have been skilled enough to collect the quality specimens and this also delayed the processing of the specimens.

Factors shown to correlate with shorter total TATs include the practice of delivering each specimen as it is collected, direct delivery route, and continuous versus batching (Hawkins, 2007). This is in agreement with the study findings which showed health facilities in Vihiga county as opposed to other Counties were delivering specimens as they are collected (no batching) and directly submitting to Alupe KEMRI Laboratory via courier services (no hubbing at the Central health facilities). The study also revealed that TAT delays were at all levels that is pre-analytical, analytical and post-analytical. This differs with study done in Australia that showed delays in TAT are most commonly pre-analytical and post-analytical (Hawkins, 2007). Specimen batching and hubbing contributes to delays in pre-analytical phase of the TAT. Inadequate capacity of the laboratory personnel both at the satellite health facilities and the Alupe KEMRI Laboratory to collect quality specimens and also to process the DBS-PCR

specimens also contributed to the long TAT.These delays could potentially be acontributor to the high MTCT rate in the studied populations.

CHAPTER SIX
SUMMARY FINDINGS, CONCLUSIONS AND RECOMMENDATIONS

6.1 Summary of findings

The study revealed that majority of HIV positive pregnant women were legally married and were aged between 24 - 49 years. Those women who tended to have HIV positive babies at 18-24 months period were older at enrollment to PMTCT than those who tended to have HIV negative babies at the same time period.The study also showed that female are more than male at birth amongst HIV positive pregnant women and that a significant proportion of babies born of HIV positive women weighed between 2.0-3.5kg though this is not conclusive given about a third of the babies' weights were not documented in the MoH registers.

This study demonstrated that HAART was the main ARV prophylaxis regimen in use and AZT and NVP were less commonly administered with AZT (with 3.3% MTCT rate) and HAART (with 5.4% MTCT rate) had the lowest HIV transmission rates at 18-24 months. Six socio-demographic correlates for MTCT were determined. The study revealed that there is a significant statistical association between marital status and babies' HIV status at 18-24 months with MTCT rate highest amongst separated, single, widowed and cohabiting women and lowest amongst the legally married HIV positive pregnant women. Babies born to mothers separated had approximately 7 times more likelyto have HIV negative results at 18-24 months as compared to widowed women. It further showed that maternal age, maternal weight and babies' birth weight, babies' sex were not associated with baby's HIV status at 18-24 months.

A number of biological and clinical correlates for MTCT rates were investigated. HIV positive pregnant women with lower CD4 counts on enrollment had a significantly higher risk of transmitting HIV to their babies as compared to those women with higher CD4 counts on enrollment with HIV positive pregnant women with CD4 counts between 350 to 500 cells/mm^3 had a higher MTCT rates at the selected time points.

This study also revealed that HIV positive pregnant women on TB treatment had a higher MTCT rates at 9-18 months and 18-24 months. This means that HIV positive pregnant women with suspected or confirmed TB have a higher MTCT rates. It also showed that the shorter the duration between enrollment and date of delivery, the lower the MTCT rates at the selected time points. Moreover, these findings demonstrated that feeding options at 6 weeks is a strong predictor of MTCT rates at the selected time periods with exclusive breastfeeding showing a strong predictor of having HIV negative babies at the selected time points.

The turnaround time for the DBS-PCR in Kakamega, Bungoma, Vihiga and Busia counties from specimen collection at the health facility and results received at the health facilities was 46.9020days while the mean duration between specimen collection at the health facility and receiving specimens at Alupe KEMRI Laboratory was 16.4553days. These were due to pooling of samples at the health facilities at low volume health facilities and hubbing at the high volume health facilities. However, a significant delay was noted in specimen processing where it took a mean of 16.805days from the time of receiving the specimens at the laboratory to testing the specimens.

6.2Conclusions

a) The study revealed that most HIV positive mothers were legally married, were young between 24 - 49 years and that those women who tended to have HIV positive babies at 18-24 months period were comparatively more mature at enrollment to PMTCT than those who tended to have HIV negative babies;

b) With regard to the socio-demographic, biological and programmatic correlates, the study revealedthat HAART was the main ARV prophylaxis regimen in use and AZT and NVP were less commonlythough AZT (with 3.3% MTCT rate) and HAART (with 5.4% MTCT rate) had the lowest HIV transmission rates at 18-24 months. Whereas MTCT rate was highest amongst separated, single, widowed and cohabiting women and lowest amongst the legally married HIV positive pregnant women, HIV positive pregnant women who are widowed more likely to have higher MTCT rates as compared to separated women at 18-24 months period. Exclusive breastfeeding at 6 weeks should be strongly encouraged since it is a key predictor of baby's HIV negative status at 18-24 months;

c) The study demonstrated that the overall TAT from specimen collection at the health facility and results received at the health facilities was 46.9020days with the mean duration between specimen collection at the health facility and receiving specimens at Alupe KEMRI Laboratory being 16.4553days. These are due to pooling of samples at the health facilities at low volume health facilities and hubbing at the high volume health facilities. Significant delay was noted in specimen processing where it took a mean of 16.805days from the time of receiving the specimens at the laboratory to testing the specimens.

6.3 Recommendations from the current study

a) Proven evidence-based interventions targeting women of 24-49 age-group and married needs to be designed and implemented as part of efforts to control HIV epidemic and eliminate Mother-To-Child HIV Transmission;

b) HIV prevention and control efforts needs to focus on widowed women since they seem to have higher rates of MTCT rates at 18-24 months, if we are to reverse the new pediatric HIV infections and attain the eMTCT goals. In addition, exclusive breastfeeding at 6 weeks should be strongly encouraged since it is a predictor of HIV negative status at 18-24 months period. Mixed feeding and exclusive replacement feeding at 6 weeks be strongly discouraged;

c) Batching of specimens at the peripheral health facilities and specimen hubbing at referral hospitals should be discouraged and specimens should be submitted directly to Alupe KEMRI Reference Laboratory as soon as possible through G4S courier servicesor any other means of transport.

6.4 Suggestions for future research

a) Further study is recommended to understand why Vihiga County records a better TAT as compared to other counties;

b) Further study is suggested to better understand why HAART prophylaxis regimen shows a higher MTCT rate as compared to AZT prophylaxis despite numerous studies showing the contrary;

c) Further study is also recommended to better understand why HIV-positive mothers in cohabiting relationships have a higher HIV MTCT rate as compared to other mothers in other relationships.

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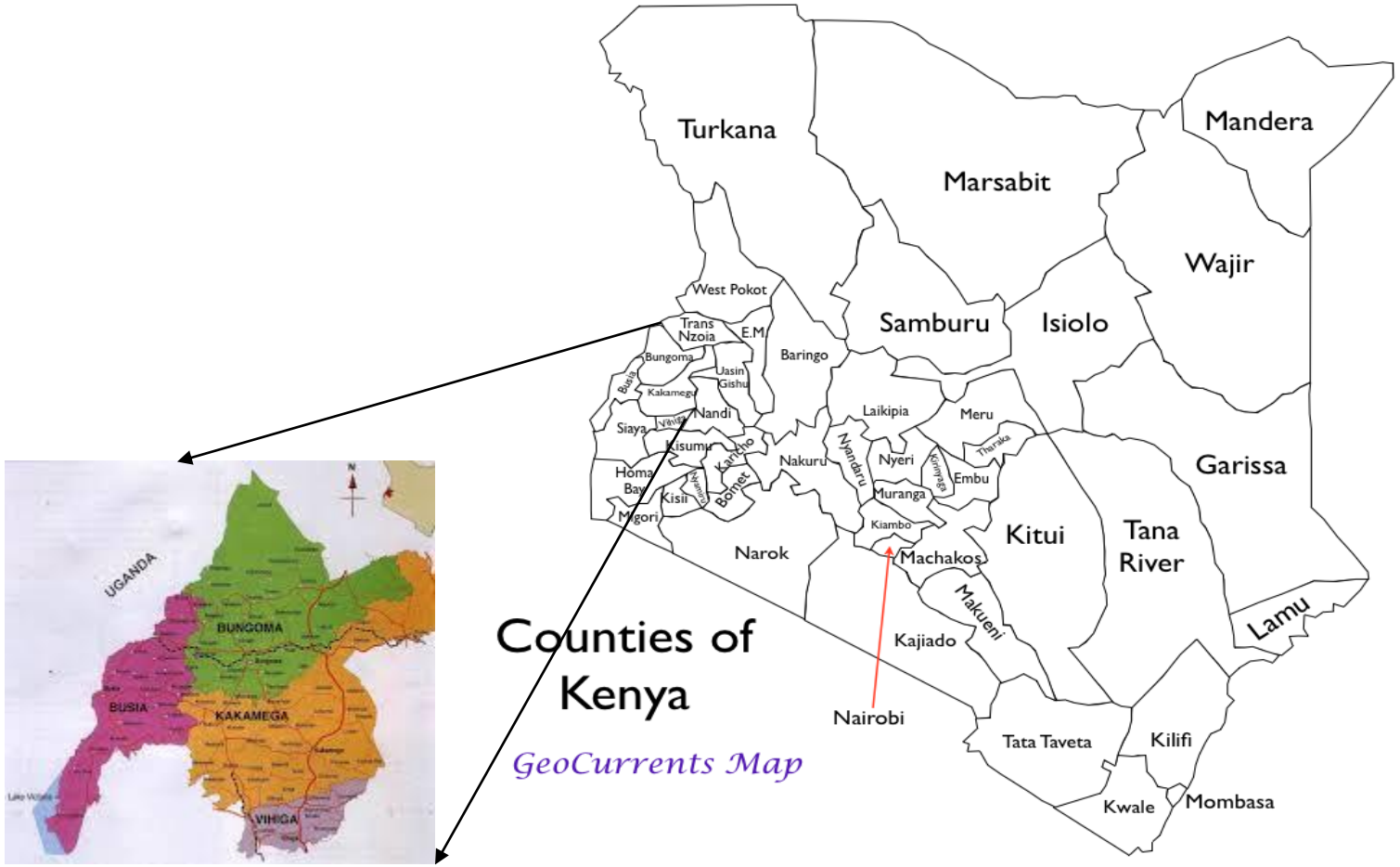
APPENDICES

Appendix 1: Map of Western Region, Kenya



Longitudes andlatitudes: Kakamega county (0.2827^0 N, 34.7519^0 E); Vihiga county (0.0816^0 N, 34.7229^0 E); Bungoma county (0.5695^0 N, 34.5584^0 E) and Busia county (0.4608^0 N, 34.1115^0 E)

Appendix 2: Sampled health facilities in Kakamega, Vihiga, Bungoma and Busia counties, Western Kenya

Mother-baby pair sampled disaggregated by level of health facility

	Frequency	Percent	Health Facilities sampled
Health Centre	372	21.2	Bumala HC, Kunyangu HC, Malakisi HC, Matayos HC, Mbale Rural HC, Naitiri HC, Nambale HC, Sabatia HC
Sub-district Hospital	267	15.2	Alupe SDH, Manyala SDH, Sio Port SDH, Sirisia SDH
District Hospital or Mission Hospital	982	56.1	Bungoma DH, Busia DH, Chwele DH, Kimilili DH, Malava DH, Matungu DH, St Mary Mumias Mission Hospital, Vihiga DH, Teso DH, Webuye DH, Mukumu Mission Hospital
Referral Hospital	130	7.4	Kakamega PGH
Total	1751	100.0	

Appendix 3: Consent form

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

Mother to child transmission of HIV in Bungoma, Kakamega, Busia and Vihiga counties, Western Region: context and rates

PRINCIPAL INVESTIGATOR
Maxwell Philip Omondi,
College of Health Sciences,
Department of Community Health, Nairobi University,
PO BOX 18717 00100,
NAIROBI.

Email: maxwellomondi@yahoo.com
Tel: 0721 208 732

Hello,
I, *Maxwell Philip Omondi*, am a doctoral student in the School of Public Health, Maseno University. I am conducting a study for the purpose of determining the mother to child HIV transmission in Bungoma, Kakamega, Busia and Vihiga counties, Western Region.

POSSIBLE BENEFITS
No direct benefits for participating in the study. However, study will help determine MTCT rates in Western region and identify correlates associated with it.
The HIV exposed babies and their mothers will be enrolled in HIV care and treatment and will be accorded the appropriate patient management as per the ministry of health/NASCOP guidelines.

CONFIDENTIALITY
All information obtained in this study will be considered confidential and not divulged to anyone not involved in the study. The participants' identification will be kept confidential. The questionnaires and discussion notes will be marked only with codes and not names. The list of numbers will be destroyed at the end of the research. The research reports and publications will only discuss large groups of participants and will not reveal individual names. Every effort will be made to protect the confidentiality of the information provided. The questionnaires will be kept under lock and key with restricted access.

COMPENSATION
We will not be able to provide you any payment or gift for being in this research.

RIGHT TO REFUSE OR WITHDRAW
A subject' participation in the study is entirely voluntary. He /she is free to refuse to take part or withdraw at any time, without affecting or jeopardizing her future medical care or career.

QUESTIONS
In case of any queries, comments or complaints, kindly contact the investigator in above mentioned address.

CONSENT
I have read/been explained to all the above and fully understand. I therefore agree/disagree to participate in the study.

Investigator
…….
Signature Date

....
Participant
…….

Signature Date

....

Appendix 4: Initial form - Sheet A

Serial No.	Infants Name	Mothers Name	CCC Number	HIV status at 6 weeks/Feeding options	HIV status at 9 months/Feeding Options	HIV status at 18months/Feeding option

Appendix 5: Abstraction form - Sheet B

Abstraction form

Date of visit	CCC Number	Mothers Names	District	Year of Birth	Marital Status	Expected Date of Delivery (EDD)	Weight (kg)	Laboratory: Haemoglobin	ART Eligibility – Assesed through?: WHO Stage	ART Eligibility – Assesed through?: CD4	Start on ART	Prophylaxis: CTX	Prophylaxis – ARV Regimen (Predominant) – Mother: NVP	Prophylaxis – ARV Regimen (Predominant) – Mother: AZT	Prophylaxis – ARV Regimen (Predominant) – Mother: HAART	Prophylaxis – ARV Regimen (Predominant): NVP for Baby	Screened f: TB	Other Conditions: 1=Hypertension 2=Diabetes 3=Epilepsy 4=Malaria in Pregnancy 5=STIs/RTI 6=Others Specify)	Date of Delivery	Place of Delivery	Mode of Delivery	Baby: Sex	Baby: Birth Weight	Baby: HIV status at 6 weeks/Feeding Options	Baby: HIV status at 9 months/Feeding Options	Baby: HIV status at 18months/Feeding Options
						(dd/mm/yy)			(Stage)		(Date)	(Y/N)	(Y/N)	(Y/N)	(P/T)	(Y/N)	(Status)					(M/F)	(in grams)			
(a)	(b)	(e)	(f)	(g)	(h)	(l)	(n)	(q)	(u)	(v)	(w)	(x)	(y)	(z)	(aa)	(ab)	(ac)	(ae)	(n)		(q)	(v)	(w)			

Appendix 6: Laboratory abstraction form – Sheet C

Facility	County	District	Patient ID	Date collected	Date received	Duration Between Collection and receiving in Days	Date tested	Duration between Received and Tested in Days	Date updated	Duration between received and updated in days	Date dispatched	Duration between received and dispatched	Date received at the facility	Duration between collected and received	Duration between dispatched and received

Appendix 7: Key Informant Guide

Participants: County and sub-county laboratory officers, Laboratory-in charges, MCH/PMTCT coordinators

1. What is the Ministry of Health protocol or algorithm in EID? Briefly explain.
    a. What protocol is used in your county, sub-county or health facility, if different from MoH?
2. What is the EID laboratory networking in place, if any? Explain
    a. How does it work?
    b. What is the DBS-PCR turnaround time (TAT)?
    c. Is it effective and efficient?
    d. What are the successes if any?
    e. What are the challenges/failure, if any?
3. What are the key programmatic and management recommendations would you suggest?
4. Any other comments

Appendix 8: KNH/UoN Ethical Review Approval

UNIVERSITY OF NAIROBI
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KENYATTA NATIONAL HOSPITAL
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Ref. No.KNH/ERC/R/78

24th June 2014

Dr. Maxwell Philip Omondi
P O BOX 18717-00100
NAIROBI

Dear Dr. Omondi

Re: Approval of annual renewal – Mother to Child Transmission of HIV in Western Province of Kenya(P666/11/2012)

Refer your communication of 30th May 2014.

This is to acknowledge receipt of the study progress report and hereby grant you annual extension of approval for ethical research Protocol **P666/11/2012.**

The approval dates are 22nd May 2014 to 21st May 2015.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN- ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.

g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN -ERC website www.uonbi.ac.ke/activities/KNHUoN

Kindly forward the informed consent documents for endorsement with updated stamp.

Yours sincerely

PROF. M.L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chairperson, KNH/UoN-ERC

Appendix 9: Missing value analysis between January 2012 to June 2013

Statistics of the Missing Values			
Independent variables	N	Missing values	
		Count	Percent
Age of enrolment in years	1751	72	4.1
Weight in Kgs	1751	154	8.8
Hb in mmHg	1751	1168	66.7
CD4ungrouped	1751	159	9.1
Age start ART	1751	355	20.3
Age At Delivery	1751	157	9.0
Birth weight in Kgs	1751	581	33.2
WHO Stage	1751	178	10.2
Marital status	1751	65	3.7
NVP prophylaxis for the Baby	1751	78	4.5
TB status of the Patient	1751	119	6.8
Other conditions	1751	474	27.1
Place of Delivery	1751	955	54.5
Mode of Delivery	1751	887	50.7
Sex of the Baby	1751	139	7.9
HIV status at 6 weeks	1751	48	2.7
Feeding options at 6 weeks	1751	171	9.8
HIV status at 9 months	1751	44	2.5
Feeding options at 9 months	1751	164	9.4
HIV status at 18 months	1751	26	1.5
Feeding options at 18 months	1751	646	36.9

Appendix 10a: Publication 1Review Approval

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Open Access to full text available at http://journals.uonbi.ac.ke/ajpt

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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[f] *African Institute for Development and Policy (AFIDEP), Nairobi, Kenya*

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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

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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).

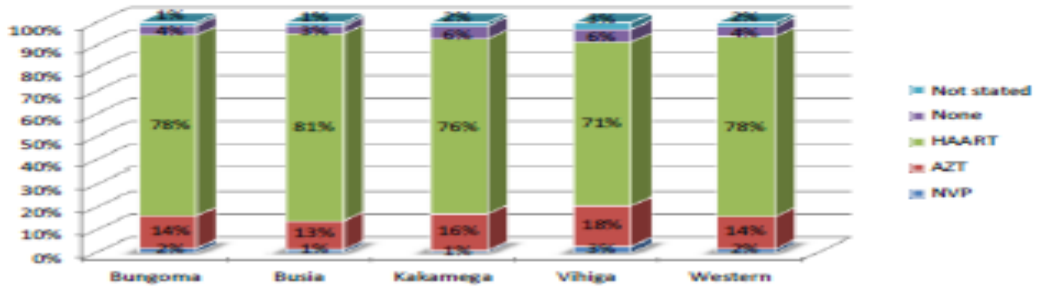

Figure 1: ARV prophylaxis regimens received disaggregated by county from January 2012 to June 2013

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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%)		

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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%

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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; Tocossi 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

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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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Appendix 10b: Publication 2

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Social and Demographic Characteristics of HIV-Positive Mother-Infant Pair and Their Association with Mother-To-Child Transmission of HIV in Vihiga, Kakamega, Bungoma and Busia Counties, Kenya: Chart Review

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Abstract:

Background: *The World Health Organization report indicates that in 2013~35 million people worldwide lived with HIV and AIDS. Of these, 3.2 million were children age <15 years. The proportion of women living with HIV has remained stable, at slightly ~52% of the global figure. There are 13 high burden countries which account for 75% of the estimated 1.5 million pregnant women living with HIV in low- and middle-income countries. Furthermore, most of the HIV-infected children live in sub-Saharan Africa and were infected by their mothers through mother-to-child transmission (MTCT). Despite these statistics, social and demographic characteristics that are associated with MTCT rate at 18-24 months remains unknown. This study aimed to describe the social and demographic characteristics of HIV mother-infant pair and their association with MTCT rate at 18-24 months in Vihiga, Kakamega, Bungoma and Busia Counties, Kenya.*

Method: *A retrospective cohort study using prospectively collected data in Kenyan Ministry of Health (MOH)HIV Exposed Infant (HEI) register from 24 health facilities sampled across the four counties were sampled. The study population was HIV mother-baby pairs enrolled from January 2012 to June 2013. The social (marital status) and demographic (maternal age, maternal weight, baby's sex, baby's birth weight, level of health facility, county name) characteristics were assessed. The main outcome measure was infant HIV status at 18-24 months. Proportions were analyzed using Chi-square tests while associations between social and demographic characteristics and outcome were established using multiple logistic regression while controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 count. P-values ≤0.05 were considered statistically significant.*

Results: *A total of 1751 HIV mother-baby pairs were enrolled in 24 health facilities. About 79.3% (1389/1751)mothers were legally married, 5.4% (95/1751) single, 5.4% (94/1751) widowed, 3.5% (62/1751) divorced, 1.8% (31/1751) cohabiting 0.9% (15/1751)separated and 3.7% (65/1751) had not stated. The MTCT rate at 18-24 months showed variations with marital status since the rates were highest amongst women in separated (26.7%), single (10.5%) and cohabiting (9.7%) relationships and lowest amongst divorced (3.2%) and legally married (4.9%) women. Separated women were about 7 times more likely to have HIV-negative babies as compared to widowed women (OR, 7.517, 95%CI, 1.344 – 42.031, p=0.022).*

Conclusion: *Separated HIV positive women are more likely to have HIV negative babies at 18-24 months as opposed to widowed woman.*

Key words: *Marital status, Mother-To-Child Transmission of HIV, socio-demographic characteristics*

1. Background

The HIV and AIDS remains one of the key challenges in the 21st century with political, economic, public health, social and scientific consequences globally. HIV and 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, especially in sub-Saharan Africa that carries 60% of the world's disease burden despite having only 10% of the world's population[1]. UNAIDS estimates that there were 33.3 million [31.4 million–35.3 million] people living with HIV at the end of 2009. The estimated number of children living with HIV increased to 2.5 million [1.7 million–3.4 million] in the same period (2009). The proportion of women living with HIV has remained stable, at slightly less than 52% globally[1]. Data show that there are 13 high burden countries which account for 75% of the estimated 1.5 million pregnant women and 75% of children living with HIV in 2007 in low- and middle-income countries. All the affected countries (except India) are in sub-Saharan Africa, Kenya inclusive[2].

Mother-to-child transmission (MTCT) occurs when an HIV-infected woman passes the virus to her baby. This can happen during pregnancy, labour and delivery, or breastfeeding. Without treatment, around 15-30% of babies born to HIV-positive women will become infected with HIV during pregnancy and delivery[3]. A further 5-20% will become infected through breastfeeding [3]. In 2009, around 400,000 children under 15 became infected with HIV, mainly through MTCT. About 90% of these MTCT infections occurred in Africa where AIDS is beginning to reverse decades of steady progress in child survival[2]. A focus on women of reproductive age in the priority countries remains central to the AIDS response. However, the number of new HIV infections among them remains high, having declined by only 17% since 2009. More effort should be made to lower the risk of women acquiring HIV. This is not only important for the woman's health, but would also achieve the goal of eliminating new HIV infections among children. Additional effort should focus on provision of treatment to pregnant women living with HIV[4].In order to eliminate MTCT among children and also keep women healthy and well, it is important to reduce new HIV infections among women of reproductive age, especially among adolescents and young women[4].

In Sub-Saharan Africa where HIV prevalence is highest, women are most affected with an average of 13 infected women for every 10 infected men[5]. This difference is more marked among young people (15-24 years) with three out of four people living with HIV being females[5]. According to Kenya AIDS Indicator Survey (KAIS) 2007, the HIV sero-prevalence in the country is 7.8% among adults aged 15-49 years, being higher in women (8.7%) than in men (5.6%)[6].MTCT is one of the biggest health and development challenges in Kenya. Numerous studies have demonstrated associations between social and demographic factors such as marital status, level of education, gender, maternal weight, maternal age, baby's birth weight and the prevalence of HIV[7-13]. However, no known study from the literature search has been done to demonstrate how they affect the mother-to-child HIV transmission at 18-24 months especially in populations resident in western Kenya. In addition, fewattempts have been made to assess the extent of mother-to-child HIV transmission in different marital relationships such as in cohabiting, with an aim of broadening andrefocusing on the HIV prevention efforts towards realization of eMTCT in Western Kenya by 2015 and beyond. This study therefore sought to determine the social and demographic characteristics of HIV positive mother-baby pairs and their association with mother-to-child HIV transmission rates at 18-24 monthsin Vihiga, Bungoma, Kakamega and Busia Counties in western Kenya.

2. Materials and Methods

Study design: Aretrospective cohort study using prospectively collected data from 24health facilities providing Prevention of Mother-to-Child-Transmission (PMTCT) and early infant diagnosis (EID) according to the Ministry of Health/NASCOP guidelines in Vihiga, Kakamega, Bungoma and Busia Counties were sampled.

Study population: The study population were HIV-positive woman who received PMTCT services during the study period (January 2012 to June 2013) and their HIV-exposed babies who were at least 18-24 months of age.

Social and demographic variables: In order to address the objective of the study, social (marital status) and demographic (maternal age, maternal weight, baby sex, baby birth weight, county and level of health facility) characteristics of the study participants were assessed as independent variables. The main outcome variable was the baby's HIV status at 18-24 months.

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. 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 period covering January 2012 to June 2013. As a result a total of 1751 mother-baby pairs data were extracted from the MOH HEI registers, which 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)The MOH registers, patient files depicted missing information in varying degrees from facility to facility and from variable to variable with the mean of 18%.

Eligibility criteria: The inclusion criteria included a) health facilities providing PMTCT and EID as per the Kenyan MOH protocol and guidelines b) In charge of health facilities who were willing to give informed consent to participate in the study c) health facilities that started providing PMTCT services from at least January 2012 d) mother-baby pairs that were enrolled in the sampled health facilities between January 2012 to June 2013 and who provided informed consent.

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 18-24 months and categorical variables. Multiple logistic regression was used to assess the association between social and demographic characteristics and baby's HIV status at 18-24 months while controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 count.*p-values* ≤ 0.05 were considered statistically significant.

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

3.1. Socio-Demographic Characteristics of Study Participants

The MOH registers which were the primary source documents for this study hadsevensocial and demographic variables: marital status, maternal age, maternal weight, baby's sex,baby's birth weight, level of health facility and county. Regarding the marital status, 15/1751 (0.9%) separated, 31/1751 (1.8%) cohabiting, 62/1751 (3.5%) divorced, 94/1751 (5.4%) widowed, 95/1751 (5.4%) single, 1389/1751(79.3%) were legally married and 65/1751 (3.7%) were not stated. There were variations in marital status across the four counties of Western Province as depicted in Table 1 below. These differences by county were statistically significant (p=0.001) with Kakamega county having proportionately less legally married woman at 69% compared to the three other counties (n=272).

When grouped into age categories, the maternal age at enrollment was as follows: 1.1% (n=20/1751) were <18 years old, 19.7% (n=345/1751) were between 18 and 24 years old, 74.8% (n=1309/1751) were aged between 25 and 49 years,0.3%(5/1751) were greater than 50 years old and 4.1%(72/1751) did not state their ages. These were further stratified by county as shown in Table 1 below and these were comparable(p=0.329).

Since it has been shown that baby's sex affects acquisition of HIV at birth, we assessed the distribution of the population based onbaby's sex. Overall 49.2% (n=861) of the babies born were females, 42.9% (n=751) were males and 7.9% (n=139) had no stated sex. Table 1 shows the differences in baby's sex by county and these differences were statistically different (p=0.001)since Vihiga County had more females while Kakamega County had less males compared to the other counties.

Table1. *Marital status, Sex of the baby and age at enrolment in MCH/PMTCT services by Counties, Jan 2012 to June 2013*

	Marital Status[a] $p<0.001$[a1]							Sex of the Baby[b] $p<0.001$[b1]			Maternal Age at enrolment in MCH/PMTCT services[c] $p=0.329$[c1]				
Counties	Cohabiting	Divorced	Legally Married	Separated	Single	Widowed	Not stated	Female	Male	Not stated	<18 years	18-25 years	>25-49 years	>49 years	Not stated
Bungoma (N=408)	3.7% (n=15)	3.2% (n=13)	79.9% (n=326)	0.7% (n=3)	6.4% (n=26)	5.6% (n=23)	0.5% (n=2)	50.7% (n=207)	43.9% (n=179)	5.4% (n=22)	2.2% (n=9)	23.8% (n=97)	72.5%(n=296)	0.2% (n=1)	1.2% (n=5)
Busia (N=817)	1.1% (n=9)	4.3% (n=35)	83.2% (n=680)	0.7% (n=6)	5.8% (n=47)	4.8% (n=39)	0.1% (n=1)	51.2% (n=418)	44.6% (n=364)	4.3% (n=35)	0.7% (n=6)	20% (n=163)	78.9%(n=645)	0.2% (n=2)	0.1% (n=1)
Kakamega (N=394)	1.8% (n=7)	2.5% (n=10)	69% (n=272)	1% (n=4)	4.6% (n=18)	5.8% (n=23)	15.2% (n=60)	42.6% (n=168)	39.8% (n=157)	17.5% (n=69)	1.3% (n=5)	14.5% (n=57)	68%(n=268)	0.5% (n=2)	15.7% (n=62)
Vihiga (N=106)	0% (n=0)	3.8% (n=4)	83.0% (n=88)	1.9% (n=2)	3.8% (n=4)	7.5% (n=8)	0% (n=0)	53.8% (n=57)	42.5% (n=45)	3.8% (n=4)	0% (n=0)	17.9% (n=19)	80.2%(n=85)	0% (n=0)	1.9% (n=2)

Legend: *[a]The number (n) and proportion (%) of different marital status are shown across the four counties. Not stated means there was no documentation of the marital status in the Ministry of Health register;[a1]Statistical analysis as determined by χ^2 statistics.[b]Legend. The number (n) and proportion (%) of females and males shown across the four counties. Not stated means there was no documentation of the sex of the baby in the Ministry of Health registers; [b1]Statistical analysis as determined by χ^2 statistics; [c]The number (n) and proportion (%) of different age brackets are shown across the four counties. Not stated means there was no documentation of the ages in the Ministry of Health registers; [c1]Statistical analysis as determined by χ^2 statistics.*

Additional analyses looked at the distribution of baby's HIV serostatus in the context of maternal age, maternal weight and baby's birth weight. The overall mean maternal age at enrollment was 29.888 years (SD 5.895). The mean maternal age at enrollment was comparable between those whose children were HIV-negative (29.853 years) and HIV-positive (31.061 years) at 18-24 months (p=0.058) (Table 2). Likewise, the overall mean maternal weight was 58.469kg (SD 10.067). The mean maternal weight at enrollment was comparable between those whose children were HIV-negative (58.559kg) and HIV-positive (57.251kg) at 18-24 months (p=0.248) (Table 2). Finally, the overall mean birth weight for the babies was 3.258kg (SD 0.644). The mean baby's birth weight at enrollment was comparable between those who were HIV-negative (3.255kg) and HIV-positive (3.321kg) (p=0.470) (Table 2). These results collectively demonstrate that maternal age, maternal weight and babies' birth weight are not associated with baby's HIV status at 18-24 months in this population.

Table2. *Association between Maternal age and weight, Baby's Birth Weight and baby's HIV serostatus at 18-24 months*

Variable		HIV Negative	HIV Positive
Maternal Age	Median age in years	29.615	30.810
	Mean age in years	29.853	31.061
	95% CI	95% CI: 29.560,30.146	95% CI: 29.847,32.274
	SD	5.905	5.828
	Range	48.510	30.130
	Interquartile range	8.430	5.810
	p-value	p=0.058	
Maternal weight	Median weight in Kgs	57.000	56.500
	Mean weight in Kgs	58.559	57.251
	95% CI	58.046,59.072	55.072,59.431

	SD	10.090	10.044
	Range	99.800	53.000
	Interquartile range	12.000	13.770
	p-value	*p*=0.248	
Birth weight	Median weight in Kgs	3.000	3.000
	Mean weight in Kgs	3.255	3.321
	95% CI	3.218,3.293	3.117,3.524
	SD	0.640	0.739
	Range	7.000	3.400
	Interquartile range	0.800	1.000
	p-value	*p*=0.470	

Legend: *the median, mean, 95% Confidence Interval, range and interquartile range were calculated for maternal age, maternal weight and baby's birth weight and comparison made between HIV positive and HIV negative babies at 18-24 months. The statistical significance was determined using the p-values.*

Using the adult females' normal physiological weight as 60.0kg, the maternal weights were then stratified by the physiological weights ≤60.0kg and >60.0kg. Mothers weighing ≤60kg were 1014/1751 (57.9%) and those weighing >60kg were 583/1751(33.3%) and 154/1751 (8.8%) had not stated their weight. Low birth weights are considered <2.0kg and overweight >3.50kg. This criterion was used to stratify the baby's birth weights. Approximately 3.5% (62/1751) of the babies had birth weights <2.0kg, 44.2% (774/1751) had birth weights between 2.0kgs and 3.50kgs while19.1% (334/1751)had birth weights >3.50kgs and 581/1751 (33.2%) had their birth weights not stated as shown in Table 3.

In order to determine MTCT rate in children aged 18-24 months, the proportion of HIV positive babies at 18-24 months in HIV exposed babies was evaluated. The MTCT rate at 18-24 months showed variations with marital status (p=0.003). The MTCT rates are highest amongst women in separated 4/15(26.7%), single10/95(10.5%) and cohabiting 3/31(9.7%) relationships and lowest amongst divorced2/60(3.2%) and legally married67/1366(4.9%) women as shown in Table 3.

In order to test the associations between the social and demographic characteristics and HIV status at 18-24 months, a bivariate analyses between baby's HIV status at 18-24 months and level of the health facility, county, maternal age, marital status, maternal body weight, sex of the baby and bays' birth weight was carried out. Results demonstrated that marital status was a significant predictor of HIV status at 18-24 months (p=0.003) as shown in Table 3. In addition, babies born to mothers separated had approximately7 times likelihood of having HIV negative results at 18-24 months as compared to widowed women (OR=7.317, 95% CI: 1.344 – 42.031, p=0.022). However, there were no associations between the maternal weight (p=0.263), maternal age (p=0.174), babies' sex (p=0.341) and the baby's HIV status at 18-24 months(Table 3) after controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 counts.

Table3. *Associations between the social and demographic characteristics and baby'sHIV status at 18-24 months*

Independent variables	**HIV status at 18-24 months**		χ^2	***p*-value**	**Odds Ratio**	**95% CI for OR**		***p*-value**
	Negative (n, %)	Positive (n, %)				Lower	upper	
Level of the health facility								0.593
County Referrals	122 (94.6%)	7 (5.4%)			Ref			
County Hospitals/ Mission Hospitals	915(94.4%)	54 (5.6%)	0.063	0.996	1.518	0.328	7.020	0.593
Sub-county hospitals	249 (94.7%)	14 (5.3%)			2.377	0.511	11.049	0.269
Health centers	343 (94.2%)	21 (5.8%)			1.785	0.414	7.701	0.437
County								0.592
Vihiga County (N=106)	94.3% (100)	5.8% (6)	0.583	0.900	Ref			

Independent variables	HIV status at 18-24 months		χ^2	P-value	Odds Ratio	95% CI for OR		P-value
Bungoma County (N=408)	93.9% (383)	6.1% (25)			1.649	0.468	5.808	1.649
Kakamega County (N=394)	94.2% (371)	5.8% (6)			1.494	0.441	5.066	0.519
Busia County (N=817)	94.9% (775)	5.1% (42)			0.995	0.258	3.839	0.994
Maternal Age at enrollment								0.031
>49years	5(100%)	0 (0%)			Ref			
<18 years	18(90%)	2(10%)	5.258	0.262	77888833.27	0.000	-	0.999
18years-25 years	325(96.7%)	11(3.3%)			21637915.58	0.000	-	0.999
25 years-49years	1216 (94%)	78 (6%)			76204025.36	0.000	-	0.999
Not stated	65 (92.9%)	5(7.1%)						
Marital status	Negative (n, %)	Positive (n, %)						0.138
Widowed	87 (93.5%)	6 (6.5%)			Ref			
Co-habiting	28 (90.3%)	3 (9.7%)			2.061	0.371	11.447	0.409
Divorced	60 (96.8%)	2 (3.2%)	**20.147**	**0.003**	1.072	0.169	6.816	0.941
Legally married	1299 (95.1%)	67 (4.9%)			1.249	0.375	4.164	0.717
Separated	11 (73.3%)	4 (26.7%)			**7.517**	**1.344**	**42.031**	**0.022**
Single	85 (89.5%)	10 (10.5%)			1.774	0.399	7.878	0.451
Not stated	59 (93.7%)	4 (6.3%)						
Maternal body weight								
≤60kg	938 (94.2%)	59 (5.8%)	1.254	0.263	Ref			
>60kg	551 (95.5%)	26 (4.5%)			1.167	0.680	2.001	0.576
Not stated	140 (92.1%)	12 (7.9%)						
Sex of the baby								
Female	811 (95.4%)	39 (4.6%)	0.907	0.341	Ref			
Male	703 (94.4%)	42 (5.6%)			0.915	0.550	1.523	0.734
Not stated	115 (88.5%)	15 (11.5%)						
Birth weight of the baby								
<2kg	58 (93.5%)	4 (6.5%)	2.270	0.321	Ref			
2-3.5kg	738 (96.1%)	30(3.9%)			1.529	0.478	4.889	0.474
>3.5kg	314 (94.3%)	19(5.7%)			0.597	0.311	1.146	0.121
Not stated	519 (92.2%)	43 (7.7%)						

Legend: *The table shows the independent categorical variables abstracted from the Ministry of Health registers with regard to the social and demographic characteristics for the mother-baby pairs. The number (n) and proportion (%) of HIV negative and HIV positive status at 18-24 months for different variables are shown. Not stated means there was no documentation in the Ministry of Health registers. The chi-square statistics and the P-value are also shown for each variable. The table also shows the results of the logistic regression analysis. The significance value, Odds Ratio and 95% confidence intervals are also shown for independent variable taking certain reference categories for each variable after controlling for possible confounders such as type of ARV prophylaxes, feeding options and CD4 count. Statistical analysis was determined by χ^2 statistics.County referral hospitals for the level of health facilities, Vihiga county for the County, >49years for maternal age, Widowed women for the marital status,≤ 60kg for maternal weight, females for sex of the baby and <2kg for baby's birth weight were considered as reference groups.Ref=Reference group.*

4. Discussion

4.1. The Social and Demographic Characteristics of HIV Positive Mother-Infant Pair in Vihiga, Kakamega, Bungoma and Busia Counties, Kenya

The MOH HEI register has seven social and demographic characteristics being recorded on a routine basis namely marital status, maternal age, maternal weight, baby sex, baby birth weight, county and level of health facility. Generally, the study revealed approximately 79% of women were legally married, 5% single, 3% widowed, 3% divorced, 2% cohabiting and 1% were separated. These observations were in agreement with a study done at a rural tertiary care hospital in Maharashtra state

of India that showed that 70.53% were married and living with their spouse, 4% unmarried, 2.5% divorced and 2% separated[16]. High number of married persons having HIV and AIDS was also reported amongst attendees in voluntary counseling and testing centers of a medical college hospital in coastal Karnataka in 2012 and among HIV-positive women in 2014 enrolled in HIV care and support service in Amhara region, Ethiopia[17, 18]. Our findings also corroborated with findings that showed that most new HIV infections in sub-Saharan Africa now occur in married and cohabiting couples [18]. Consistent with previous studies carried out elsewhere in Kenya, majority (78.3%) of women HIV-positive were married[19]. However, Kenya Demographic Health Survey for 2014 showed that of the HIV positive women,55% were married, 5.1% cohabiting/living together, and 3.7% widowed[20]. By showing that married women are the majority, it ties in with the general Kenyan population where nearly 2 out of 3 Kenyans aged 15-64 are married or cohabitating[21]. The study findings was also in tandem with results of population-based data from Demographic and Health Surveys (DHS) on heterosexual behavior in Zambia in 2001-02 and in Rwanda in 2005 that revealed that most heterosexual HIV transmission takes place within marriage or cohabitation[8]. This goes on to demonstrate that married women represent the bulk of the HIV infected population amongst the sexually active group in Western region of Kenya. Focusing on HIV prevention and control efforts to this population will be critical in reversing the trend of pediatric HIV and AIDS and also aid in controlling the HIV and AIDS related morbidity and mortality.

However, the findings of the current study were inconsistent with others reported in Mwanza region, Tanzania that demonstrated that HIV infection was associated with being separated or widowed [7]. The study was also at variance with Surveillance of HIV infections among antenatal clinic attendees in Tanzania-2003/2004 that showed HIV prevalence to be higher among single women (9.7%) than married women (8.6%)[22]. It contradicted a study done in Mainland Tanzania in 2011 that showed marital status had no statistically significant association with HIV infection [11]. These contrasting results may reflect the epidemiological shift of the HIV epidemic pattern in Sub-Saharan Africa region from affecting mostly singles, separated, divorced and widowed woman to now predominantly affecting married women/couples who now seem to be at a higher risk of HIV acquisition and transmission. The study further showed that there was a significant association between marital status and baby's HIV status at 18-24 months and that the baby is likely to be HIV positive if the mother was widowed. This concurs with our understanding that, in Western region of Kenya, the practices of widow cleansing and widow inheritance are common and viewed by many as contributing to the rapid spread of HIV in the general population. Widow inheritance is associated with apparent risk for HIV and STI acquisition and transmission since the wife inheritors don't use safer sex practices and the widows tend to have multiple partners for economic support. However, our finding contradict a prospective study in which there was no significant differences between the HIV infected and non-infected infants and mother's marital status among infants of sero-positive mothers[23].Qualitative studies is therefore needed to create a better understanding of the social, cultural and economic patterns and characteristics of the different marital relationships and further determine what could be the key determinants of the mother to child HIV transmission for different marital status beyond the known biological risk factors and whether these substantiate the quantitative results.

We also showed that the mean maternal age was 29.888 years, slightly older than most of the studies reported in the region. This finding contrast with those in Nigeria in which it was shown that HIV-positive mothers were young[16]and in Zambia where the mean age was 26.200 years [10]but compares with a study done in Western Kenya that showed the average age of women in PMTCT program was 29.400years[8]. The study also revealed that approximately 75% of women were aged between 25 and 49 years of age, the standard sexually active and productive age group. This compares favorably with findings from a study done at a rural tertiary care hospital in Maharashtra state of India in which it was demonstrated that 84.77% females were in the age group of 20-39 years[24] and in Mwanza Region, Tanzania that showed that mostly woman aged 15-34 years were HIV infected[7]. Collectively, the findings are a pointer that the bulk of HIV infected women are young adults and they constitute the majority of HIV infected women in Western Kenya. Proven evidence-based interventions targeting this age-group needs to be designed and implemented in an effort to control the HIV epidemic and eliminate Mother-To-Child HIV Transmission by 2015 and beyond.

The study also revealed that there is no association between maternal age and baby's HIV status at 18-24 months (p=0.05) and this agreed with reviewed clinical records of 1088 mother-infant pairs within the Tingo the program in Lilongwe, Malawi that showed no association between HIV transmission and maternal age (p=0.164)[25]. It also concurred with a prospective study that depicted no significant difference between the HIV infected and non-infected infants with the same mean maternal age[25].Though not necessarily a comparable study, it contradicted studies done in Tanzania in 2003/2004 and 2011 and in Gondar, Northwest Ethiopia that revealed that the risk for HIV infection was significantly higher among women aged 25-34 years[11, 13, 21]. The findings also contrasts other observations in rural Northern Tanzania that revealed that the highest HIV prevalence was among women aged between 15-19 years[15].However, the study findings agreed with a prospective study in European countries that showed that maternal age were not a factor in risk of transmission[26].It therefore seems that maternal age may not be a key predictor of the baby's HIV status at 18-24 months despite the fact that majority of the HIV infected women are young adults.

The relationship between the baby's sex and the risk of HIV acquisition from a HIV-infected mother has not been clearly documented. This study showed that 50% of the babies born were females and 43% were males giving a male to female ratio of 0.86:1. This contrasted with study done in 2012 in Nigeria among HIV positive children that showed 52.7% males and 47.3% females giving a male to female ratio of 1:0.9[27]. However, these findings may not be conclusive due to ascertainment bias when recording the sex of the baby in the MOH HEI registers. In addition, the missing data was about 7% for the entry on sex of the baby in the registers compromising conclusion on some of the infant population. The study also showed that the baby's sex had no association with baby's HIV status at 18-24 months consistent with earlier reports[26]. However, this differed with other observations that revealed significantly more girls (12.6%) than boys (6.3%) were infected with HIV and at 6 to 8 weeks more girls acquired HIV (10.0%), compared with boys (7.4%)[13].In Kenya a study demonstrated that female sex are associated with HIV-1-specific CD8+ T-cell responses in HIV-1-exposed and that female infants were also more likely to have positive Elispot assays than male infants (p = 0.046)[9]. Taken together, these data demonstrate that there could be a likelihood link between baby's female sex and risk of HIV acquisition but more studies need to be done to determine the association between baby's sex and HIV status at 18-24 months born to HIV infected women in an African context.

We further revealed that approximately 44% of babies weighed between 2.0 -3.5kgs at birth. This is not surprising given that a previous study done in Nigeria in 2012 among HIV positive children showed that 40% of children's populations under the study weighed between 2.5 and 2.9kg at birth[27].We additionally demonstrated that baby's birth weight had no association with baby's HIV status at 18-24 months. This contradicted findings from a prospective study in Europein which it was shown that low birth weight had the strongest association with vertical transmission of HIV[26].Given that there was a huge missing data for birth weight(about 33%) and the fact that the different health facilities were using different weighing scales, more studies still needs to be done to ascertain if an association exists between the birth weights and the baby's HIV status at 18-24 months.

5. MTCT Rate at 18-24 Months by Marital Status

The MTCT rate at 18-24 months showed variations with marital status. To our knowledge, this is the first epidemiological investigation of the association between HIV transmission from mother to child and the mothers' marital status. The MTCT rates at 18-24 months were highest amongst women in separated (26.7%), single (10.5%) and cohabiting (9.7%), widowed (6.5%) relationships and lowest amongst divorced (3.2%) and legally married (4.9%) women. However, this conflicts with a closely related study carried out in Nigeria that showed that HIV prevalence of divorced women were more than double those currently married/cohabiting with a sexual partner; and more than three times those that were never married [28].The current study showed that separated women are at approximately 5 times more likely to have HIV negative babies at 18-24 months post-delivery relative to widowed women (p=0.029).This probably could be due to the fact that becoming widowed is strongly associated with HIV positive status in this part of the country and HIV positive widowed women are likely to have had their spouses' die of HIV and AIDS. We hold the view that HIV among majority of widows is a result of infections acquired while in marital unions rather than as widows. The social neglect, cultural and sexual malpractices and high poverty levels could be contributing to their likelihood to have HIV positive baby at 18-24 months due to social, cultural and economic barriers.

However, no comparable studies exist in the literatures reviewed and therefore more studies with stronger designs need to be carried out to ascertain the association between marital status and risk of mother to child HIV transmission at 18-24 months and beyond. HIV counseling and testing services should reinforce efforts to provide widows with support and knowledge needed to make safe choices. Increasing financial independence through employment opportunities, income generating activities should be considered.

The greatest strength of this study is that it is 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.

6. Conclusion

We found that most HIV positive mothers were legally married and fewer were in single, widowed, separated, divorced and cohabiting unions. Maternal age, maternal weight, baby's sex, baby's birth weight, county and level of health facilitywere not predictors of baby's HIV status at 18-24 months. The study also revealedthat separated women were about 5 times more likely to have HIV negative babies at 18-24 months as opposed to widowed women. HIV prevention and control efforts needs to focus on widowed women since they seem to have higher rates of MTCT rates at 18-24 months, if we are to reverse the new pediatric HIV infections and attain the eMTCT goals by 2015 and beyond.

6.1. Competing Interests

The authors declare that they have no financial or personal relationship (s) that may have in appropriately influenced them in writing this article.

6.2. Authors Contributions

MPO, JHO, MM and CO conceptualized, designed, conducted the study, analyzed and wrote the report and the manuscript.

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Dr. Omondi is a medical doctor with over 12years' experience inpublic health, reproductive health and HIV in both development and humanitarian settings in various governmental and non-governmental organizations, including the UN. His experience includes work in Kenya, East Africa, the Great Lakes and Horn of Africa as a public health specialist and clinician and also asa lecturer in Kenyatta University and Mount Kenya University in Kenya. He has vast experience in clinical practice,programme planning, management, monitoring and evaluation and conducting research. He is experienced in working with the Ministries of Health, non-governmental organizations in the sub-Saharan Africa.Dr Omondi holds a Bachelor's degree in Medicine and Surgery (Moi University, Kenya), Master of Public Health (Nairobi University, Kenya) and Master of Business Administration (Jomo Kenyatta University of Agriculture and Technology, Kenya) and doctor in Philosophy in Epidemiology (Maseno University, Kenya).He serves as an active member of the Kenya Medical Association–Nairobi Division in the Reproductive Health and HIV Committee.

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I have had 40 years of University teaching and lecturing. During this period I have worked, visited, and did research in several institutions in the United Kingdom, Europe, the United States, Canada and Africa.My research area has basically been in Pharmacokinetics, Drug Delivery Systems and Public Health with a Drug bias. Liposomal drug Delivery is currently the major focus of my research in clinical settings.Drug use, abuse, addiction, tolerance and compliance is also an area we are exploring keenly looking at socio-economic and cultural implications. We have a large team of collaborators with different backgrounds and experiences in various Universities and research institutions.