THE IMPACT OF INTERVENTIONS TO PREVENT MOTHER TO CHILD TRANSMISSION OF HIV AT KENYATTA NATIONAL HOSPITAL.

DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS AND GYNAECOLOGY, AT THE UNIVERSITY OF NAIROBI.

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DEDICATION

To my dear son Kevin Mugo who gives me the inspiration to work!

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DECLARATION

This is to certify that this research work was managed under the supervision of senior members of staff of the department of Obstetrics and Gynaecology, University of Nairobi.

The work submitted in this book is original and has never been presented for a degree for membership in any other university.

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DECLARATION

I declare that this research work for the dissertation in part fulfillment of the Masters of Medicine degree in Obstetrics and Gynaecology is my original work and, to the best of my knowledge, has not been presented to any university forum.

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ABBREVIATIONS

AIDS	=	Acquired Immunodefiency Syndrome
ANC	=	Antenatal Clinic
ARVs	=	Antiretroviral drugs
ART	=	Antiretroviral Therapy
AZT	=	Azidothymidine (Zidovudine)
C.C.C	=	Comprehensive Care Center
C/S	=	Caesarean Section
CDC	=	Centre for Disease Control
CD4	=	Strictly, refers to all cells bearing the CD4 receptor (including Langerhan cells and dendritic cells). In the context of this study, it was used to refer to CD4+ T lymphocytes.
D4T	=	Stavudine
DNA	=	Deoxyribonucleic Acid
ECS	=	Elective Caesarean Section
HAART	=	Highly Active Antiretroviral Therapy
HIV	=	Human Immunodeficiency Virus
KEMRI	=	Kenya Medical Research Institute
KNH	=	Kenyatta National Hospital
MTCT	=	Mother to Child Transmission
NEV	=	Nevirapine
PCR	=	Polymerase Chain Reaction
PEPFAR	=	President's Emergency Plan for HIV/AIDS Relief
PLWHA	=	People Living With HIV/AIDS
PMTCT	=	Prevention of Mother to Child Transmission
RNA	=	Ribonucleic acid
STIs	=	Sexually Transmitted Infections
SPSS	=	Statistical Package for Social Sciences
3TC	=	Lamivudine
UNAIDS	=	United Nations Program on HIV/AIDS
WHO	=	World Health Organization

ABSTRACT

The study aimed to establish the impact of the various interventions used for Prevention of Mother to Child Transmission (PMTCT) of Human Immunodeficiency Virus (HIV) infection at Kenyatta National Hospital (KNH), a national referral and teaching hospital in Nairobi, Kenya.

RESEARCH QUESTION: What effect has provision of Antiretroviral drugs (ARVs), mode of delivery and mode of infant feeding had on the Mother to Child Transmission (MTCT) of HIV infection at KNH?

OBJECTIVES

- To describe the social and demographic characteristics of mothers on PMTCT program.
- To determine the prevalence of HIV infection in infants of HIV positive mothers on PMTCT program at KNH.
- To determine the correlation between maternal CD4 cell count and transmission of HIV to the infant.
- To determine the correlation between ARV regime used, mode of delivery and infant feeding option and the risk of transmission of HIV infection to the infant.

STUDY DESIGN: This was a cross-sectional study.

SETTING: The study was conducted in clinic 18(the postnatal clinic) of Kenyatta National Hospital, Nairobi.

STUDY POPULATION: HIV positive mothers and their infants attending high risk postnatal clinic at KNH.

SAMPLE SIZE: 207 mother-infant pairs.

DATA COLLECTION AND ANALYSIS: Mothers' bio-data, CD4 cell count, ARV regime used ,mode of delivery, mode of infant feeding and infants PCR results were entered in the data collection form (appendix II) and analyzed using the SPSS computer package.

PRIMARY OUTCOME MEASURE: Detection of HIV infection, at age 6 weeks, in infants born to mothers in the PMTCT program at KNH.

ETHICAL CONSIDERATION: Mothers were informed of the study procedure and assured of their confidentiality. Only those who consented participated in the study. Those who declined were offered equal treatment. Ethical approval to conduct the study was sought from the Ethics and Research committee of Kenyatta National Hospital.

RESULTS: Majority of the mothers attending the high risk postnatal clinic were 25 to 34 years old (74.9%) while 59.4% had attained at least secondary level of education. The overall Mother to Child Transmission rate at six weeks of age was 2.4%. Fifty per cent of the mothers had a CD4 cell count of more than 500 cell/ml while 21% had CD4 cell count of below 200 cells/ml. Mothers with CD4 cell count of below 200 were likely to transmit HIV infection to their infants, p=0.04. Zidovudine was the most commonly used ARV regime (58.5%). Others used triple therapy (29.5%), Nevirapine only (10.6%) and PEP (1.4%). There was no significant association between the ARV regime used and PCR status of the infant, p=0.804. Most infants (95.2%) were born at term, 72.5% were born through elective caesarean section and weighed more than 2500 grams (94.2%). Seventy per cent of the infants were put on formula feeding while 28% were exclusively breastfed. There was no significant association between the mode of feeding and the likelihood of transmitting HIV infection from the mother to her infant, p=0.269.

CONCLUSIONS: The reported MTCT rate without any interventions ranges between 20 and 45% in breastfeeding populations. The study showed an MTCT rate of 2.4%. Thus, PMTCT interventions particularly antiretroviral drugs were shown to be significantly associated with lower MTCT of HIV infection at KNH.

RECOMMENDATIONS: PMTCT services should be promoted and provided to all HIV infected pregnant mothers. Mothers with low CD4 cell count should be offered HAART for treatment of their HIV infection which also lowers vertical transmission of HIV. A larger study following up the infants until after cessation of breastfeeding is needed in order to assess the effect of breastfeeding on MTCT.

INTRODUCTION

Mother to child transmission (MTCT) is one of the main routes of HIV transmission. By the end of the year 2006, approximately 39.5 million people were infected with HIV worldwide, 2/3 of who were in sub-Saharan Africa. Two and a half million children <15 years of age are living with HIV/AIDS. The number of children orphaned by HIV/AIDS approaches 13.2 million. Over 80% of the cases of AIDs in women occur in women of reproductive age, making heterosexual and perinatal transmission of HIV important concerns [1].

According to the Kenya Demographic and Health Survey (KDHS) 2003 [2], the number of People Living with HIV/AIDS (PLWHA) were estimated at 1.1m adults between 15-49years, 60,000 adults above the age 50 years and approximately 100,000 children below the age of 15 years. More than 90% of these children had acquired the disease from their mothers.

HIV may be acquired through sexual contact which accounts for more than 70% of all the transmissions [3], parenteral exposure to blood or bodily fluids or from an infected woman to her foetus or infant (MTCT). Without any intervention the risk of MTCT is 15-30% in non-breastfeeding populations and 20-45% in breastfeeding populations [4]. MTCT occurs most commonly in the perinatal period [5].

Strategies to reduce MTCT include prevention of unintended pregnancies among HIV infected women, application of safe obstetric practices during delivery, safe feeding practices and use of antiretroviral drugs. The rate of MTCT is about 1% in women who are receiving combination antiretroviral therapy for their HIV infection [3, 5, 6 and 7].

Table 1: ARV regimes used with the respective effectiveness.

REGIME (References)	ANC PERIOD	INTRAPARTUM	POSTPARTUM	INFANT	% MTCT REDUCTION
HAART (7)	Triple Therapy*	Triple Therapy	Triple Therapy	AZT 4mg/kg twice daily for 1 week	Up to 90%
LONG COURSE AZT(8)	AZT 300mg starting anytime between 14-34 weeks	I.V AZT 2mg/kgin first hr of labour I.V 1mg/kg of AZT every 3hrs until delivery		AZT 2mg/kg given four times per day for 6 weeks	67%
SHORT COURSE AZT(9)	AZT 300mg twice daily from 34-36 weeks until onset of labour	AZT 300mg every 3hrs from onset of labour until delivery		AZT 4mg/kg Twice daily for 4 weeks	50%
PETRA "A"(10)	AZT 300mg twice daily + 3TC 150mg from 36 weeks	AZT 300mg every 3 hrs +3TC 150mg every 12hrs	AZT 300mg bid for 1 week	AZT 4mg/kg twice daily +3TC for 1 week	50%
HIV NET 012(11)		Nev 200 mg at onset of labour		Nev 2mg/kg Within 72hrs of birth	47%
PEP** (12)				Nev 2mg/kg stat AZT 4mg/kgfor 1 week	47%

*Triple therapy refers to a combination of three drugs either for treatment or for PMTCT prophylaxis. The recommended first line combination in pregnancy is AZT+3TC+NVP.

** PEP means post exposure prophylaxis

Table 2: ARV protocols used for PMTCT at KNH

REGIME	ANC PERIOD	INTRAPARTUM	POSTPARTUM	INFANT
HIV NET 012		Nev200mg at onset of labour		Nev 2mg/kg within 72hrs of birth
SHORT COURSE AZT	AZT 300mg twice daily from 34-36weeks until onset of labour	Nev 200mg at onset of labour+ AZT 600mg stat		Nev 2mg/kg within 72hrs AZT 4mg/kg twice daily for 1 week
LONG COURSE AZT	AZT 300mg twice daily from 28 weeks until onset of labour	Nev 200mg + AZT 600mg stat at the onset of labour		Nev 2mg/kg within 72hrs + AZT 4mg/kg twice daily for 1 week
POST EXPOSURE PROPHYLAXIS OF PMTCT				Nev 2mg/kg within 72hrs of birth+ AZT 4mg/kg twice daily for 1 week
HAART	Triple Therapy	Triple Therapy	Triple Therapy	Nev 2mg/kg within 72hrs of birth + AZT 4mg/kg twice daily for 1 week or for 4 weeks if the mother received ART for less than 4 weeks prior to delivery.

LITERATURE REVIEW

Mother to child transmission (MTCT) is the predominant source of HIV infection in young children. In the absence of preventive interventions, the probability that an HIV- positive woman's baby will become infected is approximately 25% to 45% [4].WHO recommends the 4 pronged approach to PMTCT that includes primary prevention of HIV, prevention of unintended pregnancies in HIV infected women, PMTCT and care and support of HIV infected women, infants and their families [18]. The complete PMTCT package includes comprehensive antenatal care, modified obstetric practices, antiretroviral therapy and infant feeding counselling and support ad linkage for care and treatment. HIV transmission from infected mother to child is mainly prevented by antiretroviral drugs (ARV) prophylaxis to the mother and baby, replacement feeding and elective caesarean section. MTCT rate of less than 2% have been reported from countries where ARV prophylaxis, caesarean section and replacement feeding is practiced [6, 7].

The first major breakthrough in the prevention of MTCT came in 1994 with the three-part Paediatric AIDS Clinical Trials Group (PACTG) 076 trial, which demonstrated that long-course Zidovudine (AZT) prophylaxis given early in pregnancy and

intravenously during delivery to the mother and for six weeks to the infant dramatically reduced the risk of vertical transmission from 25% to 8%[8]. This regimen was adopted by countries in Europe and North America. Although effective, the PACTG 076 regime was too costly and complex for many parts of the world where there is high prevalence of HIV. This necessitated the need for studies to evaluate cheaper, shorter, simpler yet effective regimes. A lot of studies have been undertaken in many low and medium economy countries to evaluate these cost-effective regimes.

A study done in Thailand to investigate safety and efficacy of short-course oral Zidovudine administered during late pregnancy and labour, showed the estimated transmission risks to be 9.4% on Zidovudine and 18.9% on placebo. In this study all the babies were formula fed. The authors concluded that a short course of twice daily oral Zidovudine was safe and well tolerated and, in the absence of breastfeeding, can lessen the risk for mother to child transmission by half (that is 50% reduction in MTCT)[9].

A similar study was done in West Africa with the aim of assessing the safety and efficacy of short course perinatal oral Zidovudine in reducing MTCT in breast feeding population. Mothers were assigned to either Zidovudine or placebo. All

babies were breastfed. At age 3 months, the transmission rate was 26.1% in the placebo and 16.5% in the Zidovudine arm. This represented a 37% reduction in MTCT of HIV [13].

Thus, even in breastfeeding populations there was significant efficacy of short course perinatal Zidovudine. Maternal CD4 count cell was found to have a correlation in transmission of HIV from a HIV positive mother to her infant. Another study done in West Africa to assess the efficacy of short course Zidovudine to prevent MTCT in breastfeeding population showed a 59% reduction in MTCT. The result was realized in the Zidovudine arm but only in those mothers whose CD4 cell count was equal to or above 500 cells/ml. Among children born to women with CD4 cell counts less than 500 cells/ml, the risk of MTCT was similar in placebo and Zidovudine arms[14].

Though the above short course Zidovudine regimes showed reduction in MTCT, there was need to assess the optimal duration of Zidovudine administration to prevent perinatal MTCT. Lallemant et al conducted a randomized trial of Zidovudine starting in the mother at 28 weeks' gestation, with 6 weeks of treatment in the infant(the long-long regime) and Zidovudine starting at 35 weeks' gestation, with 3 days of treatment in the infant(short-short regime).The rate of in utero transmission was significantly higher in regimens with a short

maternal treatment (5.1%) than with the regimens with long maternal treatment (1.6%). Thus, longer maternal treatment duration resulted in lower transmission rates [15].The WHO recommends starting AZT at 28 weeks' gestation [18].

However, WHO also recommends an intrapartum and postpartum component of both Zidovudine and Lamivudine [18]. The Petra Study was a randomized, double-blind, placebo-controlled trial aimed at evaluating the efficacy of short course regimens of Zidovudine and Lamivudine in preventing early and late transmission of HIV-1in a predominantly breastfeeding population. This study revealed a remarkable reduction in transmission rates at 6 weeks in infants whose mothers were put on Zidovudine and Lamivudine during prenatal, intrapartum and postpartum periods. However, this benefit was significantly reduced at 18 months ostensibly because of breastfeeding. Although short-course regimens are effective in reducing HIV-1 transmission, there is need for incorporation of interventions to minimise the risk through breastfeeding [10].

Use of Zidovudine for PMTCT was an eye opener in efforts to reduce MTCT.The economic situation in most of HIV endemic areas called for a search of simpler and cost-effective regimes. Moreover, antenatal services in these countries are not very

elaborate. One such study that came to the rescue of resource constrained countries was the HIV NET 012 study. This study sought to compare the efficacy of a short course of Nevirapine and efficacy of Zidovudine for PMTCT. The primary objective of this study was to determine the rate of HIV-1 infection in infants in each arm of the study. This landmark study found that a short intrapartum/ neonatal regimen of Nevirapine given to the mother at the onset of labour and to the infant within 72 hours of life reduced the risk of perinatal HIV among breast feeding women by 47% at 14-16 weeks and by 42% at 18 months compared to a short intrapartum/ neonatal regimen of AZT [11]. This regimen has been adopted as the standard care in many resource-limited countries and was endorsed by UNAIDS and many other international health organizations [1].

The PETRA study findings were corroborated by the South African Intrapartum Nevirapine Trial (SAINT) study. In this study, mothers were randomized to either nevirapine during labour and post delivery or to AZT/3TC during labour and for one week post delivery. In both treatment arms, about 40% of infants were breast fed. Eight weeks after birth, there was no significant difference observed between the rate of HIV infection or death across the two treatment arms, with a rate of 14.3% in the simpler nevirapine arm and 12.5% in the more

involving and expensive dual therapy arm[16]. This added credence to the use of single dose nevirapine as a minimum standard of care for HIV infected women [18].

Leroy et al did a study to compare the efficacy of different antiretroviral regimens in reducing the risk of 6-week MTCT rate in African breastfeeding populations. Mothers were assigned to different regimes or placebo. These regimes were derived from findings of the various clinical trials undertaken in the continent. Only the longest regimen of ZDV+3TC was significantly more effective than single dose NVP and short-course ZDV [17]. Thus, where resources permit, combination regimes are more effective in reducing risk of MTCT of HIV.

The WHO HIV/AIDS department revised recommendations to provide improved interventions for PMTCT are [18]:

- Intrapartum single dose Nevirapine for MTCT programmes is only the minimum standard of care for pregnant women living with HIV and that instead combination regimes of AZT and Nevirapine are more effective than a single dose Nevirapine regimen for both breast feeding and non breast feeding populations.

- Combination of AZT and 3TC at tail end (postpartum) should be used to reduce the potential resistance to Nevirapine.
- The criteria for commencing pregnant women on ARV treatment: Recommend that all mothers in stage 3 without CD4 cell count or stage 3 with CD4 count <350cells/ml and those in stage 4 should be initiated on ARVS.

Many workers have compared the efficacy of single agent regimens against combinations of two or more agents. Triple therapy or HAART when combined with elective caesarean section and avoidance of breastfeeding can reduce risk of MTCT to as low as <2% [6, 7]. During the 2006 PEPFAR Implementers' meeting held in Durban, South Africa, Dr Mbori-Ngacha, Chief of PMTCT section of CDC in Kenya, presented a table (table 3) showing sequential improvements that have been made in the regimens over the past several years [19].

Table 3 showing MTCT rates in respect to various regimens.

No Intervention	22%
AZT monotherapy	13%
Single dose Nevirapine	12%
Short course AZT+3TC	9.3%

Short course AZT+ sd. Nevirapine	6.5%
Short course AZT+3TC+sd.NVP	4.7%
Triple ART	<1%

Use of HAART is common in the developed countries. However, with the excellent results that studies on HAART for PMTCT have shown, combination therapy is the way forward. In the AmRo study done in the Netherlands, Boer K et al assessed the efficacy of HAART in PMTCT of HIV. All mothers were put on HAART. Elective caesarean delivery was planned at 38-39 weeks for those whose viral load was > 500 copies /ml otherwise those with viral load < 500 copies/ml were scheduled for vaginal delivery. MTCT was 0% in both treatment arms [7].

The mechanism by which triple therapy works is by suppression of maternal viraemia. Perinatal transmission of HIV is low in women who receive ARVs during pregnancy, have low viral loads, high CD4 counts and delivers via an elective caesarean section. Shapiro et al followed up 1202 women with HIV RNA viral loads <1000 copies/ml. Transmission rate was 1% in the group receiving antiretroviral treatment compared with 9.8% for untreated mothers. Transmission was lower with antiretroviral therapy, caesarean section, greater birth weight and higher CD4 cell count. They

concluded that perinatal HIV-1 transmission occurs in only 1% of treated women with viral loads <1000 copies/ml and may be almost eliminated with antiretroviral prophylaxis [6].

Combination regimens work best with avoidance of breastfeeding. A study done in Uganda evaluated the impact of different modalities of infant feeding on HIV transmission in children. Participants were offered short course ARV regimes and formula feeding provided free of charge for women who choose not to breast feed. HIV status was assessed at 6 weeks and at 6 months. The Exclusive Breast Feeding (EBF) and Mixed Feeding (MF) groups were associated with a significantly higher risk of HIV transmission than the Exclusive Formula Feeding (EFF) group [20].

The above findings are supported by the results of The Mashi Study. Lockman et al did a study to compare the efficacy and safety of two infant feeding strategies (breastfeeding for 6 months plus Zidovudine compared to formula feeding plus Zidovudine) for prevention of postnatal mother to child transmission of HIV. They concluded that HIV transmission was lower in the formula fed group [21].

Studies done locally have showed a significant risk of transmission of HIV through breast milk. In their study, Nduati et al found the frequency of transmission of HIV-1 at 24 months that could be attributed to breast milk to be 16.2%. Majority of these infections occurred early during breast feeding. The use of breast milk substitutes prevented 44% of infant infections and was associated with significantly improved HIV-1 free survival [22]. WHO recommends replacement feeding if this is acceptable, feasible, affordable, sustainable and safe.

Even though exclusive formula feeding is associated with higher reduction in MTCT, many populations in Africa cannot always afford formula feeds. For the breast feeding populations, the choice of ARV regimen may determine the risk of peripartum transmission of HIV. Kiarie et al did a study to compare the effect of perinatal regimens of short course Nevirapine and Zidovudine on breast milk viral shedding and perinatal transmission during the first 6 weeks postpartum. At 6 weeks, the HIV-1 perinatal transmission rate was significantly lower among those who took Nevirapine than Zidovudine (6.8% vs 30.3%). They concluded that compared to a peripartum Zidovudine regimen, Nevirapine was significantly more likely to decrease HIV-1 RNA in breast milk during the first week and through the third postpartum week. Sustained

breast milk HIV-1 suppression may contribute to the ability of Nevirapine to decrease perinatal transmission of HIV-1 [23].

Another hindrance to effective PMTCT strategies especially in the developing world is poor access to health services. It means that a number of pregnant women are delivering at home or only comes to hospital to deliver. For the HIV infected pregnant mothers who present late in labour or after delivery, routine testing is done postpartum. In this regard, studies have been done to evaluate the effectiveness of post exposure prophylaxis for PMTCT. A study done in Malawi showed a MTCT of 15.3% at 6-8 weeks in babies who received nevirapine and Zidovudine and 20.9% MTCT in babies who received Nevirapine only. The authors concluded that post exposure prophylaxis can offer protection against HIV infection to babies of women who missed opportunities to be counselled and tested before or during pregnancy. The nevirapine and Zidovudine regimen is safe and easy to implement [12].

Gray et al compared the efficacy of Single dose nevirapine given to the infant soon after delivery with Zidovudine given to the baby for 6 weeks. Interestingly, postexposure prophylaxis using a single dose of nevirapine was found to be more effective than a 6 weeks course of Zidovudine for reducing MTCT. The MTCT rate at 12 weeks in the group that was

given nevirapine was 7.9% compared with an MTCT rate of 13.1% in the group that used Zidovudine for 6 weeks [24].

The mode of delivery may have an impact on MTCT of HIV infection. Initial studies showed that mothers who were delivered by elective caesarean section before onset of labour or rupture of membranes had a lower transmission rate than those who were delivered vaginally. Elective caesarean delivery is also beneficial in mothers with high viral loads and low CD4 cell counts [6, 7]. Caesarean section decreases the risk of intrapartum transmission of HIV by decreasing transplacental haemorrhage during labour and reducing the length of exposure of baby to vagino-cervical secretions.

A meta-analysis of 15 cohort studies done in Europe and North America showed a 50% reduction of vertical transmission of HIV with elective caesarean section as compared to other modes of delivery. The likelihood of transmission was reduced by approximately 87% with both elective caesarean section and receipt of antiretroviral therapy during the prenatal, intrapartum and neonatal periods, as compared with other modes of delivery and the absence of therapy. Among the mother-infant pairs receiving antiretroviral therapy during the prenatal, intrapartum, and neonatal periods, rates of vertical transmission were 2%

among those who underwent elective caesarean section and 7.3% in those with other modes of delivery [25].

Mandelbrot et al sought to ascertain the interaction between Zidovudine prophylaxis and mode of delivery. In their study, they found no association between the mode of delivery and transmission risk in the mothers who were not put on Zidovudine prophylaxis. However, in the mothers who were given Zidovudine prophylaxis, there was a significant reduction in transmission rate in those who were delivered by elective caesarean section than in those who were delivered by either emergent caesarean section or vaginal delivery [26].

Caesarean deliveries are associated with a five fold increase of morbidity compared to vaginal deliveries. Read et al carried out a review of articles on clinical trials on the efficacy (reducing MTCT of HIV) and safety of elective caesarean section. The authors concluded that elective caesarean section is an efficacious intervention for prevention of MTCT in HIV infected women not taking ARVs or only on Zidovudine. However, the risk of postpartum morbidity was found to be higher with elective caesarean section than that associated with vaginal delivery. The authors also noted that the risk of MTCT according to mode of delivery among HIV infected mothers with low viral loads is unclear. They recommended a large

randomized trial to assess the effectiveness of elective caesarean section in mothers with undetectable viral loads [27].

Although operative delivery is associated with risks, it is important to quantify their incidence and severity. There were few complications and no serious adverse events after elective procedures among HIV infected women in a large European trial [28]. In this study, an even lower vertical transmission risk of HIV was noted in mothers assigned to undergo elective caesarean section.

Elsewhere, Shah did a randomized trial comparing elective caesarean and vaginal delivery in mothers who are put on antiretroviral therapy and abstain from breast feeding their infants. He concluded that elective caesarean section and vaginal delivery are as effective as each other for prevention of HIV when added with antiretroviral therapy and no breastfeeding [29].

The above studies shows that use of ARVs for PMTCT significantly reduces the rate of MTCT to a varying degree. Use of ARVs should be accompanied by application of safe obstetric practices like minimizing unnecessary vaginal examinations during labour. Mode of delivery should be

individualised based on receipt of antiretroviral drugs and viral loads. Mothers who miss ARVs, gets poor prenatal care, have high viral loads may benefit from elective caesarean section. Avoidance of breastfeeding confers a reduction in MTCT. Studies are on going to evaluate the effect of HAART in lowering MTCT of through breast milk. Giving antiretroviral drugs to infants whose mothers missed ARVs is an effective strategy to prevent mother to child transmission of HIV.

STUDY JUSTIFICATION

Ten per cent of AIDS cases in Kenya are children below 5 years of age. Over 90% of HIV infection in children is due to perinatal HIV transmission. The Ministry of Health in collaboration with donor agencies have put in place programs for PMTCT at referral, provincial, district and mission hospitals. At KNH, PMTCT program was started in the year 1998. Since then, there have been programs for following up progress of PMTCT. The MTCT rates range from below 1% when combination therapy is used [6, 7] to more than 20% when no intervention is instituted [4]. Information on MTCT pattern at the institution is limited. This study is therefore aimed at determining the effect of the various interventions that are employed for PMTCT at KNH. The results realized by the study will shed light on gains so far in PMTCT at the institution. These results will also inform KNH, the Ministry of Health and other stakeholders when formulating cost effective strategies for PMTCT.

RESEARCH QUESTION

What effect has provision of ARVs, mode of delivery and mode of feeding had on the MTCT of HIV at KNH?

STUDY OBJECTIVES

Main objective:

The study aimed at determining the effect of various interventions in prevention of mother to child transmission of HIV infection at KNH.

Specific objectives:

1. To describe social and demographic characteristics of HIV positive mothers on PMTCT program.
2. To determine the prevalence of HIV infection in infants of HIV positive mothers on PMTCT program at KNH.
3. To determine the correlation between maternal CD4 cell count levels and the risk of transmission of HIV to the infant.
4. To determine the correlation between the ARV regime, mode of delivery, infant feeding option and the risk of transmission of HIV infection.

METHODOLOGY

Study design

This was a hospital based cross-sectional study in which the impact of PMTCT interventions was evaluated.

Study population

This comprised of HIV positive mothers and their infants attending high risk postnatal clinic, who met the inclusion criteria.

Study setting

The study was conducted at clinic 18 (the postnatal clinic) of Kenyatta National Hospital (KNH). KNH is a 2000 bed tertiary care facility and a national referral and teaching hospital. The obstetric unit is responsible for about 8000 deliveries per year. The Obstetrics department runs its antenatal, post natal and gynaecology clinics at clinic 18. The clinics are run by consultants, senior registrars and registrars with the help of the nursing staff. The post natal clinic is held on Friday mornings. All mothers who deliver at the institution are booked for follow up at the post natal clinic. The post natal clinic is run by three senior house officers. This clinic is divided into two sections. Mothers who are HIV negative attend the regular postnatal follow-up while HIV positive mothers are followed up at the high risk postnatal clinic.

The high risk postnatal clinic is run by two registrars who include a resident Obstetrician and a resident Paediatrician.

Other personnel involved in running the high risk clinic include a nurse trained in PMTCT and a laboratory technician.

About 20 to 30 mothers and their infants attend the high risk clinic every week. Mothers and their infants are followed up in this clinic up to six months after which they are discharged to be followed up in the Comprehensive Care Centre (C.C.C). The first visit is at 2 weeks then at 6, 10 and 14 weeks. The mother and her infant are subsequently seen once per month until 6 months when they are discharged through C.C.C.

The mother is first seen by the obstetrician. The obstetrician seeks to attend to any puerperal complications that the mother may have. Counselling on her hygiene, nutrition, breast care, resumption of sexual and physical activities as well as contraception is done. The postnatal visit presents a good opportunity for the obstetrician to review what ARVs the mother might be on and to re-emphasize on adherence. Appropriate investigations e.g CD4 cell count, total blood count, liver function tests and renal function tests are ordered where applicable.

After the review by the obstetrician, the mother is referred to the Paediatrician who reviews the infant. The paediatrician enquires about the ARVs that the baby was put on and whether this was adhered to. The paediatrician also seeks to enquire about infant feeding and whether there is any deviation to the mode of feeding adopted. Those who are formula feeding their babies are

counselled and reminded to ensure best feeding practices. All HIV exposed infants are put on Cotrimoxazole from 6 weeks of age until proven HIV negative by way of PCR testing. Those who require supplements like Multivitamins are put on them.

Having been attended to by the Paediatrician, the mother and her infant are then referred to the PMTCT nurse. The nurse doubles up as the records clerk for PMTCT program. The nurse is responsible for recording all the details of the mothers and infants attending the high risk clinic. Infants who have attained the age of 6 weeks are eligible for the PCR testing for HIV. The nurse takes the mother through pre and post test counselling before the infants blood is withdrawn for PCR testing.

Infants who are aged 6 weeks are then referred to the laboratory technician who withdraws the infants blood, processes it into a dried blood sample then sends the sample to the KEMRI laboratories where the PCR testing is carried out. The results of the PCR test are availed to the mother after about one month. While conveying the PCR results, the nurse takes the mothers through post test counselling explaining the implications of the PCR results. After PCR testing, the babies and their mothers are seen once per month until they are aged 6 months after which they are discharged from the high risk clinic to be followed up at the C.C.C.

SAMPLE SIZE AND SAMPLING METHOD

Sample size

The sample size was determined using the following formula:

$$n = \frac{4*(Zcrit)^2 *P(1-P)}{D^2}$$

Where:

n =required sample size

P = the average rate of MTCT after putting mothers on ARVS. The 2001 recommendation by UNAIDS assumes default MTCT rate of 32% without any interventions [32].The average reduction rate of most ARV regimes is 50%. Thus, the average rate of MTCT after ARVs is 16%.

D = the precision of the study set at 0.1

Zcrit = this is the cut off points along the x-axis of the standard normal probability distribution that represents probabilities matching the 95% confidence interval (1.96).

Substituting the values above, we get:

n= 206.5244

n=207

A sample size of 207 mother-child pairs was required.

Sampling Method

All mothers attending high risk postnatal clinic, who met the inclusion criteria and gave consent to participate in the study, were recruited and enrolled sequentially until the sample size was attained.

Every week, about 20 to 30 mothers attended the high risk postnatal clinic. However, not all mothers and their infants were eligible for recruitment into the study. This is because some mothers were attending the clinic before 6 weeks while others may have been recruited in previous visits. Thus, only about a third had their infants' PCR results ready.

Inclusion and exclusion criteria

a) Inclusion criteria:

1. HIV positive mothers and their infants attending postnatal clinic at 6 weeks or beyond.
2. Infants whose PCR test results were availed
3. Patients who consented to the study.

b) Exclusion criteria:

Patients whose vital records including ARV regime used, CD4 count levels, mode of delivery and infant feeding option could not be authenticated.

Recruitment of research assistants

Data collection was done by the investigator with the help of two nurses trained on PMTCT. The principal investigator explained to the assistants the objectives of the study, discussed how to obtain and record patient details in the data collection form and how to maintain patient confidentiality. The training of the assistants was done one week before the commencement of the study.

The training of the research assistants was carried out in the postnatal clinic where the investigator demonstrated the patient flow. The assistants were shown where to position themselves when interviewing the patients.

Pre-testing of data collection tools

To ensure that the requisite information for the study was duly obtained, the data collection form was pre-tested one week prior to the start of the actual data collection. The pre-testing of the data collection forms was done during one of the postnatal clinics at clinic 18 (data collection site). The investigator and his two assistants did the pre-testing of the data collection tools. Five data collection forms were used for pre-testing. The pre-testing entailed getting the consent from the participants, interviewing them, going through the patients' files and antenatal cards to confirm that all the information will be sourced from these tools. The information obtained from the pre-

testing was used to modify the data collection form to ensure that all details will be obtained. The pre-tested forms were not included in the actual data collection.

DATA COLLECTION

Data was collected from November 2007 to August 2008.

Data collection was done by the principal investigator with the help of two nurses. All patients attending the high risk postnatal clinic were evaluated for eligibility and upon meeting the inclusion criteria were recruited into the study.

During the period of study, the investigator and/or his trained assistants were at the clinic every week. The investigator or his assistants interviewed the mothers after they had been attended to by the resident obstetrician and paediatrician. The data was collected during the visit at 10 weeks. This was the time that the DNA PCR results were availed to the mothers. For those whose DNA results were delivered late, the data collection was done at the 14^{th} week visit or any other time that the PCR results were availed. Thus the key item determining eligibility for the study was the availability of the infants' DNA PCR results. The PCR status of the infant provided the main outcome measure for this study.

The patients recall, her hospital file, her antenatal card and the PMTCT register were used to obtain the vital records.

Three interventions aimed at prevention of mother to child transmission of HIV were studied. These were ARV regime used, mode of delivery and infant feeding option.

The antenatal card and the file provided the information about when ARVs were started, which ARVs were given to the mother and infant. Mothers CD4 cell counts were correlated with ARV regime used. Mothers with CD4 cell count of over 350 were put on AZT prophylaxis from 28 weeks through to delivery. Mothers with CD4 cell count below 350 were put on HAART for treatment of their HIV infection.

The second intervention for PMTCT that was studied was the mode of delivery. This information was also furnished from the records. Details pertaining to labour progress, duration of rupture of membranes, obstetric interventions or any complications during vaginal delivery were noted. For those who delivered through caesarean section, it was noted whether this was emergency caesarean delivery or if it was planned. Any complications encountered during caesarean deliveries were also recorded.

Another intervention that was studied was the mode of infant feeding. Mothers were asked about which mode of infant feeding that they had adopted. Those who chose to give formula were asked about the availability, affordability of the formula feeds and hygiene conditions of feeding. Those who chose to exclusively breast feed were asked about adhering to the feeding

and whether they had introduced any foods while breastfeeding. Any breast or babies' infections were noted.

This information was recorded in the data collection form (Appendix Π).

QUALITY CONTROL

The data collection form was pre-tested before commencement of the study and appropriate modifications made to minimize errors. Data collection was only done either by the principal investigator or by his trained assistants.

To avoid recruiting one participant twice, the hospital numbers were indicated on the data collection form.

DATA ANALYSIS

Information on socio-demographic characteristics and vital statistics concerning the mother and her infant were entered in a data collection form (appendix Π). The data was checked for completeness, consistency and accuracy. Data entry was done by the investigator while consulting with the statistician. It was then transferred into a coded sheet for computer analysis (SPSS package) with the help of a statistician. Comparison of the results was done by cross tabulation and Chi-square tests. The results were then presented in tabular form.

STUDY LIMITATIONS

1. Since the study was done after the mothers had been put on the various ARV regimes, it was difficult to verify that the mothers actually adhered to the treatment instructions.
2. It is likely that not all HIV positive mothers who delivered at KNH came for follow up visits in the high risk clinic. This group of mothers and their infants were not captured by this study.
3. Most mothers who had attended antenatal clinic elsewhere did not have complete records detailing the ARV regimes used. This category was also excluded.

ETHICAL CONSIDERATION

The study was done after approval by the ethical committee of KNH. Study participants were inducted only on voluntary consent. Patients who accepted to participate in the study were assured of their confidentiality. Patients were only identified by their hospital numbers. Those who declined to consent for the study were reassured and given the same treatment as those in the study. Those who participated in the study were not given any inducements. The study participants did not incur any extra costs due to their participation save for about 15 minutes of their time that was spent during the interview.

The results of the study will be published and used only for purposes of improvement of service provision

STUDY RESULTS

The study participants were 207 HIV positive mothers and their infants attending the high risk postnatal clinic during the study period who met the inclusion criteria.

Table 4: Socio-demographic characteristics of the mothers

Socio-demographic characteristic	Frequency (%)
Age in years	
18 – 24 yrs	36 (17.4%)
25 – 29 yrs	87 (42.0%)
30 – 34 yrs	68 (32.9%)
35 – 39 yrs	15 (7.2%)
>= 40 yrs	1 (0.5%)
Education level	
No formal education	6 (2.9%)
Primary level	78 (37.7%)
Secondary level	99 (47.8%)
College/university	24 (11.6%)
Marital status	
Single	49 (23.7%)
Married	151 (72.9%)
Divorced	7 (3.4%)
Occupation	
House wife	78 (37.7%)
Employed	53 (25.6%)
Self employed	76(36.7)

Most mothers were aged between 25 and 34 years (74.9%). The majority had either attained primary level of education (38%) or had at least secondary level of education (59.4%). Married women comprised 73% and 62.3% had a source of income (Table 4).

Table 5: Obstetric characteristics and ARV regimes used

Obstetric characteristic	Frequency (%)
Mothers' parity	
1	72 (34.8%)
2 - 4	131 (63.3%)
>= 5	4 (1.9%)
Mothers' CD4 cell count	
> 500	110 (53.1)
200 - 499	76 (36.7%)
< 200	21 (10.1%)
Mothers' ARV regime	
HAART	61 (29.5%)
AZT	121 (58.5%)
Nevirapine only	22 (10.6%)
PEP	3 (1.4%)
Gestation age at delivery	
Term (> 37 wks)	197 (95.2%)
Pre-term (35 or 36 wks)	9 (4.3%)
Very pre-term (< 35 wks)	1 (0.5%)
Mode of delivery	
Vaginal	40 (19.3%)
Emergency caesarean section	17 (8.2%)
Elective caesarean section	150 (72.5%)
Complications during delivery	
None	198 (95.7%)
PROM	3 (1.4%)
PET	1 (0.5%)
APH	1 (0.5%)
PPH	2 (1.0%)
Endometritis	1(0.5%)
Anaemia	1 (0.5%)

Majority of the mothers had 2-4 children (63.3%). A high CD4 cell of more than 500 cells/ml was found to be in 53.1% of the mothers. Use of single agent Zidovudine for prophylaxis accounted for 58.5%.Most babies (95.2%) were born at term with the majority of the mothers (72.5%) undergoing elective caesarean section. The incidence of delivery complications was found to be rare. Complications occurred in 9(4.4%) participants. Two of the 5 mothers whose babies turned HIV

positive had complications during delivery. These included one who had anaemia and another who had premature rupture of membranes. However, no statistical significance could be attached to the incidence of the complications and risk of MTCT of HIV (Table 5).

Table 6: Birth weight, Infant feeding option, ARV regime and DNA PCR status.

Health characteristic	Frequency (%)
Infant birth weight	
> 2500 grams	195 (94.2%)
1500 – 2500 grams	11 (5.3%)
< 1500 grams	1 (0.5%)
Infant feeding option	
Exclusive breastfeeding	58 (28.0%)
Formula feeding	145 (70.0%)
Mixed feeding	4 (1.9%)
Infant ARV regime	
Nevirapine and AZT	207 (100%)
Infant PCR status at 6 weeks of age	
HIV Negative	202 (97.6%)
HIV Positive	5 (2.4%)

Most babies (94.2%) weighed more than 2500grams. Only one baby (0.5%) weighed below 1500 grams. Seventy per cent of the babies were put on replacement feeding while 28% were exclusively breastfed. Four mothers mix fed their infants. All infants were given a single dose of Nevirapine and continued on Zidovudine for a further one week. Five infants out of the 207 sampled turned positive. This translated into a 2.4% prevalence of HIV infection in infants at 6 weeks of age (Table 6).

Table 7: Infant PCR status and the mothers CD4 cell count

Infant HIV status	Mother's CD4 count			Total	p VALUE
	> 500	200 - 499	< 200		
HIV positive (Prevalence)	3 (2.7%)	0 (0.0%)	2 (9.5%)	5 (2.4%)	0.04
HIV negative	107	76	19	202	
Total	110	76	21	207	

Three (2.7%) of the mothers whose infants turned out to be HIV positive had CD4 cell count of more than 500 cells/ml. Two of the mothers had CD4 cell count below 200cells/ml. HIV infection was significantly more prevalent in infants whose mothers had CD4 count less than 200, P = 0.04 (Table 7).

Table 8: PMTCT interventions and the Infant PCR status

PMTCT INTERVENTION	INFANT PCR STATUS			
	POSITIVE	NEGATIVE	TOTAL	p VALUE
Mother's ARV Regime				
HAART	2(2.2%)	59	61	
AZT	2(1.6%)	119	121	
Nevirapine	1(4.5%)	21	22	0.804
PEP	0(0%)	3	3	
Total	5(2.4%)	202	207	
Mode of Delivery				
Vaginal	2(5%)	38	40	
Emergency c/s	1(5.9%)	16	17	0.253
Elective c/s	2(1.3%	148	150	
Total	5(2.4%)	202	207	
Infant Feeding Option				
Breast feeding	3(5.2%)	55	58	
Formula	2(1.4%)	143	145	0.269
Mixed Feeding	0(0%)	4	4	
Total	5(2.4%)	202	207	

The mothers of two of the HIV positive infants (3.3%) had used triple therapy for treatment of their HIV infection. Two had been put on Zidovudine only (1.6%) while one used Nevirapine only (4.5%). There was no significant association between infant PCR status and the mothers ARV regime, P = 0.804.
Two of the HIV positive infants (5%) were delivered vaginally, two (1.3%) were delivered through elective caesarean section while one (5.9%) was delivered through emergency caesarean

section. Although the infant HIV infection appeared to be more prevalent in infants delivered by vaginal and emergency caesarean section (5 % and 5.9% respectively), there was no statistically significant association between infant HIV PCR status and the mode of delivery, P = 0.253.

Three (5.2%) of the infants who became HIV positive were exclusively breastfed. Two (1.4%) of the HIV positive infants were placed on formula feeding. Although the infant HIV infection appeared to be more prevalent in infants put on exclusive breast feeding, there was no statistically significant association between infant HIV status and the infant feeding option, P = 0.269 (Table 8).

Table 9: Infant Birth Weight and PCR status

PCR STATUS	Infant Birth Weight			Total	P Value
	>2500gms	1500- 2500	<1500		
HIV Positive(Prevalence)	4 (2.1%)	1 (9.1%)		5 (2.4%)	
HIV Negative	191	10	1	202	0.331
Total	195	11	1	207	

Four babies who tested positive for HIV weighed more than 2500gms (2.1%). One baby who weighed between 1500 and 2500gms became HIV positive (9.1%). The only baby who weighed less than 1500gms turned out to be HIV negative. Although babies weighing between 1500 and 2500gms appeared to have a higher likelihood of contracting HIV infection from their mothers (9.1%), there was no statistical significance between birth weight and infant PCR status, p=0.331(Table 9).

DISCUSSION

Most of the mothers followed up at the postnatal clinic were between the age of 25 and 29 years (42%). In the French Perinatal cohort study, the mean age of mothers was 28 years [26]. Most had attained at least secondary level of education (59.4%). The vast majority of the mothers (72.9%) were married as at the time of study. Thirty eight per cent of the mothers were unemployed while 36% were engaged in self-employment. Most mothers had between 2 and four children (63.3%). Although the relationship between parity and likelihood MTCT was not tested in this study, it is interesting to note that Christian et al, in their study, concluded that primiparous women appear to transmit HIV to their children at a higher rate [30].

The reported overall Mother to Child Transmission rate (MTCT) of HIV infection in the absence of any interventions is 20-45% [4]. Prevention of Mother to Child transmission of HIV entails efforts aimed at reducing the likelihood of an HIV positive mother passing the infection to her unborn baby or infant. These efforts include provision of antiretroviral drugs, safe obstetric practices during delivery, delivering mothers through elective caesarean section and avoidance of breastfeeding.

The results of this study revealed an MTCT rate of HIV of 2.4% at Kenyatta National Hospital. This is lower than transmission rates reported by other studies in Africa. In these studies workers compared the difference in MTCT rates at 6 weeks in infants of HIV infected mothers who were put on different ARV regimes. In Malawi, Taha et al reported MTCT rates of between 15.3% and 20.9% at 6 weeks [12]. In South Africa, one study noted an HIV prevalence of between 12.5% and 14.3% at 6 weeks [16]. In Kenya, Kiarie et al found a MTCT prevalence of 6.8% and 30.3% at 6 weeks [23].

The transmission rate was at six weeks of age. This was done for all babies whether they were put on formula feeding or they were breastfed. The ultimate transmission rate can only be estimated after re-testing the babies 3 months after cessation of breastfeeding. Nevertheless, this transmission rate attests to the fact that antiretroviral drugs and other PMTCT strategies are effective in lowering the MTCT rate of HIV.

MTCT of HIV has been shown to be lower in mothers with high CD4 cell counts [6]. Most mothers had a CD4 cell count of more than 500 cells/ml. This comprised of 53% of all mothers. It compares well with studies done elsewhere [26]. Of the infants who were HIV positive, 3 were of mothers with CD4 cell count

of more than 500cells/ml while 2 were of mothers with CD4 cell count of less than 200 cells/ml. Mother to child transmission of HIV infection was significantly more in mothers with CD4 cell count of less than 200 cells/ml, p=0.04. Mothers with CD4 cell counts of below 200/ml or those in stage 4 disease are counselled and started on HAART for treatment of HIV infection. If started early, this treatment lowers the viral load thus also reducing vertical transmission of the HIV infection. In most developed countries, all HIV positive mothers are given HAART for PMTCT [7].

The policy at KNH is to start mothers on HAART if they have CD4 cell counts of less than 350cells/ml if in stage 3 or if in stage 4 HIV disease. The majority (58%) of mothers had been put on Zidovudine for PMTCT. This was in keeping with the distribution of the mothers as per their CD4 cell status. Mothers who had been put on HAART comprised of 30%. All these had been put on the combination therapy for treatment of their HIV disease. There was no significant association between the ARV regime used and the likelihood of transmitting the HIV infection to the infant, p=0.804. A vast number of studies have been done to evaluate the efficacy of different ARV regimes in PMTCT. In their review of these studies, Leroy et al [17] concluded that only regimens given for a long period antepartum and also for a further long period in the postpartum period showed a higher

efficacy in PMTCT. When HAART is given for PMTCT and combined with ECS and avoidance of breast feeding, MTCT rates of <2% have been reported. WHO recommends a single dose of Nevirapine as a minimum standard of care for HIV positive pregnant mothers [18].

Studies done in North America and Europe showed a reduced transmission risk if mothers were delivered through elective caesarean section [7, 25, 26 27]. Elective caesarean section was the commonest mode of delivery for the mothers. This accounted for 72.5%. The rest delivered either by the vaginal route (19.3%) or by emergency caesarean section (8.2%). Although most of the HIV positive infants were born to mothers who delivered vaginally (5%) and those who delivered by elective caesarean section (5.9%), there was no significant association between the mode of delivery and the PCR status of the infant, p= 0.253. The high uptake of elective caesarean section can be attributed to the policy of counselling all HIV positive mothers to deliver by elective caesarean section. Only those who do not consent are delivered vaginally. In countries where all mothers are put on HAART for prophylaxis, those with low viral loads (<1000 copies/ml) or high CD4 counts are assessed for vaginal delivery.

Breast milk confers an added risk of transmission of HIV infection from the mother to her infant [20, 21]. The vast majority of the infants were formula fed (70%). Twenty eight per cent of the mothers chose to exclusively breastfeed their infants while 4% introduced formula feeds while breastfeeding at the same time. Three out of the 5 infants who became HIV positive had been exclusively breastfed. The other two were formula fed. There was no significant association between the PCR status of the infant and the mode of feeding, p= 0.269. The risk of transmission of HIV through breast milk is directly related to the duration of exposure. Infants who breastfeed for a long duration have a higher chance of contracting HIV infection through breast milk [4]. WHO recommends formula feeding if this is affordable, available, accessible and safe. However, in the developing countries where replacement feeding may not be readily available, mothers may opt to exclusively breast feed their infants. Studies are on going to evaluate the effect of HAART on lowering transmission of HIV through breast milk.

All infants of HIV positive mothers should be put on antiretroviral drugs. The policy at the institution is to put all babies born of HIV positive mothers on Nevirapine as a stat dose and Zidovudine for one week. In this study, all the infants were put on this regime. Most babies were delivered at term (95.2%) and weighed more than 2500grams (94.2%) at birth.

Only 1 baby was delivered before 35 weeks, it weighed less than 1500grams at delivery (0.5%). Four out of the 5 infants who were HIV positive weighed more than 2500grams at delivery while 1 weighed between 1500 and 2500 grams. There was no significant association between birth weight and PCR status of the infants, p=0.331.

Most mothers experienced no complications at delivery (95.7%). The rest had delivery complications including 3 who had premature rupture of membranes, 2 who had postpartum haemorrhage, 1 each who had anaemia, antepartum haemorrhage and endometritis. Two out the 5 infants who became HIV positive were born by mothers who experienced complications at delivery. This comprised one mother who had antepartum haemorrhage and another who had anaemia. However, due to the small number of complications noted in the study, it was difficult to test for any association between the complications at delivery and the PCR status of the infants. Mandelbrot et al also reported the intrapartum risk factors to be rare. However, in their study, procedures like amniocentesis and amnioscopy, STIs during pregnancy, premature rupture of membranes, haemorrhage in labour and bloody amniotic fluid were associated with increased MTCT of HIV [31].

CONCLUSIONS

- The MTCT rate at 6 weeks at KNH was noted to be 2.4%. Compared to reported MTCT rates elsewhere in Africa, this study shows that provision of various interventions aimed at PMTCT have had a great impact in lowering vertical transmission of HIV infection at the institution.
- Mothers with low CD4 cell counts were noted to have a higher likelihood of transmitting HIV infection to their infants.
- The study did not reveal a statistically significant correlation between ARV regime, mode of delivery or mode of infant feeding and likelihood of HIV transmission to the infant.
- The PMTCT program at Kenyatta National Hospital is on course to achieving the lowest possible MTCT rate. However, there is still a lot to be done.

RECOMMENDATIONS

- PMTCT interventions especially provision of affordable ARVs should be made readily available in all health institutions that offer maternity services.
- There is need for the government, health institutions, the media and other stakeholders to sensitize pregnant women to go for voluntary counselling and testing in order to access the services of the PMTCT program.
- Mothers with low CD4 cell counts should be counselled and offered ARVs for treatment of their HIV infection and for PMTCT.
- A larger study encompassing a larger sample size is required in order to follow-up the babies who are breastfed until 3 months after cessation of breastfeeding so as to factor in any infants who may have contracted the HIV infection through breast milk as well have more power thus allowing more conclusive inferences to be made from the results.

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APPENDIXES

APPENDIX I- GENERAL PATIENT INFORMATION AND CONSENT FORM

I, Dr Stanley Wamwea Mugo, MMED student at the University of Nairobi, department of Obstetrics and Gynaecology, am the principal investigator for this study. I wish to invite you to participate in the study.

This study includes only patients who choose to take part. Please take your time to decide on whether to participate or not. In this study, we would like to know what proportion of mothers that we put on antiretroviral drugs (ARVs) for Prevention of Mother to Child Transmission of HIV (PMTCT) pass on the HIV infection to their babies, at KNH. When we know this, we will be able to formulate the most cost effective strategies for PMTCT in the future.

Some of your expected questions are answered below, but if you have any other questions, feel free to ask.

- **What is my role in this study?**

If you are recruited to participate in the study, you will undergo the same treatment, investigations and follow-up just like those not taking part in the study. In addition to this, you will be asked a few questions concerning you and your infant. This is not an examination and you only answer to the best of your knowledge.

The answers you give will not be shown or discussed with anyone else. This exercise will take an extra 20-30 minutes of your time but it will only be done after you and your baby have been attended to by the doctor.

- **What is the cost of participating in this study?**

Participating in this study will not amount to an extra cost on what you are expected to pay for your mediacation or consultation. You will not make any extra visits to the hospital for the purpose of the study. You will not be admitted to hospital for the purpose of the study.

- **Are there any benefits for those who participate?**

No material benefits will be advanced to those who chose to participate. By participating, there may or may not be direct medical benefits to you. We hope whatever we learn from this study will benefit other patients enrolled in the PMTCT program in the future.

- **What are my rights as a participant?**

Taking part in this study is voluntary. You may chose to not to take part or may stop participating at any time. Refusal to participate will not compromise your management in any way. No benefits to which you and your baby are entitled to as a patient will be lost.

- **What about my confidentiality?**

Efforts will be made to keep your personal information confidential. Records of you and your baby's details while in

this study will be kept in confidential form. An anonymous code will be used to refer to your details such that no one can trace who the information belongs to.

- **What will you do with the information you get?**

The information we get might not be of immediate help to you but might help us manage patients in future. Like all scientific information, we will share our findings with our colleagues. Therefore, we may publish our findings in scientific journals or present them at scientific meetings.

If you want to discuss this matter with your relatives, friends or associates before giving consent, you are free to do so. If you are satisfied with our explanation and have chosen to participate in this study, please fill and sign the consent form below.

CONSENT FOR STUDY

I ..... of

.....

ID No ..... Study No.

..... do hereby consent to be included in this study on effectiveness of ARVs in PMTCT at the Kenyatta National Hospital. The nature of the study has been fully explained to me by

Dr/Mr/Mrs..... I have not been promised any material gain to be included in this study.

Signed.....

(Self/parent/guardian)

Date .....

INVESTIGATOR'S STATEMENT

I confirm that I have fully explained the above study participant the nature of the study and she has understood and accepted to take part in this study on her own volition.

Signature .....

(Investigator or his assistant)

Date .....

APPENDIX II – DATA COLLECTION FORM

IP No.....

1. STUDY No.....

2. What is your age (years)?

a)<18 [ ]

b) 18-24 [ ]

c)25-29 [ ]

d) 30-34 [ ]

e)35-39 [ ]

f) 40 and above [ ]

3. What is your marital status?

a) Single [ ]

b) Married [ ]

c) Divorced [ ]

d) Widowed [ ]

4. What is your education level?

a) No formal education [ ]

b) Primary level [ ]

c) Secondary level [ ]

d) College/ University [ ]

4. How many children do you have?

a) 1 [ ]

b) 2-4 [ ]

c) 5 and above [ ]

5. What is your occupation?

   a) Housewife [ ]

   b) Employed [ ]

   c) Self employed [ ]

6. What was the maternal CD4 cell count before starting ARV for PMTCT (or the lowest CD4 cell count ever recorded)

   a) > 500cells/ml [ ]

   b) 200-499 cells/ml [ ]

   c) < 200 cells/ml [ ]

7. At what gestation was the mother started on ARVs?

   a) Had been on triple therapy even before conception [ ]

   b) 28 weeks or immediately thereafter [ ]

   c) 34-36 weeks [ ]

   d) At onset of labour [ ]

   e) Was not put on any ARVs [ ]

8. What ARVs was the mother put on antenatally?

   a) AZT 300mg twice daily [ ]

   b) Triple therapy [ ]

   c) None [ ]

10. What ARVS was the mother put on during labour?

    a) Nevirapine 200mg only [ ]

    b) Nev 200mg + AZT 600mg stat at onset of labour [ ]

    c) AZT 300mg every 3 hours + 3TC 150mg 12 hourly [ ]

    d) Triple therapy continued throughout labour [ ]

e) None [ ]

11. What ARVs was the mother put on after delivery?

a) AZT 300mg twice daily for 1 week [ ]

b) AZT 300mg bid+ 3TC 150 mg bid for 1 week [ ]

c) Triple therapy continued [ ]

d) None [ ]

12. What ARVs was the infant put on?

a) Nevirapine 2mg/kg stat [ ]

b) Nev 2mg/kg stat + AZT 4mg/kg for 1 week [ ]

c) AZT 4mg/kg bid for 1 week [ ]

d) AZT 4mg/kg bid for 4 weeks [ ]

e) None [ ]

13. What was the gestation age at delivery?

a) Term (>37 completed weeks) [ ]

b) Preterm (35 or 36 weeks) [ ]

c) Very preterm (< 35 weeks) [ ]

14. What was the mode of delivery?

a) Vaginal [ ]

b) Emergency caesarean section [ ]

c) Elective caesarean section [ ]

15. Were there any complications

	Yes	No
a) Vaginal	[ ]	[ ]
b) Caesarean section	[ ]	[ ]

16. If yes, what were the complications?

	Yes	No
a) Prolonged rupture of membranes	[ ]	[ ]
b) Prolonged labour	[ ]	[ ]
c) Antepartum haemorrhage	[ ]	[ ]
d) Postpartum haemorrhage	[ ]	[ ]

e) Other (specify) .....

17. Were there any obstetric manoeuvres or procedures undertaken during delivery?

	Yes	No
a) Artificial rupture of membranes	[ ]	[ ]
b) Episiotomy	[ ]	[ ]
c) Forceps or vacuum extraction	[ ]	[ ]
d) Repair of perineal tear	[ ]	[ ]

e) Other (specify) .....

18. What was the birth weight of the infant?

a) >2500gm [ ]

b) 1500-2500 gm [ ]

c) < 1500gm [ ]

19. What was the infant feeding option adopted by the mother?

a) Exclusive breastfeeding [ ]

b) Formula/ Replacement feeding [ ]

20. Did the mother adhere to the feeding option?

Yes	No
[ ]	[ ]

If no, state the nature of the diversion from the original method of feeding

.....

21. What was the HIV PCR test result for the infant?

POSITIVE	NEGATIVE
[ ]	[ ]

UNIQUE FINDING

This paper was presented at the 2nd NATIONAL PMTCT GRAND ROUND held at Nairobi, Kenya, on 27th and 28th November, 2008.

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21st November 2007

Dr. Stanley Wamwea Mugo
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Mugo

RESEARCH PROPOSAL: "TO DETERMINE THE EFFECTIVENESS OF ANTIRETROVIRAL DRUGS IN PREVENTION OF MOTHER TO CHILD TRANSMISSION OF H.I.V AS SEEN AT K.N.H" (P223/8/2007)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your revised research proposal for the period 21st November 2007 – 20th November 2008.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

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