ASSESSMENT OF OUTCOMES FROM BIRTH TO SIX WEEKS IN

PREMATURE BABIES OF LESS THAN 1500g

BORN TO HIV-1 INFECTED MOTHERS AT DR. GEORGE MUKHARI

ACADEMIC HOSPITAL IN PAEDIATRIC DEPARTMENT

M MED (PAEDIATRICS & CHILD HEALTH)

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ASSESSMENT OF OUTCOMES FROM BIRTH TO SIX WEEKS IN PREMATURE BABIES OF LESS THAN 1500g BORN TO HIV-I INFECTED MOTHERS AT DR. GEORGE MUKHARI ACADEMIC HOSPITAL IN PAEDIATRIC DEPARTMENT

By

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RESEARCH DISSERTATION

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Supervisor: Prof MPB Mawela

2011
DECLARATION

I declare that the dissertation hereby submitted to the University of Limpopo, for the degree of M MED Paediatrics & child health has not previously been submitted by me for a degree at this or any other university; that it is my work in design and in execution, and that all material contained herein has been duly acknowledged.

M. Musasa (Dr) 12 September 2011
Student Number: 200729530
DEDICATION

To my beautiful wife, Thola
for her unconditional love, support and encouragements

My father, Pascal Tshibanda
for leading me into intellectual pursuits

My sons, Vassili and Samuel
My daughters, Celeste and Paula
Who brighten my every day

Pastor Walter Nzongo
for his spiritual support

In memory of

Don de Dieu
ACKNOWLEDGEMENTS

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- All the doctors and nurses in neonatal and Kangaroo Mother Care Units of Dr George Mukhari Academic Hospital.
ABSTRACT

BACKGROUND
Mother to child transmission of HIV infection accounts for 90% of Paediatric AIDS cases and new HIV infections in children. Preterm birth is reported to be associated with a higher transmission of HIV infection but little is known about the infection rate, morbidity and mortality. The objective was to determine HIV infection rate at birth and six weeks of age, comorbidities and mortality in a cohort of preterm babies born to HIV infected mothers.

METHODS
Mother-infant pairs admitted to the neonatal ward of Dr George Mukhari Academic Hospital between December 2008 and March 2010 were enrolled according to the inclusion criteria. The infants were premature of less than 1500g born to HIV-I infected mothers. Blood samples were taken for HIV DNA PCR test at birth and six weeks of age. Babies were assessed at birth, one, two, four and six weeks of life.

RESULTS
A total of 120 mother-infant pairs were enrolled on the study, 106 completed the study. 75 were formula fed and 31 were breastfed. The overall HIV transmission rate was 7.5% at birth and 12.3% at six weeks of age. The additional risk of transmission through breastfeeding was estimated at 12.9% with four more infants infected at six weeks in the breastfeeding arm vs. one in the formula feeding arm (p=0.02). Vaginal delivery was associated with an increased risk of HIV transmission compared to Caesarian-section (87.5% vs. 12.5% at birth and 76.9% vs. 23.1% at six weeks) (p=0.03).
We found a significant statistical difference in co morbidities between the formula fed and breastfed groups in the second week of life with sepsis as the leading co morbidity (49 episodes) followed by necrotizing enterocolitis (35 episodes), pneumonia (30 episodes) and failure to thrive (10 episodes)(p=0.02).
CONCLUSION
HIV transmission rate at six weeks of age was high in the breastfed group compared to formula feed counterpart. Formula feeding was associated with an increased morbidity and mortality during the first six weeks of life. Sepsis was the leading comorbidity and remained the major cause of death.
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LIST OF ABBREVIATIONS

AAP - American Association of Pediatrics
AFASS- Affordable, Feasible, Accessible, Safe and Sustainable
AIDS - Acquired Immunodeficiency Syndrome
ANC - Antenatal Care
ART - Antiretroviral Therapy
AZT - Zidovudine
BFHI - Baby Friendly Hospital Initiative
CDC - Centers for Disease Control
CTX - Cotrimoxazole
C/S - Caesarian – Section
d 4T - Stavudine
DNA PCR- DNA-based Polymerase Chain Reaction Test
DGMH- Dr George Mukhari Academic Hospital
EBF - Exclusive Breastfeeding
EFF - Exclusive Formula Feeding
ELISA- Enzyme – linked Immuno Absorbent
EPI - Expanded Programme of Immunisation
GA - Gestational age
HAART- Highly Active Antiretroviral Therapy
HIV - Human Immunodeficiency Virus
IUGR - Intra Uterine Growth Restriction
KMC - Kangaroo Mother Care
MRSA- Methicillin Resistant Staphylococcus Aureus
MTCT- Mother-to-child Transmission of HIV
NVD - Normal Vaginal Delivery
NVP - Nevirapine
POPD- Paediatrics Out Patient Department
PMTCT- Prevention of Mother-to-child Transmission of HIV
Sd NVP - Single dose Nevirapine
3TC - Lamivudine
UNAIDS- Joint United Nations programme on HIV/AIDS
UNICEF - United Nations International Children’s Emergency Fund
VCT - Voluntary Counselling and Testing
WHO - World Health Organisation
CHAPTER 1
INTRODUCTION

1.1 **BACKGROUND**
Paediatric HIV infection is an important health problem especially in developing countries. Mother-to-child transmission of HIV-I (MTCT) accounts for 90% of paediatric AIDS cases and almost all new HIV infections in children. Without antiretroviral prophylaxis, the risk of MTCT is 15% to 45% with the highest rates reported in sub-Saharan Africa. Post natal transmission through breastfeeding is estimated to contribute one third to half of HIV infection in children worldwide (Bulterys and Fowler, 2000).

Early studies from sub-Saharan Africa suggest that infants of HIV-infected mothers may be at increased risk of adverse pregnancy outcomes such as lower birth weight, prematurity, and prenatal and neonatal death (Rollins et al., 2007). It has also been shown in developed country settings that highly active antiretroviral therapy (HAART) begun before pregnancy or in early pregnancy may been associated with an increased risk of premature delivery (Lorenzi et al., 1998).

1.2 **MOTIVATION FOR THE STUDY**
The relationship between prematurity and HIV infection has not been extensively studied. To date few studies are available on this subject. In Dr George Mukhari Academic Hospital prematurity accounts for 30% to 40% of all admissions to the neonatal unit every year. With the high prevalence of HIV in pregnant women in South Africa, 29% according to the 2008 estimate of the antenatal clinic prevalence, a sizeable number of these babies can be assumed to be exposed to HIV. The primary objective is to determine the HIV transmission rate, the co morbidities and mortality during admission in premature HIV exposed babies. The secondary objective is to determine the same outcomes in relation to the mode of feeding in these HIV exposed premature babies.

1.3 **OBJECTIVES OF THE STUDY**
1. To determine the HIV transmission rate in premature babies of less than 1500g born to HIV-I infected mothers at Dr George Mukhari Academic Hospital at birth and six weeks of age using the HIV DNA PCR test.
2. To determine co morbidities in premature babies of less than 1500g born to HIV-I infected mothers at Dr George Mukhari Academic Hospital in general and in relation to feeding modality.

1.4 EXPLANATION OF TERMS
- HIV-I: Human immunodeficiency virus type 1. It is the more common and widely distributed type of HIV infection compared to HIV-2
- MTCT: mother-to-child transmission of HIV or vertical transmission of HIV from HIV infected mother to a child during pregnancy, delivery or breastfeeding.
- PMTCT: prevention of mother-to-child transmission
- EXCLUSIVE BREASTFEEDING: giving an infant no other food or drink, not even water, apart from breast milk with the exception of drops of syrups of vitamins, mineral supplements or medicines deemed necessary and essential for the baby.
- FORMULA FEEDING: giving an infant any food or drink marketed or otherwise represented as a partial or total replacement for breast milk whether or not suitable for that purpose.
- EXCLUSIVE FORMULA: giving an infant no breast milk but a diet providing adequate nutrient until the age at which the baby can be fully fed family foods.
- MIXED FEEDING: giving an infant both breast milk and formula.
- HIV-I INFECTED: infant with a positive HIV DNA PCR test
- HIV EXPOSED: infant born to a mother living with HIV until HIV exposure stops and infection can be excluded.
- ELBW: Extremely low birthweight, baby weighing less than 1000g at birth.
- VLBW: Very low birthweight, baby weighing less than 1500g at birth.
- BOOKED MOTHER: Mother who attended antenatal care clinic during pregnancy.
- UNBOOKED MOTHER: Mother who did not attend antenatal care clinic during pregnancy.
- PREMATURE: infant born prior 37 completed weeks.
2.1 **EPIDEMIOLOGY OF MOTHER TO CHILD TRANSMISSION OF HIV-1**

2.1.1 **EPIDEMIOLOGY**

Since the early 1980’s, more than 45 million people have become infected with HIV worldwide and it is estimated that in 1998 alone nearly six million adults and children acquired HIV infection (UNAIDS, 1999). The prevalence of HIV has been reported as one to three per 1000 pregnant women in urban areas such as London, Paris, Barcelona and Roma with a lower prevalence (<0.5 per 1000) in Scandinavian countries (Cazein et al., 1998). The introduction and widespread use of combination antiretroviral treatment in the late 1990 resulted in a steady decline of AIDS incidence. HIV AIDS disproportionately affects sub-Saharan Africa which comprises less than 10 % of the World’s population, but has 90 % of the paediatric cases of HIV and 68 % of the adult cases of HIV (Zanoni, 2009).

The U.S Bureau of Census estimated that by 2010, the infant mortality rate would more than double from an expected 30 per 1000 without AIDS in 2001 to 71 per 1000 in Zimbabwe and from 26 to 66 per 1000 in Botswana. In Kenya the infant mortality rate was projected to be 70 % higher, in Zambia 60 % higher and in Malawi, Tanzania and Uganda 40 % higher (Kozinetz, 2001).

South Africa has an estimated 5.5 million people infected with HIV, the highest in the world. The number of people living with AIDS is higher than the entire combined population of Swaziland, Lesotho and Botswana (Zanoni, 2009).

South Africa also has one of the highest antenatal clinic HIV prevalence rates in the world 29.1 % in 2006 after a peak of 30.2% in 2005 (Zanoni, 2009). The 2008 estimate of the antenatal clinic prevalence is 29 % (prevalence of pregnant women attending Public Health Care clinics). The total HIV prevalence rate in South Africa is 12 % whereas 20 % of adults between the ages of 20 and 64 are estimated to be HIV positive (Nathea, 2008).
Antenatal clinic HIV rates are not evenly distributed throughout the country. The province of Kwa-Zulu Natal stands out at 39.1% with intra provincial rates as high as 46%. Despite these rates, only 66% of HIV positive pregnant women received antiretroviral to reduce mother to child transmission of HIV and 42% of adult and children with advanced AIDS were receiving ARV therapy in 2007 (Zanoni, 2009).

Fig 1: National Antenatal clinic HIV prevalence rates in sub-Saharan countries 2006
(Data Source: UNAIDS 2007)
Figure 3 depicts the prevalence of the HIV epidemic in 2008 in each of the nine provinces. From the graph it is clear that the epidemic is still growing rapidly in the Eastern Cape and to a lesser extent in the Western Cape, Northern Cape and Limpopo, whereas it has matured in the other provinces.

A mature epidemic means that new infections and deaths are more or less at the same level so that total numbers of infected people remains constant.

Where HIV prevalence declines, it can often be attributed to the number of AIDS deaths being higher than new infections and does not necessarily imply that new infections are declining.

Among females, HIV prevalence is higher in those between 25 and 29 years; among males, the peak is in the group aged 30-34 years.

HIV seroprevalence is higher in blacks than whites, coloured or indians. Informal settlements in urban areas showed the highest HIV prevalence rate when compared with urban formal areas, rural informal areas or rural formal areas (Connolly et al., 2004)

The variable social, economic and environmental conditions play a role in the distribution and determinants of the disease.


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<th>POPULATION GROUP</th>
<th>PREVALENCE (%)</th>
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<tr>
<td>White</td>
<td>0.3</td>
</tr>
<tr>
<td>Coloured</td>
<td>1.7</td>
</tr>
<tr>
<td>Indian</td>
<td>0.3</td>
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2.1.2 MOTHER TO CHILD TRANSMISSION OF HIV-I (MTCT)

The HIV epidemic among children is closely linked to that among women since the vast majority of paediatric infections are the result of vertical transmission from mother-to-child. In 2006, in South Africa there were more than 1,400 new HIV infections per day, which was equivalent to nearly one infection every minute (Zanoni, 2009).

More than 90% of newly infected children are babies born to women with HIV. Over nine-tenths of such transmission occur in sub-Saharan Africa (UNAIDS 2009).

MTCT encompasses transmission from an infected pregnant woman to her foetus during pregnancy (in utero) or labour and delivery (intrapartum) and through breastfeeding (postpartum). Rates of vertical transmission in the absence of specific interventions ranges from 16% to 20% in large-cohort studies in Europe and North America to 25% to 40% in sub-Sahara Africa (Fowler et al., 2000).

The reasons behind these variations include different prevalences of breastfeeding, maternal and obstetric risk factors as well as methodological differences between studies.

Attempts have been made to categorize infant infections by timing of transmission because the magnitude of risk, prevention and disease progression differ according to the three periods of infection in the foetus and the infant (Fowler et al., 2000).

a. **In utero transmission:**

   In utero transmission most likely occurs through placental transmission of HIV. In uterotransmission can be enhanced by membrane inflammation. HIV infected infants with a positive HIV DNA PCR in the first two days of life are usually assumed to have had intrauterine acquisition of infection (Thorne and Newell, 2000).

b. **Intrapartum transmission:**

   Intrapartum transmission occurs in a variety of ways including direct contact of the foetus/infant with infectious maternal secretions during birth, ascending infection after rupture of membranes, materno-foetal micro transfusions during uterine contractions and
absorption of the virus through the infant’s digestive tract following ingestion of infected amniotic fluid. The HIV DNA PCR test taken in the first week of life will test negative, but positive after that if the child is infected intrapartum (Thorne and Newell, 2000).

c. **Postpartum transmission:**

Postpartum transmission most likely occurs through frequent and prolonged exposure of an infant’s oral and gastrointestinal tract to infected breast milk.

Although in breastfeeding populations it is difficult to distinguish intrapartum from early postnatal acquisition of infection, the additional risk of transmission through breastfeeding over and above that of intrauterine or intrapartum transmission is estimated to be between 7% and 22% (Bertolli et al., 1996).

Three groups of variables have been associated with the risk of vertical transmission: maternal, obstetric and infant related factors.

The most important maternal factor is the viral load. Further maternal risk factors include a high frequency of unprotected sex and illicit drug use in pregnancy (Rodriguez et al., 1996).

Obstetric risk factors associated with an increased risk of mother-to-child transmission include vaginal delivery, prolonged rupture of membrane, chorioamnionitis, invasive obstetric procedures and co infection with another sexually transmitted infection (European Collaborative Study, 1996).

Specific risk factors for post natal transmission include breast health, such as the presence of mastitis or an abscess (Sembra et al., 1999), and the pattern of feeding, with mixed feeding reportedly associated with a higher risk than exclusive breastfeeding (Coutsoudis et al., 1999).

Perinatal transmission of HIV-I can be lowered from 40% to < 2% with the use of a combination of antiretroviral drugs during pregnancy and labour (with or without Caesarean section), infant prophylaxis with antiretroviral agents and avoidance of breastfeeding. However this reduction can be achieved only when there is awareness of the presence of maternal HIV-infection and interventions can be implemented.
Primary HIV infection is associated with very high level of HIV-1 RNA (Lindback et al., 2000). In turn, the maternal HIV-1 RNA level is one of the most important predictors of perinatal HIV-1 transmission. It is therefore not surprising that very high rates of MTCT have been observed among women who experienced seroconversion during pregnancy or breastfeeding (Palasanthiran et al., 1993).

The South African Prevention of Mother-to-child transmission of HIV programme (PMTCT), conceptualized in 2000 has been implemented at pilot sites since 2001 and nationally since 2002. In February 2008 the National Department of Health and the South African PMTCT published a revised policy and guidelines for the implementation of the PMTCT programme.

The policy seeks to provide continued guidance toward successful reduction of MTCT, building on work done in the past decade.

In summary to maximally reduce risk of MTCT and to ensure women who could benefit from HAART receive it, specific categories of women were defined, as shown below. The use of ARV’s in infants was also detailed. The following treatment protocol was therefore recommended:

a. Pregnant women not eligible for HAART i.e. CD$_4$ cell count >200 cells/mm$^3$ (WHO Stage I-III) or CD$_4$ cell count unknown should, at a minimum receive a dual therapy PMTCT regimen initiated at 28 weeks of pregnancy or as soon as possible thereafter. Where the CD$_4$ cell count is unknown, AZT should be prescribed and commenced if the woman is >28 weeks of pregnancy and blood should be sent for a CD$_4$ cell count. If the CD$_4$ cell count indicates the need for HAART, AZT should be continued up to the point that HAART is initiated when PMTCT regimen will be substituted by HAART.

The same recommendation applies for women with WHO stage IV disease. Women started during pregnancy with the PMTCT regimen should be counseled on early presentation for delivery.
b. Pregnant women with a CD$_4$ cell count $<200$ cells/mm$^3$ or WHO stage IV should be initiated onto HAART.

The choice of HAART in this group would be regimen 1b of the National Adult ARV treatment guidelines i.e. d4T, 3TC, NVP. All doses to be consistent with Adult ARV guidelines and are the same as for non-pregnant women. Prophylaxis with cotrimoxazole should also be commenced.

c. Women already on HAART before pregnancy should continue with treatment. A woman who becomes pregnant whilst on HAART should have efavirenz switched to NVP in the first trimester. After the first trimester there is no need for the switch. Adverse event monitoring is critical in all cases and should be ongoing including foetal anomaly scans.

d. Pregnant women presenting in labour who are not on any antiretroviral drugs (either unbooked, or HIV status unknown) should be offered VCT in the 1st stage of labour, if found to be HIV-positive they should be given antiretroviral drugs in the form of SdNVP during labour. Decisions around supporting women’s choices of infant feeding after delivery need to be made at the time of initiation of HAART.

e. Infants born to women who receive optimal PMTCT or HAART (group A-C above that have had more than four weeks of treatment) should receive SdNVP as soon after birth as possible within a 72 hour period. AZT prescribed according to regulatory requirements should be commenced soon after birth and be administered for seven days.

f. Infants born to women who received suboptimal PMTCT or HAART

-where no maternal ARV’s were taken

-where maternal ARV’s (PMTCT or HAART regimen) were taken for less than four weeks

-where women received only SdNVP

These infants should receive SdNVP as soon after birth as possible, preferably within six hours of birth but not later than after 72 hours after birth. AZT should be commenced soon after birth and be administered for 28 days.
2.2 **HIV INFECTION AND PREMATURITY**

Frequencies of low birth weight (LBW) (Birth weight <2500g), prematurity (Gestational age < 37 weeks), and intra uterine growth restriction (Low birth weight and gestational age > 37 weeks) are generally high in Africa, independently of HIV serostatus. They are associated with poor maternal nutritional status, related to combined determinants like low dietary intake and exhausting work. HIV infection could represent an additional factor inducing a high frequency of LBW in settings where prevalence of HIV infection is elevated. It has been shown that HIV+ patients often show deficiencies in micronutrients such as Vitamin E, Vitamin A, selenium, and Zinc. Maternal Vitamin A deficiency is common in developing countries and is associated with mother-to-child transmission of HIV and a higher mortality in children, possibly via its role in immunity and mucosal integrity (Castetbon et al., 1999).

In the European collaborative study (ECS) infants born before 37 weeks were approximately 2.5 times more likely to acquire HIV infection than infants born at term (European Collaborative Study, 1999).

**RISK OF HIV TRANSMISSION IN PREMATURE BABIES**

**Breastfeeding**

Premature babies are at high risk of developing necrotizing enterocolitis from immaturity of key functions especially gastro intestinal motility, digestive ability, circulatory regulation, intestinal barrier function and immune defenses (Lin and Stoll, 2006). This lack of intestinal barrier function may also expose premature babies to transmission of HIV infection via infected breast milk.

**Maternal HIV infection**

The relationship between HIV infection and prematurity has not been studied extensively. Studies on this subject do not show consistent findings. HIV infection in premature babies may be associated with variety of morbidities as found in different studies.

In a study done in Rwanda in 1998, maternal HIV infection was shown to have a significant effect by increasing the frequency of adverse obstetrical and neonatal outcomes (Leroy et al., 1998). Although there was no influence of HIV on congenital malformations and neonatal mortality, maternal HIV infection increased the risk of prematurity by 62% and the risk of
LBW by 58%. Prematurity was estimated to be caused by the direct effect of maternal HIV infection or by a causal pathway implicating other risk factors such as sexually transmitted diseases or malaria.

The risk of stillbirth was not significantly increased in HIV positive compared with HIV negative women as reported in previous studies (Braddick et al., 1990).

In a meta analysis of the association between maternal HIV and perinatal outcomes, the risk of premature delivery (before 37 weeks) and low birth weight (<2500g) was nearly doubled in HIV infected women compared to uninfected controls (Brocklehurst and French, 1998).

In the European Collaborative Study (ECS), a prospective study following up children born to HIV infected women, the overall premature delivery rate was 15 % (341/2299). Birth weight was available for 2274 (99 %) of these mother-child pairs and ranged from 700g to 5300g with a mean of 2932g (median 2970g). Overall, 19 % (433/2874) of infants were of low birth weight.

In a US study of 600 infants born to HIV infected women, a slightly higher rate of prematurity (19 %) was found with 18 % of neonates having low birth weight and 3% very low birth weight (Martin et al., 1997).

In another study done in Rwanda, prematurity was almost twice more frequent in infants born to HIV positive women than in infants born to HIV negative women. Similarly the frequency of intra uterine growth restriction was almost three times higher in infants born to HIV positive women than in infants born to HIV negative women (Castetbon et al., 1999). This could be explained by dietary intake reduction, intestinal malabsorption, and metabolic disturbances, which are frequent in HIV positive patients and can, occur early in the course of infection. HIV positive women gained less weight during pregnancy than did HIV negative women, and had not recovered their pre-pregnancy weight nine months after delivery.

In Cote d’Ivoire, a study found that birth weight and gestational age were not significant risk factors for HIV transmission at one or 24 months as described in previous studies (Jamieson et al., 2003).
In Tanzania, lower birth weight babies born to HIV infected mothers were five times more likely to die than babies with normal birth weight. HIV transmission, especially early infection, was strongly related to post neonatal and infant mortality (Wei et al., 2004).

A recent study in Kwa-Zulu Natal, South Africa found that maternal HIV infection was associated with reduced birth weight (45% increased risk). The risk of HIV transmission was inversely associated with birth weight and maternal CD4 count with a higher risk when birth weight was <2500g and maternal CD4 count was <200.

The effect of low birth weight or mortality was substantial by six weeks of age in HIV infected mothers (7.7%) vs. HIV uninfected mothers (2.2%).

Paradoxically in the same study, maternal HIV was not significantly associated with early infant mortality. The six weeks mortality was similar to the 1.8% mortality reported in a previous study in Harare, Zimbabwe as well as 1.0% mortality in breast fed vs. 3.9% mortality in formula fed infants in Nairobi, Kenya (Rollins et al., 2007).

2.3 HIV AND INFANT FEEDING PRACTICES

2.3.1 Background

In its 1997 policy statement on the use of formula milk, the American Association of Pediatrics acknowledged that human milk is beneficial in the management of premature infants due to improvement in host defense, digestion and absorption of nutrients, gastrointestinal function, neuro development outcomes and maternal psychological well being: one major protective effect of human milk on recipient infant operate through the enterommary immune system. Exposure of mother to the environment of neonatal nurseries through skin to skin contact with their premature infant induces specific antibodies against nosocomial pathogens in nurseries (Schanler, 2001).

However, breastfeeding is not without controversy when the mother is HIV positive. It can lead to mother to child transmission of HIV. According to UNAIDS statistics, breastfeeding was responsible for one-third to one half of the 640 000 new HIV infections in infant each year (Blais and Altosaar, 2007).
In sub-Saharan Africa, women infected with HIV continue to breastfeed their infants for several reasons. Breastfeeding satisfies the nutritional need of an infant and is frequently encouraged by other family members as a cultural norm. Women who do not initiate and maintain breastfeeding raise suspicions in the community about their HIV status, and this may lead to discrimination of the HIV positive women by her family and community.

Furthermore, substitutes for breast milk are either expensive or not safe to use owing to a lack of safe water. Breastfeeding carries a risk for HIV transmission but improves survival. Formula feeding carries zero risk for transmission but increased risk for mortality. There is a high incidence of deaths associated with unsafe formula feeding.

Milk formulae still lack a key advantage that breast milk offers to the newborn (i.e. the ability to supplement and stimulate the developing immune system and gastro intestinal tract with immune and growth factors through passive immunity).

No current feeding method is risk free for most of the HIV infected mothers in under privileged countries and therefore exclusive breastfeeding remains the safest option. A South African study demonstrated that the transmission rate with exclusive breastfeeding at six months was 4%. When solids were given in addition to breast milk, there was 10-fold increase in risk for transmission and a 21.8 fold risk when formula was given in addition to breast milk (Coovadia et al., 2007).

To counter balance the benefits and risks of breastfeeding when the mother is infected with HIV, WHO, UNICEF and others have developed guidelines to assist women in making an informed decision about feeding choices. A variety of additional approaches may decrease breast milk transmission of HIV-I except avoidance of breast milk. These include pasteurization of expressed breast milk, early weaning, maternal HAART, maternal short cause antiretroviral and infant antiretroviral prophylaxis.

For HIV infected mothers the WHO issued two recommendations (WHO on behalf of the Inter-Agency Task Team, 2006)

i. avoiding breastfeeding entirely when replacement milk is acceptable, feasible, affordable, sustainable and safe.
ii. otherwise, breastfeeding exclusively during the first four to six months of the infant’s life. Despite the WHO guidelines, exclusive breastfeeding by HIV infected mothers is rarely practiced in many resource constrained countries (Bland et al., 2002).

In some area, as many as 90 % of breastfed neonates are given non breast milk fluids or infant formulae on the result of social pressures, maternal illnesses or breast milk insufficiency. With reduced intake of growth factors and cytokines in non breast milk fluid, mixed feeding can compromise the integrity of the neonatal gastro intestinal epithelium and consequently facilitate the GIT entry of HIV present in breast milk. Mixed fed newborn are four times more susceptible to HIV infection than exclusively breastfed neonates (Illiff et al., 2005).

2.3.2 BREASTFEEDING VS FORMULA FEEDING

Counselling on infant feeding has been one of the weakest components of the current SA PMTCT programme. In many instances health care personnel have interpreted the UN recommendations as “promoting replacement feeding” or “avoiding breastfeeding”. In South Africa programmatic data show that quality of infant feeding counselling is poor and that women’s choices are not being guided by the AFASS criteria (Doherty et al., 2007). South African data shows that at least three conditions need to be met before formula feeding may be beneficial i.e. piped water must be available in the house or yard, and fuel must be regularly available and the woman should have disclosed her HIV status (Doherty et al., 2007). Data from the Good Start study show that 33 % of women made an inappropriate choice to exclusively formula feed (intending to formula feed but not meeting these three criteria) and 16 % made an inappropriate choice to exclusively breastfeed (intending to exclusively breastfeed and meeting these three criteria).(Doherty et al.,2007).

In an intention to treat analysis of the randomized clinical trials of breastfeeding versus formula feeding in Kenya, women were more likely to die within two years after delivery if randomized to the breastfeeding arm (Nduati et al., 2001). However data from a South African study suggested no difference in mortality of HIV infected mother according to their children’s feeding modality (Coutsoudis et al.,2001). A meta analysis by the Breastfeeding and HIV transmission International Study group using data from several clinical trials in Africa done in 2004 did not show a significant difference of mother’s mortality according to children’s feeding modality.
A study on early exclusive breastfeeding to reduce risk of post natal HIV transmission showed a post natal transmission rate of 3.9 %, 7.7 % and 12.1 % at six, 12 and 18 months respectively. A total of 68.2 % of all post natal transmission rate occurred after six months. Mixed breastfed babies had a significantly greater post natal transmission risk. The Mashi study in Botswana to evaluate both perinatal and post natal interventions for Combating MTCT showed that infant formula feeding was found to be more effective than breastfeeding with Zidovudine prophylaxis (5.6 % vs. 9.0% infection rate, a 38 % difference). However, formula use was associated with a higher mortality rate at seven months (9.3 % and 4.9%). Both strategies achieved similar HIV free survival at 18 months (13.9 % and 15.1 %). These results demonstrated the vulnerability of young infants and underscored the risk of formula feeding for infants in less developed settings (The Mashi Study Team, 2006).

In Lusaka, Zambia a study demonstrated a survival benefit from breastfeeding among children infected post partum versus children infected during pregnancy or delivery and a benefit from increased breastfeeding duration among infected children (20 % of the intra uterine and intra partum/ early post partum group died by 100 days after infection whereas nearly 10 % of the post partum group had died by this time). After adjusting for birth weight, maternal CD4 cell count, breastfeeding and maternal death, children infected post partum had one quarter the mortality rate of those infected in utero. Stopping breastfeeding increased mortality in infected children (Fox et al., 2008).

An evaluation of two cohorts studies in Mozambique (Palombi et al., 2007) reported that the provision of free formula feeding plus water filters and nutritional supplement for six months was an inferior option to breastfeeding plus HAART. At one month of age, the HIV-I transmission rate was 1.2 % among breastfed infants and 0.8 % among formula-fed infants. At six months of age HIV-I MTCT rate was 0.8 % among breastfed infants of women receiving HAART and 1.8 % among formula-fed infants (chi = 0.77, p = 0.38). The cumulative incidence rate of six months of age was 2.7 % for formula-fed infants vs. 2.2 % for breastfed infants (chi = 0.27, p = 0.60). There was a trend for HIV-I infection rates to be slightly greater among formula-fed infants, but overall mother-to-child transmission rates in both cohorts were extremely low. Most infants did relatively well on both feeding regimens.
An urban cohort study from Cote D’Ivoire demonstrated similar morbidity and mortality outcomes at two years between breastfed and formula fed infants. The duration of breast feeding was four months (Becquet et al., 2007).

Presently, there is no clear evidence that universal maternal HAART would be superior to infant antiretroviral prophylaxis for mother-infant pairs who receive tiered PMTCT (i.e. maternal HAART if eligible and combination short course antiretroviral if ineligible for HAART). In the study by Taha and colleagues, HAART ineligible women comprised \~70\% of the cohort, even with a higher CD$_4$ cell count cut off (CD$_4$ cell count >350 cell/mm$^3$) it is likely that >50\% of women would be ineligible for HAART and have a lower transmission risk than HAART eligible women. HAART ineligible women in the study had a transmission risk of 3.66 per 100 person years after 14 weeks, and the authors speculated that infant prophylaxis may decrease this by 67\% (Taha et al., 2009).

2.3.2 SAFE INFANT FEEDING PRACTICES

The South African national PMTCT programme adopts an approach to infant feeding that seeks to maximize child survival with the following considerations:

Infant feeding counselling should take cognizance of the specific circumstances of the pregnant woman/mother, including her individual ability to meet the AFASS criteria so that appropriate infant feeding choices are made.(Appendix 1). Thus detailed, comprehensive and individualized feeding counselling is critical to enable women to make the feeding choice that will maximize HIV free survival.

The South African infant and Young child feeding policy and implementation guidelines and the Baby Friendly Hospital initiative (BFHI) including the ten steps to safe infant feeding, as outlined in the BFHI provide a framework to facilitate feeding support for HIV positive and HIV negative women.

2.4 SUMMARY OF LITERATURE REVIEW

HIV/AIDS disproportionately affects Sub-Saharan African with 90\% of children infected with HIV. The vast majority of paediatric infections are the result of vertical transmission form mother-to-child which can take place in utero, during delivery and postnatally through
breastfeeding with about three-quarters of infections occurring around the time of delivery in non breastfeading populations.

Breastfeeding carries a risk for HIV transmission but improves survival, whereas formula feeding carries zero risk for transmission but increased risk for morbidity and mortality.

An association between maternal HIV infection and prematurity and/or low birth weight is a consistent finding of epidemiological studies. Premature delivery may therefore be a consequence of maternal HIV infection, with very premature infants more susceptible to intrapartum acquisition of infection than those born at term. With antiretroviral treatments and the avoidance of breastfeeding, rates of vertical transmission have occasionally been virtually eliminated in developed countries. These rewarding experiences have been difficult to reproduce in developing countries due to the lack of infrastructure and the need to continue breastfeeding because of the hazard of replacement feeding for overall child health.
CHAPTER 3
METHODOLOGY

3.1 STUDY DESIGN:
This is an observational analytic study conducted at the neonatal ward and the KMC units of Dr George Mukhari Academic Hospital, a tertiary hospital linked to the University of Limpopo (Medunsa Campus) situated in Ga-Rankuwa, Gauteng Province.

3.2 SAMPLE SELECTION
3.2.1 ENROLMENT
All mother-infants pairs admitted to neonatal unit of Dr George Mukhari Academic Hospital satisfying the inclusion criteria were enrolled into the study over a 15 month period. All the eligible patients were identified by the researcher and an assistant asked potential participants if they would be willing to participate in the study using the information leaflet (Appendix 2) as a guide. Mothers willing to participate in the study were enrolled after a consent form was signed. (Appendix 3)

3.2.2 INCLUSION CRITERIA
- Premature and/or VLBW infants of less than 1500g born to HIV infected mothers and admitted to Dr George Mukhari Academic Hospital neonatal unit.
- Mother has been counselled on feeding choice and has made an informed choice before enrolment.
- Available written informed consent to participate in the study.

3.2.3 EXCLUSION CRITERIA
- Identifiable congenital abnormalities
- Failure to meet inclusion criteria
- No available informed consent to participate in the study.
3.2.4 **SELECTION OF STUDY POPULATION**

A convenience sampling method was used. Premature and/or VLBW infants of less than 1500g born to HIV infected mothers and admitted to the neonatal unit were enrolled over a 15 month period. All study patients were followed up by the researcher according to the study protocol.

3.3 **DATA COLLECTION**

Enrolled mothers were counselled (Appendix 2) and a consent form was signed (Appendix 3). Data for all eligible patients was recorded on a data collection sheet (Appendix 4). The infants were assessed at birth, one, two, four, and six weeks of life. These assessments were done while the infant was still in hospital and at the outpatient neonatal clinic during routine follow up visits if the infant was discharged prior to six weeks of age.

The mother’s demographic details were recorded by the researcher. All mother-pairs from local communities who missed follow up were contacted telephonically. If after this contact the patient could not be traced the patient was excluded from the study. The infant HIV status was determined by DNA PCR analysis (Roche Amplicor, Version 1.5, Roche Molecular Systems) done at the National Health Laboratory Services (NHLS). An infant was considered as HIV infected if two separate HIV DNA PCR tests were positive and as not HIV infected if two separate HIV DNA PCR tests were negative.

The gestational age was determined using the modified Ballard score (Rennie, 2005), a scoring system using the neuromuscular maturity and physical maturity. Co morbidities were determined by the researcher using standard diagnostic criteria. A diagnosis of hyaline membrane disease (HMD) was made if the infant had features of respiratory distress within hours of birth and there was radiological confirmation according to standard criteria. Pneumonia was diagnosed in the presence of signs of respiratory distress accompanied by signs of systemic sepsis such as a rise in the CRP or an abnormal WBC count and there was radiological confirmation according to standard criteria.

Sepsis was diagnosed clinically and with laboratory evidence of a rise in the CRP or a positive blood culture or an abnormal, WBC count.
Necrotizing enterocolitis (NEC) was diagnosed with a clinical presentation associated with an abnormal Abdominal X-Ray according to standard criteria. Failure to thrive was diagnosed when an infant was failing to grow as expected.

3.4 **THE RESEARCH ASSISTANT**
A Research Assistant assisted with communication with participants in SETSWANA according to the participation information leaflet and consent form.

3.5 **QUALITY CONTROL**
On a daily basis the researcher inspected data collection sheets for completeness in recording. Errors and omissions were identified and corrected.

3.6 **DATA ANALYSIS**
Data were captured by double entry on the computer using Epi Info (TM) version 3.5, a Database and statistics software for public health professionals (2008/04/29). Data entries were compared to the original record sheet to verify their accuracy. Data was analyzed using descriptive statistics. Frequency distributions for every variable were calculated and different variables were compared between the two feeding choices.

3.7 **ETHICS**
Permission to conduct the study was obtained from the Superintendent of Dr George Mukhari Academic Hospital and the Head of Department of Paediatrics and Child Health. The protocol was approved by the Medunsa Research & Ethics Committee (MREC.M.215/2008 = PG) (Appendix 5). The nature of the study was explained to mothers and those willing to participate gave written consent (Appendix 3). The study records were kept confidential and participants were free to withdraw at any time during the course of the study.
CHAPTER 4
RESULTS

4.1 DEMOGRAPHICS:

4.1.1 BABIES

During the study period, a total of 940 premature infants were admitted to the Neonatal unit of Dr George Mukhari Academic Hospital. 120 premature infants were enrolled into the study according to the inclusion criteria. 106 (88.3 %) HIV exposed premature infants completed the study and 14 (11.7 %) did not. All those who did not complete the study died during the course of follow up. 54 (50.9 %) were males and 52 (49.1 %) females. 14 (13.2 %) infants were extremely low birth weight and 92 (86.8 %) very low birth weight. The gestational age ranged from 25 weeks to 36 weeks with a peak around 29-31 weeks (Figure 6). 92 were singletons and 14 twins.

Fig 5: Gestational age distribution of study population

The majority of mothers (70 %) opted for formula feeding (Figure 6). This feeding choice remained the actual feeding practice during the study period.
4.1.2 MOTHERS
A total of 106 mothers were enrolled in the study group. The maternal age ranged between 15 and 41 years. 83 mothers were booked vs. 23 unbooked. 56 (52.8 %) mothers delivered vaginally and 50 (47.2 %) by Caesarian Section.

CD4 Results
Antenatal CD4 results were recorded for 46 mothers only. In 60 mothers (56.6 %) there was no record of the CD4 result.
Where the CD4 count was recorded:
23 (21.7 %) had CD4 count less than 200 cells/mm$^3$
19 (17.9 %) had a CD4 between 200-500 cells/mm$^3$
And 4 (3.8 %) had a CD4 count above 500 cells/mm$^3$

Antiretrovirals
81 (76.4 %) mothers received PMTCT prophylaxis (AZT + SdNVP or SdNVP) during pregnancy/labour, 18 (16.9 %) were on HAART and seven (6.6 %) did not receive either HAART or PMTCT prophylaxis. 75 (70.8 %) mothers opted for formula feeding vs. 31 (29.2 %) who opted for breastfeeding (Figure 6).
Fig 7: Flow diagram of participants: feeding option and infant outcomes

120 Mother-infant pairs enrolled

35 Breastfeeding arm
- 0 Maternal death
- 4 Infant deaths
- 31 alive infants (29.2 %)

Outcomes:
- HIV infection at birth: 3
- HIV infection at six weeks: 7
- Cumulative co-morbidities:
  - HMD: 23
  - Pneumonia: 15
  - Sepsis: 25
  - NEC: 14
  - FTT: 3

85 Formula feeding arm
- 4 Maternal deaths
- 10 Infant deaths
- 75 alive infants (70.8 %)

Outcomes:
- HIV infection at birth: 5
- HIV infection at six weeks: 6
- Cumulative co-morbidities:
  - HMD: 52
  - Pneumonia: 41
  - Sepsis: 56
  - NEC: 27
  - FTT: 8
4.2 HIV INFECTION OUTCOMES

4.2.1 INUTERO INFECTION (AT BIRTH)

Eight infants (7.5 %) in the study had a positive HIV DNA PCR at birth. Five of these babies were born to mothers with unknown CD₄ count, two were born to mothers with CD₄ counts <200 cells/mm³ and only one to a mother with a CD₄ count >500 cells/mm³.

TABLE 2: MATERNAL CD₄ COUNT IN RELATION TO BIRTH HIV PCR

<table>
<thead>
<tr>
<th>Mother CD₄ Count in cells/ mm³</th>
<th>BIRTH HIV PCR</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n(%)</td>
<td>Positive n(%)</td>
<td>Total</td>
</tr>
<tr>
<td>&lt;200</td>
<td>21 (91.3)</td>
<td>2 (8.7)</td>
<td>23 (100.0)</td>
</tr>
<tr>
<td>&gt;500</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
<td>4 (100.0)</td>
</tr>
<tr>
<td>500-200</td>
<td>19 (100.0)</td>
<td>0 (0.0)</td>
<td>19 (100.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>55 (91.7)</td>
<td>5 (8.3)</td>
<td>60 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (92.5)</td>
<td>8 (7.5)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Chi-square 3.39, P = 0.33

Seven of these babies with a positive HIV DNA PCR at birth were delivered vaginally and only one baby was delivered by Caesarean section.
TABLE 3: BIRTH HIV PCR IN RELATION TO DELIVERY MODE

<table>
<thead>
<tr>
<th></th>
<th>DELIVERY MODE</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>NVD n(%)</td>
<td>C/S n(%)</td>
<td>TOTAL n(%)</td>
</tr>
<tr>
<td>BIRTH HIV PCR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>49 (50.0)</td>
<td>49 (50.0)</td>
<td>98 (100.0)</td>
</tr>
<tr>
<td>Positive</td>
<td>7 (87.5)</td>
<td>1 (12.5)</td>
<td>8 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>56 (52.8)</td>
<td>50 (47.2)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Odd ratio 0.14; 95 % CI 0.00 – 0.98; P = 0.02

Six (75 %) of these babies with a positive HIV DNA PCR at birth were born to mothers not on PMTCT prophylaxis and two (25 %) were born to mothers on PMTCT prophylaxis.

TABLE 4: MATERNAL HAART IN RELATION TO BIRTH HIV PCR

<table>
<thead>
<tr>
<th></th>
<th>BIRTH HIV PCR</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n(%)</td>
<td>Positive n(%)</td>
<td>Total n(%)</td>
</tr>
<tr>
<td>MATERNAL HAART</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (88.9)</td>
<td>2 (11.1)</td>
<td>18 (100.0)</td>
</tr>
<tr>
<td>No</td>
<td>82 (93.2)</td>
<td>6 (6.8)</td>
<td>88 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (92.5)</td>
<td>8 (7.5)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Odds ratio 0.58; 95 % C.I.0.10-3.16;P = 0.27

4.2.2 HIV INFECTION AT SIX WEEKS

At six weeks of age 13 (12.3 %) infants had a positive HIV DNA PCR test. Six of these babies were born to mothers with unknown CD₄ counts, four were born to mothers with CD₄ counts < 200 cells/mm³, two to mothers with CD₄ counts between 500-200 and only one to a mother with aCD₄ count >500 cells/mm³.
TABLE 5: MATERNAL CD4 COUNT IN RELATION TO SIX WEEKS HIV PCR

<table>
<thead>
<tr>
<th>Mother CD4 count in cells/mm3</th>
<th>SIX WEEKS HIV PCR</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n(%)</td>
<td>Positive n(%)</td>
<td>Total n(%)</td>
<td></td>
</tr>
<tr>
<td>&lt; 200</td>
<td>19 (82.6)</td>
<td>4 (17.4)</td>
<td>23 (100.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;500</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
<td>4 (100.0)</td>
<td></td>
</tr>
<tr>
<td>500-200</td>
<td>17 (89.5)</td>
<td>2 (10.5)</td>
<td>19 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>54 (89.5)</td>
<td>6 (10.5)</td>
<td>60 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>93 (87.7)</td>
<td>13 (12.3)</td>
<td>106 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

Chi square 1.50; P = 0.68

10 of these babies with a positive HIV DNA PCR at six weeks were delivered vaginally and three by Caesarian section.

TABLE 6: SIX WEEKS HIV PCR IN RELATION TO DELIVERY MODE

<table>
<thead>
<tr>
<th>SIX WEEKS HIV PCR</th>
<th>DELIVERY MODE</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NVD n(%)</td>
<td>C/S n(%)</td>
<td>Total n(%)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>46 (49.5)</td>
<td>47 (50.5)</td>
<td>93 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>10 (76.9)</td>
<td>3 (23.1)</td>
<td>13 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56 (52.8)</td>
<td>50 (47.2)</td>
<td>106 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio 0.29; 95 % C.I 0.07-1.13; P = 0.03
10 (76.9 %) of these babies with a positive HIV DNA PCR at six weeks were born to mothers not on PMTCT prophylaxis and three (23.1 %) were born to mother on PMTCT prophylaxis.

TABLE 7: MATERNAL HAART IN RELATION TO SIX WEEKS HIV PCR

<table>
<thead>
<tr>
<th>MATERNAL HAART</th>
<th>SIX WEEKS HIV PCR</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n (%)</td>
<td>Positive n (%)</td>
<td>Total n (%)</td>
</tr>
<tr>
<td>Yes</td>
<td>15 (83.3)</td>
<td>3 (16.7)</td>
<td>18 (100.0)</td>
</tr>
<tr>
<td>No</td>
<td>78 (88.6)</td>
<td>10 (11.4)</td>
<td>88 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>93 (87.7)</td>
<td>13 (12.3)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Odds ratio 0.64; 95 % CI 0.15-2.60; P = 0.26

4.2.3 HIV INFECTION OUTCOMES IN RELATION TO FEEDING MODE

Eight (7.5%) infants had a positive HIV DNA PCR test at birth and 13 (12.3 %) infants had a positive HIV DNA PCR test at six weeks of age. Five more infants in the study acquired HIV infection at six weeks of age, four in the breastfed group and only one in the formula fed group. The additional risk of HIV transmission through breastfeeding is estimated at 12.9 %.

TABLE 8: ACTUAL FEEDING PRACTICE IN RELATION TO BIRTH HIV PCR

<table>
<thead>
<tr>
<th>ACTUAL FEEDING PRACTICE</th>
<th>Birth HIV PCR</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n(%)</td>
<td>Positive n(%)</td>
<td>Total n(%)</td>
</tr>
<tr>
<td>Breastmilk</td>
<td>28 (90.3)</td>
<td>3 (9.7)</td>
<td>31 (100.0)</td>
</tr>
<tr>
<td>Formula</td>
<td>70 (93.3)</td>
<td>5 (6.7)</td>
<td>75 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (92.5)</td>
<td>8 (7.5)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Odds ratio 0.66; 95 % C.I. 0.14-2.97; P = 0.30
<table>
<thead>
<tr>
<th>ACTUAL FEEDING PRACTICE</th>
<th>SIX WEEKS HIV PCR</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative n(%)</td>
<td>Positive n(%)</td>
<td>Total n(%)</td>
</tr>
<tr>
<td>Breast milk</td>
<td>24 (77.4)</td>
<td>7 (3+4) (22.6)</td>
<td>31 (100.0)</td>
</tr>
<tr>
<td>Formula</td>
<td>69 (92.0)</td>
<td>6 (5+1) (8.0)</td>
<td>75 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>93 (87.7)</td>
<td>13 (12.3)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Odds ratio 0.29; 95% C.I 0.09-0.97; P = 0.02

4.2.4 **COMORBIDITIES**

Sepsis was the leading co morbidity (81 episodes) followed by hyaline membrane disease (75 episodes), pneumonia (56 episodes), necrotizing enterocolitis (41 episodes) and failure to thrive (11 episodes). The overall incidence of infant co morbidities according to feeding choice is presented in Figure 8.

Fig 8: Overall incidence of co morbidities by feeding modality

(Chi square 1.20, P=0.99)
During week one, hyaline membrane disease was the leading co morbidity (75 episodes) followed by sepsis (62 episodes) and pneumonia (31 episodes). There was a higher incidence of co morbidities in formula feeding arm compared to breastfeeding arm with hyaline membrane disease 52 vs. 23, sepsis 44 vs. 18 and pneumonia 25 vs. 6 % (p=0.48).

During week two, sepsis was the leading co morbidity (49 episodes) followed by necrotizing enterocolitis (35 episodes), pneumonia (30 episodes) and failure to thrive (10 episodes). There was a significant statistical difference between the two arms (p=0.02) with a higher incidence of co morbidities in the formula feeding arm compared to breastfeeding arm, sepsis 36 vs. 13, necrotizing enterocolitis 24 vs. 11, Pneumonia 20 vs. 10, and failure to thrive 8 vs. 2.

![Incidence of co morbidities by feeding modality during week two](image)

Fig 9: Incidence of co morbidities by feeding modality during week two

Chi square 0.91; P=0.02

During week four, sepsis was still the most common co morbidity (27 episodes) followed by pneumonia (20 episodes) and necrotizing enterocolitis (11 episodes). Formula feeding arm has higher incidence of co morbidities without statistical significance with sepsis 16 vs. 11, pneumonia 15 vs.5 and necrotizing enterocolitis 6 vs.5 (p=0.59).
Week six was characterized by a low incidence of co morbidities with no statistical significance between the two arms. Sepsis was the only co morbidity with 3 in breastfeeding arm vs. 4 in formula feeding arm (p=0.07).

4.3 MORTALITY

4.3.1 INFANT MORTALITY
Of the 120 enrolled infants, 14 (11.7%) died during the course of follow up, 10 (71.4 %) in the formula feeding arm vs. 4 (28.6%) in breastfeeding arm (p=0.49). Although there was no statistical significance, a trend of increased mortality was observed in the formula feeding arm compared to the breastfeeding arm.

13 (92.9 %) infants died during neonatal period vs.1 (7.1 %) during post neonatal period. Among deaths, four were early neonatal deaths and nine late neonatal deaths.

They were all HIV non infected at birth. Sepsis was the most common cause of death (71 %) followed by pneumonia (21 %) and severe hyaline membrane disease (8 %). Among the 10 diagnosed with sepsis, five were non specific sepsis, two were due to methicillin resistant staphylococcus aureus, one Candida non albicans, one Escherichia coli and one Enterococcus Faecalis. Six were formula fed and four breastfed.

4.3.2 MATERNAL MORTALITY
In the study population, four mothers died and were all in the formula feeding arm. Two had a CD4 count <200 and 2 unknown CD4 count. Their infants were all alive and non HIV infected at birth and six weeks of age.

The causes of maternal death were: sepsis in two mothers, one had severe eclampsia, one cardiac failure due to mitral valve disease.

4.4 SUMMARY OF RESULTS
The following results were statistically significant (p<0.05).

The HIV transmission rate was 12.3% at six weeks of age with an additional risk of HIV transmission through breastfeeding estimated at 12.9%.
HIV transmission was higher in the vaginal delivery group than in the Caesarian section group.

There was a significant difference in co morbidities between the two feeding arms during week two with sepsis as the leading co morbidity followed by necrotizing enterocolitis, pneumonia and failure to thrive.

There were no statistically significant differences (p>0.05) between the two arms in the following:
HIV infection rate at birth between the two arms.
Effect of maternal CD$_4$ count on HIV transmission at birth and at six weeks of age.
HIV transmission at birth or six weeks whether mother on HAART or not.
Co morbidities during week one, week four and week six.
Mortality and feeding modality.
5.1 SAMPLE SIZE
Compared to similar studies, the number of enrolled mother-infant pairs was low despite the extended period of enrollment. Mbori-Ngacha et al. (2001) followed up 425 mother-infant pairs in their study on morbidity and mortality in breastfed and formula fed infants of HIV-I infected women. Becquet et al. (2007) followed up 557 live born babies in a study on two year morbidity and mortality of infants born to HIV infected mothers. Thior et al. (2006) during a randomized trial comparing outcomes in breastfeeding mothers with formula feeding mothers followed up 1200 infants. All these studies were not limited to premature infants and the enrollment period was long.

In this study, there was no loss to follow up except for 14 infants who died during the course of the study. Most infants were still in neonatal unit during follow up.

5.2 DEMOGRAPHICS
The prevalence of formula feeding was high (70.8 %) compared to breastfeeding (29.2%), this was also observed in previous similar studies. Thior et al. (2006) had 602 infants in the formula feeding arm vs. 598 infants in the breastfeeding arm. Becquet et al. (2007) had a slightly higher number of infants in the formula feeding arm compared to the breastfeeding arm, respectively 295 vs 262. Mbori-Ngacha et al. (2001) had almost a similar number of infants in both arms, 186 infants in the formula feeding arm vs. 185 infants in the breastfeeding arm.

However, Otieno et al. (2007) in their study on HIV disease progression in breastfeeding and formula feeding mothers had a high prevalence of breastfeeding (198 mothers) compared to formula feeding (98 mothers).

In our study, the difference between the two arms might be related to our small sample size or biased counselling on feeding choice by health professionals. This could have influenced our results.
5.3 **HIV INFECTION**

In this study, breastfeeding was associated with higher rate of HIV transmission at six weeks compared to formula feeding with a statistical significance ($p=0.02$). The additional risk of transmission of HIV through breastfeeding was estimated at 12.9% in keeping with what Bertolli et al. (1996) estimated to be between 7-22%. Palombi et al. (2007) found a low HIV transmission rate at one month of age in the formula feeding arm (0.8%) compared to the breastfeeding arm (1.2%) but high HIV transmission rate at six months in the formula feeding arm (1.8%) compared to the breastfeeding arm (0.8%) ($p=0.38$). Formula feeding plus water filter option was inferior to the breastfeeding plus HAART option for a number of reasons; it was technically difficult and extremely expensive. Adherence to formula was poor because women mixed breast milk with formula.

Nduati et al. (2000) also found a high HIV infection rate at 24 months in the breastfeeding arm (36.7%) compared to the formula feeding arm (20.5%) ($p=0.01$). 44% of HIV infection in the breastfeeding arm was attributed to breast milk. Most breast milk transmission occurred early with 75% of the risk difference between the two arms occurring by six months.

Iliff et al. (2005) in their study on early exclusive breastfeeding to reduce the risk of postnatal HIV transmission observed a postnatal transmission rate of 3.9%, 7.7 and 12.1% at six, 12 and 18 months respectively. The overall positive HIV test after the six weeks negative test was 12.1% similar to the additional risk of HIV transmission through breastfeeding in our study (12.9%). Nduati et al. (2000) observed a HIV transmission rate of 16.2% through breastfeeding in their randomized clinical trial and majority of infections occurred early during breastfeeding.

Among variables associated with the risk of vertical transmission of HIV, low maternal CD$_4$ count was the primary maternal risk factor of HIV transmission to the infant. Paradoxically, our study did not show a statistical significance of the effect of maternal CD$_4$ count on HIV transmission, this might be due to a higher number of mothers with unknown CD$_4$ count results as shown in table 2 and 5 previously.
Vaginal delivery was associated with a higher HIV transmission rate at birth and six weeks of age with a statistical significance (p=0.02 at birth and p=0.03 at six weeks) as described in previous studies (European Mode of Delivery Collaboration, 1999).

Maternal HAART was associated with reduced HIV transmission rate at birth and six weeks of age, although there was no statistical significance.

5.4 **CO MORBIDITIES**

The study results are consistent with previously published observational studies in which breast milk has been most protective against co morbidities in the first three months of life compared to formula feeding. (Coutsoudis et al., 2003). An overall increased incidence of co morbidities was observed in the formula feeding arm with sepsis as the leading co morbidity. The South African Vit A study on morbidity in children born to women infected with HIV according to feeding modality showed that 60 % of infants who were never breastfed had three or more morbidity episodes compared with 32 % of breastfed children (p=0.05). During the first two months of life, never breastfed infant (regardless of HIV status) were nearly twice as likely to have an illness episode than the breastfed infant (p=0.006)(Coutsoudis et al., 2003).

However, other studies did not find the same observations. Becquet et al.(2007) observed similar morbidity at two years between breastfed and formula fed infants. The duration of breastfeeding was four months, the two year probability of presenting with a severe event was the same among formula fed (14 %) and short term breastfed children (15 %)(p=0.44).

Because prematurity was the main reason for admission to the neonatal unit, HMD was the leading co morbidity during the first week. We found a significant statistical difference in co morbidities in week two between the two feeding modalities(p=0.02) with sepsis as the leading co morbidity in formula feeding arm as compared to breastfeeding arm. Formula feeding seemed to potentiate the inherent lack of immunity in premature HIV exposed babies. Necrotizing enterocolitis was the second co morbidity during week two, this was expected in keeping with its natural history of late onset (2nd, 3rd week) in premature infants with formula as a risk factor.
There was a trend for the breastfeeding arm to have better nutritional status than Formula feeding arm: Failure to thrive occurred in 7.5 % of Formula fed infants vs. 1.8 % breastfed infants with a statistical significance during week two (p=0.02).

5.5 **MORTALITY**

Although there was no statistical significance (p=0.49), formula feeding was associated with an increased risks of dying during the first six weeks of life (71.4 % vs. 28.6 %). This has been described in previous studies like 1.0 % mortality in breastfed infants vs. 3.9 % in formula fed infants in a study done in Kenya (Rollins et al., 2007).

Thior et al.(2006) in the Mashi study observed more deaths in the formula feeding arm compared to the breastfeeding arm. The cumulative incidence of infant death was significantly higher in the formula-fed group up to seven months of age (p=0.003). The increased mortality was mostly due to common infections of infancy. By seven months of age 9.3 % infants died in the formula feeding arm compared to 4.9 % in the breastfeeding arm. Mbori-Ngacha et al.(2001) observed similar two year mortality rates in the formula feeding arm (20.0 %) compared to the breastfeeding arm (24.4 %) (95% confidence interval 0.5-1.3) even after adjusting for HIV-I infection status (95 % confidence interval 0.7-1.7). Nduati et al.(2000) also found similar two years mortality rates in both arms (24.4 % in the breastfeeding vs. 20.0 % in formula feeding arms, p=0.01).

Intrauterine/Peripartum infection seems not to increase mortality in our study as opposed to a study done in Zambia (Matthew et al., 2008) where 20 % of intrauterine/peripartum group dies by 100 days vs. 10 % of postpartum group. All infants who died in our study were HIV negative at birth. Feeding modality and prematurity were associated with poor infant outcomes. All infants who died were below 30 weeks gestational age and majority was in formula feeding arm.

5.6 **SUMMARY**

The study results are similar to previously published studies. The majority of mother choose formula feeding than breastfeeding. The additional risk of HIV transmission through breastfeeding was 12.9% and formula feeding was associated with increased co morbidades and mortality.
CHAPTER 6
CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS
6.1.1 THE MAIN OBJECTIVE
The main objective of the study was to determine the HIV infection rate of premature babies of less than 1500g born to HIV-I infected mothers at Dr George Mukhari Academic Hospital at birth and at six weeks of age using the HIV DNA PCR test.

The HIV transmission rate was 7.5 % at birth and 12.3 % at six weeks of age with an additional risk of HIV transmission through breastfeeding estimated at 12.9 %. Vaginal delivery was associated with an increased risk of HIV transmission at birth and six weeks of age. The higher number of mothers without CD4 count results and the smaller number of mothers on HAART in our study population might have influenced the non significance of these risk factors on HIV transmission rate.

6.1.2 THE SECOND OBJECTIVE
The second objective was to determine co morbidities in general and in relation to feeding modality. An overall increased incidence of co morbidities was observed in the formula feeding arm compared to the breastfeeding arm. A statistically significant difference in co morbidity between the two arms was observed during the second week of life with sepsis as the leading co morbidity followed by necrotizing enterocolitis, pneumonia and failure to thrive.

6.2 RECOMMENDATIONS
6.2.1 RECOMMENDATIONS FROM STUDY
The HIV transmission rate is high in premature infants. Breastfeeding is associated with an increased risk of post natal HIV transmission and formula feeding is associated with increased co morbidities and mortality.

Health Care personnel should provide high quality, unambiguous, unbiased information about the risk of HIV transmission through breastfeeding and risks of Formula feeding to enable women to make the feeding choice that will maximize HIV free survival of their infants.
6.2.2 RECOMMENDATIONS FOR FUTURE STUDIES

We recommend that a larger sample of mother-infant pairs be followed up to make the results more applicable to the general population.
REFERENCES:


Policy and Guidelines for the implementation of the PMTCT programme in South Africa. National Department of Health.  


APPENDIX 1

AFASS CRITERIA

Acceptable: the mother perceives no barrier to choosing and executing the option for cultural or social reason, or for fear of stigma and discrimination.

Feasible: The mother (or family) has adequate time, knowledge, skills and other resources to prepare and feed the infant and the support to cope with family, community and social pressures.

Affordable: The mother and family, with available community and/or health system support, can pay for the purchase/production, preparation and use of the feeding option, including all ingredient, fuel and clear water and equipment without compromising the health and nutrition spending of the family.

Sustainable: Availability of a continuous and uninterrupted supply and dependable system of distribution for all ingredient and commodities need to safely implement the feeding option, for as long as the infant needs it.

Safe: Formula/milk would be correctly and hygienically prepared by clean hands, using clean, safe and clear utensils. Nutritionally adequate quantities of formula milk would be regularly available, clear water and food would be regularly available and formula milk would be fed using clean hands and utensils and preferably with cups rather than bottles.
INTRODUCTION.

I am Dr Mudibo Musasa. I am conducting research on the assessment of outcomes from birth to six weeks in premature babies of less than 1500 g born to HIV infected mothers at Dr George Mukhari hospital in the Paediatric Department. This information leaflet will help you decide whether you agree to take part in the study or not. Before you decide to take part, you should understand what the study involves and ask questions if you need more information.

THE AIM AND OBJECTIVES OF THE STUDY

To determine the rate of HIV infection both at birth and at six weeks of age in premature babies of less than 1500g born to HIV infected mothers.

To determine the effect of feeding choice on the baby's health status.

WHO WILL BE INVOLVED IN THE STUDY?

Premature babies of less than 1500 g born to HIV infected mothers, admitted at Dr George Mukhari hospital or discharged and attending neonatal clinic.

WHAT DOES THE STUDY INVOLVE?

If you agree to participate in this study, it will be voluntarily and you will not be forced to answer any questions if you don’t want to. You are also free to withdraw from the study at anytime if you wish without giving reasons. You will not be pressurised to participate. This study will have no influence on the regular treatment and care that holds for your baby condition.
If you decide to participate, you will be enrolled in the study and every information will be kept confidential. Your baby will be assessed at birth, one week, two weeks, four weeks and six weeks while still in hospital or being discharged and attending neonatal clinic to determine the HIV status of the baby and the effect of feeding choice on the baby’s health status. The continuous assessment of your baby will include weighing your baby, examining for illnesses and taking blood samples for HIV testing.

**WHAT ARE THE POSSIBLE RISK OF BEING IN THE STUDY?**

No risks are anticipated.

**WHAT ARE THE POSSIBLE BENEFITS OF BEING IN THE STUDY?**

As an observational study, no benefits are expected.

**PRIVACY AND CONFIDENTIALITY**

The information obtained from your baby’s file will be kept confidential. Data that will be reported will not include any information which identifies you as participant in the study. Results of the study will be used for further scientific studies without your identity being divulged.

**ETHICAL CONSIDERATIONS**

This research will be conducted after approval by the Medunsa Research Ethics committee. You will be asked to sign an informed consent form to acknowledge your decision to participate in the study.

**Contact person: Dr. M. Musasa. Cell 0827095720**
MOMELLO YA 2

TOKOMANA YA TSHEDIMOSETSO KA GA GO TSAYA KAROLO MO THUTO PATLISISONG

SETLHOGO SA THUTO-PATLISISO

TEKANYETSO YA DIMORAGO MO MASEENG A A SA TSWANG GO BELEGWA GO FITLHA

GO A DIBEKE TSE THATARO A A BELEGWANG PELE GA NAKO A BOIMA JO BO KWA

TLASE GA 1500G, A BELEGWA KE BATSETSI BA BA NANG LE TSHWAETSO YA HIV.

MATSENO

Ke nna Dr Mudibo Musasa. Ke dira dipatlisiso ka ga go lekanyetsa dimorago mo maseeng a a sa tswang go belegwa go fitlha go a dibeke tse thataro a a belegwang pele ga nako, a boima jo bo kwa tlase ga 1500g, a belegwa ke batsetsi ba ba nang le tshwaetso ya HIV mo sepetleng se sa Dr George Mukhari, mo lefapheng la tsa masea. Tokamana e ya tshedimosetso e ya go go thusa gore o tseye tshwentso ya go tsaya karolo kgotsa nnyaa. Pele o tsaya tshwentso ya go tsaya karolo, o tshwanetse go tlhaloganya se thuto-patlisiso e se akaretsang, le go botsa dipotso fa o tlhoka tshedimosetso.

MAITHHOMO LE MAIKAELELO A THUTO-PATLISISO

Go lekanyetsa boemo jwa tshwaetso ya HIV mo maseeng a a sa tswang go belegwa le a dibeke tse thataro a a belegwang pele ga nako a boima jwa 1500g ke batsetsi ba ba nang le tshwaetso ya HIV.

Go lekanyetsa kamego ya mofuta wa phepo ya lesea mo maemong a gagwe a pholo.

BATSAYA KAROLO MO THUTO-PATLISISONG KE BOMANG?

Masea a a belegwang pele ga nako a boima jo bo kwa tlase ga 1500 g ke batsetsi ba ba nang le tshwaetso ya HIV mo sepetleleng sa Dr George Mukhari bo le mo sepetlele kgotsa ba tsamaya kliniki ya bana.

THUTO-PATLISIISO E AKARETSA ENG?

Fa o dumela go tsaya karolo mo thuto-patlisisong e, e tla bo e le ka go ithaopa, e bile ga o ne o patelediwa go araba dipotso fa o sa battle.O lokologile go ikogela morago nako nngwe le nngwe fa o eletsa jalo kwa
ntle ga go lebaka /mabaka. Ga o gatebwe go tsaya karolo. Thuto-patlisiso e ga e na tlhotheletso epe mo kalafing le thokomelo e lesea la gago le leng mo go yoneka tsa kalafi.

Fa o dumela go tsaya karolo, o ya go kwadisiwa mo thuto-patlisisong e bile tshwaelo nngwe le nngwe e ya go nna khupamarama /sephiri. Lesea la gago le ya go lekanyediwa fa le belegwa, fa le fetsa beke ya ntlha, ya bobedi, ya bone le ya borataro mo sepetlele sa Dr George Mukhari kgotsa o le tsamaisa kliniki ya bana mo go sone sepetelele se, go lekanyetsa boemo jwa tshwaetsa ya HIV mo go lone, le kamego ya mofuta wa phepo ya lona mo pholog ya lesea. Tswelediso ya tekanyetsa ya lesea la gago e ya go akaretsa go mo kala, go tlhatlhoba malwetsi a a ka nnang teng, le go tsaya dikao madi go tlhatlhobela HIV.

KE MATSHOSETSIS AFE A A KA TLHAGELANG LESEA MO GO TSEYENG KAROLO?
Ga go matshosetsi a a lebeletsweng.

KE DIPOELO DIFE TSE KE DI SOLOFELANG?
Thuto-patlisiso e key a tshekatsheko fela, ka jalo ga go dipelo dipe tse di ka solofelwang.

BOSEPHIRI LE KHUPAMARAMA
Tshedimosetso e e yang go tsewa mo faeleng ya lesea la gago e ya go nna sephiri. Tse di yang go begwa mabapi le diphitlhello, ga di na go senola wena kgotsa lesea e le batsaya karolo. Dipholo tsa thuto-patlisiso di ya go dirisediwa dipatlisiso tsa tsa saense mo nakong e e tlang, ntle le go pepentsha leina la gago kgotsa la lesea.

TSA TSA SETHO
Thuto-patlisiso e e ya go tsamaisiwa morago ga go fiwa tetla ya tiriso ke komiti ya Medunsa ya tsadithuto-patlisiso le diphasalatso ya tsa setho.O ya go kopiwa go saena foromo ya tulumano ka kutlwisiso go tiisa tshwetsa ya gago go tsaya karolomo thuto-patlisison

Ikgolaganye le Dr M. Musasa mo : 0827095720.
APPENDIX 3

CONSENT FORM.

Statement concerning participation in the study.

Name of Project

Assessment of outcomes from birth to six weeks in premature babies of less than 1500 g born to HIV-1 infected mothers at Dr George Mukhari Hospital.

I have read the information on / or* heard the aims and objectives of the proposed study and was provided the opportunity to ask questions and given adequate time to rethink the issue. The aim and objectives of the Study are sufficiently clear to me. I have not been pressurised to participate in any way.

I understand that participation in this Project is completely voluntary and that I may withdraw from it or withdraw my permission for review of my child’s medical record at any time and without supplying reasons. This will have no influence on the regular treatment that holds for my child’s condition neither will it influence the care that I or my child receives from my regular doctor.

I know that this Study has been approved by the Research, Ethics and Publications Committee of Medunsa / Dr George Mukhari Hospital. I am fully aware that the result of this Study will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in the Study and for my child’s medical record to be reviewed:

..............................................................................................................
Name of patient
..............................................................................................................
Signature of patient or guardian

..............................................................................................................
Place
..............................................................................................................
Date
..............................................................................................................
Witness

Statement by the researcher
I provide verbal and/or written* information regarding this study.
I agree to answer any future questions concerning the Study as best as I am able.
I will adhere to the approved protocol.

..............................................................................................................
Name of Researcher
..............................................................................................................
Signature
..............................................................................................................
Date
..............................................................................................................
Place

Delete whatever is not applicable.
MOMELLO YA 3

TOKOMA YA TUMELANO KA KUTWISISO GO TSAYA KAROLO MO THUTO-PATLISISONG

SE TLHOGO SA THUTO-PATLISISO

TEKANYAETSO YA DIMORAGO MO MASEENG A A SA TSWANG GO BELEGWA GO FITLHA GO A DIBEKE TSE THATARO A A BELEGWANG PELE GA NAKO A BOIMA JO BO KWA TLASE GA 1500g, A BELEGWA KE BATSETSBA BA BA NANG LE TSHWAETSO YA HIV.

Ke buisitse / ke utlwile maikaelelo le maitlhomo a thuto-patlisiso e e tshitshintsweng e. Ke filwe sebaka le tetla ya go botsa dipotso, ka be ka fiwa nako ya go naganisisa lebaka le. Ke tlhaloganya sentle maikaelelo le maitlhomo a thuto-patlisiso e. Ga ke a gatellwa ka gope gore ke tseye karolo.

Ke tlhaloganya gore go tsaya karolo ga me mo thuto-patlisisong e, ke ka go ithaopa, e bile ke ka ikgogela morago mo go tseyeng karolo nako nngwe le nngwe kwa ntle ga go fa lebaka. Se ga se kitla se nna le kgoreletso kgosla tlhotlheletso epe mo go tsa ngwana / lesea tsa tlwaelo tsa kalafi, le fa e le go kgoreletsatlhokomela e a e amogelang go tswana go ngaka ya ngwana ya tlwaelo.

Ke itse gore thuto-patlisiso e, e reboetswe tiriso ke komiti ya Medunsa ya tsa dithuto-patlisiso le diphasalatso ya tsa setho. Ke lemoga ka botlalo gore dipholo tsa thuto-patlisiso e di ya go dirisediwa tsa saense, le gore di ka phasaladiwa. Ke dumelana le se, fa fela ke tiisediwa gore tsotlhe e ya go nna sephiri.

Ke dumelana le go tsaya karolo mo thuto-patlisisong e.

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Leina la motsetsi    Saena    Lefelo    Letlha    Paki

Bopaki ka mmatlisisi

Ke file tshedimosetso ka molomo/ ka bokomana ya tshedimosetso mabapi le thuto-patlisiso e. Ke dumela go tla araba dipotso dife kappa dife tse di amanang le thuto-patlisiso e, ka moo ke ka kgonang.

Ke tla tshegetsatsotlhe ka ga thuto-patlisiso e e reboletswang tiriso.

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Leina la mmatlisisi    Saena    Letlha

51
# APPENDIX 4

## RECORD SHEET

**STUDY NUMBER:**

### 1. Mother

<table>
<thead>
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<th>Parity</th>
<th>Gravidity</th>
<th>Stillborn Abortion</th>
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<tr>
<td>CD 4 Count</td>
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<td>HAART</td>
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<tr>
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<td>Review date after DIC</td>
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### 2. Baby

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<td></td>
<td>Gestational Age (weeks)</td>
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<td>AZT</td>
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<td></td>
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<tr>
<td>Feeding Choice</td>
<td>Breast milk</td>
<td>Formula</td>
<td></td>
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</tr>
<tr>
<td>Actual feeding practice</td>
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<td>Formula</td>
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<td>HIV PCR at birth</td>
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<tr>
<td>Weight</td>
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<td>2 weeks</td>
<td>4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Co-Morbidities</td>
<td>1 week</td>
<td>2 weeks</td>
<td>4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>HIV PCR at 6 weeks</td>
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<td>Negative</td>
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<td></td>
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<tr>
<td>Outcome</td>
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<td>Dead (time + cause)</td>
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</table>
MEETING: 08/2009

PROJECT NUMBER: MREC/M215/2009; PG.

PROJECT:

Title: Assessment of outcomes from birth to six weeks in premature babies of less than 1500g born to HIV+ infected mother at Dr George Mukhari Hospital in Paediatric Department.

Researcher: Dr M Musasa
Supervisor: Dr M Mavulu (Paediatrics and Child Health)
Hospital Superintendent: Dr Nathan (Dr George Mukhari Hospital)
Department: Paediatrics and Child Health
School: Medicine
Degree: M MED (Paeds)

DECISION OF THE COMMITTEE:

MREC approved the project.

DATE: 07 October 2009

Note:

1) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.

2) The budget for the research will be considered separately from the protocol. PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.