

**A Retrospective Analysis  
of  
Prevention of Mother to Child Transmission  
(PMTCT)  
outcomes in a group of infants  
attending  
Paediatric Practices in Central Durban**

**submitted to**

**NELSON R MANDELA SCHOOL OF MEDICINE  
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**In partial fulfilment of the academic requirements for the degree  
Master of Public Health**

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## ABSTRACT

The vast majority of paediatric HIV occurs in sub-Saharan Africa and could be averted through implementation of effective Prevention of Mother to Child Transmission (PMTCT) strategies. At the United Nations General Assembly Special Session on HIV/AIDS in 2001, members committed themselves to the goal of reducing paediatric HIV by 20% by 2005 and by 50% by 2010. In South Africa, rates of HIV infection range between 28% in KwaZulu-Natal and 16% in the Western Cape. The South African National Department of Health has, over the past few years, phased in a comprehensive package for PMTCT of HIV. KwaZulu-Natal implemented its programme in 2002. The South African private healthcare sector follows guidelines of those of developed countries for PMTCT. Not much data is available of the outcome of infants born to HIV positive mothers managed in private practice. In view of this, the present study aimed to assess success or otherwise of PMTCT in private paediatric practice in South Africa.

Eight of the 20 private paediatricians, in the central region of Ethekeweni Metro of KwaZulu-Natal (Durban Central Area), agreed to participate in a retrospective study. Data for all their HIV exposed infants between January 2004 and June 2005 were reviewed. One hundred and one Black African infants were born to 100 HIV positive women aged 29.85 years (SD 5.38; range 18-44 years). The median CD4 count was 426 (IQR 244-613). The median viral load at first presentation was 3.97 logs (IQR 1.6-5.8) or 11 391 copies/ml (IQR 2 013-41 502). Eighty six women had HAART, nine had other antiretroviral therapy and five had no prophylaxis. Treatment started before 34 weeks in 72 women. There were 93 caesarean sections.

There were 20 low birth weight neonates, 18 were preterm and all had been formula fed and received AZT for six weeks. Of the 92 tested, two (one preterm) were positive. Although caesarean deliveries, both these mothers had not adhered to the optimal treatment protocol. Of the rest, eight did not return for HIV testing and one died (the only neonatal death). This death was unlikely to have been HIV related. The transmission rate of less than one percent in those women who followed the protocol optimally is much better than that in the SA public sector, and is consistent with transmission rates in the developed world.

## **DECLARATION**

This Master of Public Health dissertation is my own work and all primary and secondary sources have been appropriately acknowledged. The dissertation has not been submitted to any other institution as part of an academic qualification.

This dissertation is prepared in partial fulfilment of the requirement of the Master of Public Health degree at the School of Family and Public Health Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa.

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## ACRONYMS AND ABBREVIATIONS

AfA	Aid for AIDS
AGA	Appropriate for gestational age
AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal clinic
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT	Zidovudine
CDC	Centres for Disease Control and Prevention
ELISA	Enzyme linked immunosorbent assay
HAART	Highly active anti retroviral therapy
Hb	Haemoglobin
HIV	Human immunodeficiency Virus
IQR	Interquartile range
IUGR	Intrauterine growth retardation
KZN	KwaZulu-Natal
MDGs	Millennium Development Goals
MTCT	Mother to Child transmission of HIV
NVP	Nevirapine
PCP	Pneumocystis jirovecii pneumonia
PCR	Polymerase Chain Reaction
PIH	Pregnancy induced Hypertension
PMTCT	Prevention of mother to child transmission
sdNVP	Single dose Nevirapine
3TC	Lamivudine
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNGASS	United Nations General Assembly Special Session
UK	United Kingdom
USA	United States of America
VCT	Voluntary Counselling and Testing

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# **CHAPTER 1**

## **INTRODUCTION AND LITERATURE REVIEW**

## 1.1 Introduction

Since the beginning of the HIV/AIDS epidemic, almost two and a half decades ago, it continues to take its devastating toll, wreaking havoc as it continues to march unrelentingly. During 2007 alone, 33 million people were living with HIV/AIDS.<sup>1</sup> Sub-Saharan Africa is worst hit by this catastrophe where a quarter of a million people are living with HIV/AIDS.<sup>2</sup> Every day a staggering six thousand people die in Africa of AIDS and its related complications. Sadly, last year 2.7 million people had become newly infected with HIV. Its social and economic consequences are widely felt, in all sectors of society such as health, education, industry, agriculture, transport, human resources and the economy. In Africa, HIV/AIDS is not just a health issue. It poses a barrier to development, halting and reversing decades of progress. It affects every part of life, community and development.<sup>2</sup>

Almost 40% of the population in Botswana and Swaziland are living with HIV/AIDS. South Africa with its estimated 5.7 million people living with HIV has the largest number of infections in the world. Estimates suggest 18.1% of adults (15-49 years) were living with HIV in 2007, 3.1 million of them women.<sup>2</sup> Unfortunately there is no sign yet of a decline in the epidemic. More than half (55%) of all South Africans infected with HIV live in the KwaZulu-Natal (KZN) and Gauteng provinces. KZN has consistently reported the highest HIV prevalence in the country. The national HIV prevalence estimate stands at 28.0% (CI:26.9%-29.1%). HIV prevalence among pregnant women in the various provinces is as follows KwaZulu-Natal (39%) highest, Northern Cape (15%) lowest, Western Cape (16%) and Limpopo (19%).<sup>3</sup>

Children are the innocent victims of this deadly epidemic. Last year, just over a quarter of a million children died of HIV/AIDS. Currently there are 2 million children infected with HIV in the world. In more than nine times out of ten, children become infected with HIV through mother to child transmission (MTCT). The tragedy is that although we presently have the knowledge and the means of preventive measures, to cut down drastically on this terrible situation, yet the figures continue to rise.<sup>4</sup>

The vast majority of paediatric HIV occurs in sub-Saharan Africa and could be largely averted through effective use of MTCT prevention strategies. HIV-infected newborns are becoming uncommon in the USA and Europe.<sup>1</sup> At the United Nations General Assembly Special Session (UNGASS) on HIV/AIDS in 2001, member states committed themselves to the goal of reducing the proportion of infants infected with HIV by 20% by 2005 and by 50% by 2010.<sup>5</sup>

The achievement of three of the Millennium Development Goals (MDGs) to be met by 2015 is directly linked to reducing vertical transmission of HIV as follows:

- 4<sup>th</sup> MDG: Reduce by two thirds the mortality rate among children under five.
- 5<sup>th</sup> MDG: Reduce by three quarters the maternal mortality ratio.
- 6<sup>th</sup> MDG: Halt and begin to reverse the spread of HIV/AIDS.<sup>6</sup>

HIV transmission from infected mother to the infants takes place in utero, intrapartum, and postnatally through breastfeeding. The in utero rate is 5-10%, intrapartum rate is 10-20%, and the postnatal (breastfeeding) rates vary according to the duration of breastfeeding. In the absence of any preventative strategy there is a 30-45% possibility of overall vertical transmission in developing countries.<sup>4</sup>

The risk of MTCT is affected by a number of factors, maternal, foetal, viral and behavioural. The main maternal factors are advanced disease, high viral load, and HIV infection acquired during pregnancy or breastfeeding and sexually transmitted disease. The obstetric factors are vaginal delivery as opposed to caesarean, prolonged rupture of membranes, invasive procedures and episiotomy. The infant factors are prematurity, breastfeeding and lesions of skin and/or mucous membranes.<sup>7</sup>

Prevention of Mother to Child Transmission (PMTCT) of HIV encompasses the following aspects:

- Primary prevention of HIV infection among parents to be.
- Prevention of unwanted pregnancies. A cost-effectiveness study of PMTCT in eight African countries demonstrated that lowering HIV prevalence among women by

1.25% or reducing unintended pregnancies among HIV-infected women by 16%, yielded an equivalent reduction in HIV-infected infant transmissions to that achieved by PMTCT using single-dose nevirapine (sdNVP).<sup>4</sup>

- Prevention of viral transmission from mother to child as part of routine antenatal care. This PMTCT is achieved by various approaches: antiretroviral prophylaxis for the mother, prophylaxis to the infants, implementation of safe delivery practices, and use of safe alternatives to breastfeeding.
- The provision of treatment, care and support occurs not only for the HIV-infected mother but should include their infants and family. This must be fully integrated into ongoing efforts to improve maternal and child health services, and be tailored to the needs of women for safe and effective antenatal, obstetric and reproductive health services.

## **1.2 Prevention Trials**

### **1.2.1 Developed Countries**

In 1994, administration of zidovudine (AZT) to the mother during pregnancy and labour, and to the infants was shown to reduce perinatal transmission.<sup>8,9</sup> The AZT regimen started from 14 to 34 weeks and it included antepartum AZT (100 mg orally five times daily), intrapartum AZT (2 mg/kg given intravenously over a one-hour period, then 1 mg/kg per hour until delivery), and AZT for the newborn (2 mg/kg orally every six hours for six weeks). A regimen consisting of AZT given antepartum and intrapartum to the mother and to the newborn for six weeks reduced the risk of MTCT HIV transmission by approximately two thirds (68%). This study was crucial in establishing the principle of ARV usage.<sup>10</sup>

Incorporation of this regimen into clinical practice in the USA and other more developed countries, and avoidance of breastfeeding, resulted in falling perinatal transmission rates to as low as 2-4%. Further decrease in transmission rates of 2% or less had been reported when AZT was combined with elective caesarean delivery or when women were treated

with combination antiretroviral (ARV) regimens that reduce maternal viral load to undetectable levels.<sup>11</sup>

The Women and Infants Transmission Study demonstrated that very low rates of vertical transmission were achievable with the use of highly active antiretroviral therapy (HAART). The protective effect of therapy increased with the complexity and duration of the regimen.<sup>12</sup> The more recent European Collaborative Study added that caesarean section delivery to all HIV-infected women, even in areas where HAART is available, is appropriate clinical management, especially for persons with detectable viral loads.<sup>13</sup>

Some of the developed countries have reached a stage where elimination of paediatric HIV can be contemplated. For example, in Sweden vertical transmission fell from 24.7% in 1985-1993 to 5.7% in 1994-1998 and 0.6% in 1999-2003.<sup>14</sup> PMTCT uptake increased from 2.3% to 91.6% during the same period, and the elective caesarean delivery rate increased from 8.0% to 80.3%. No vertical transmission of HIV occurred in Sweden after 1999.

### **1.2.2 Developing countries**

In less developed countries the situation is vastly different. The above regimens were far too expensive at that time. The complex nature of their usage was also a barrier for the majority of the public. Trials over the past decade have now proven the efficacy of several ARV interventions. Several simpler, more affordable short ARV regimens have been shown to decrease vertical transmission in less resourced countries, with reduced but persistent efficacy in breastfeeding populations.<sup>4</sup> Studies in Thailand among non-breastfeeding populations and in Africa among breastfeeding populations informed the decisions for ARV usage in the developing countries.

Among non-breastfeeding women the short course CDC Thai regimen using AZT from week 36 of pregnancy through labour and delivery, reduced transmission to 9.4% at six months with a 50.1% absolute reduction.<sup>15</sup> Other studies also using AZT, compared different duration of AZT given to the women and infants. These studies suggested that in utero transmission was significantly higher with shorter maternal treatment (5.1%) than

with longer maternal treatment (1.6%) and, although beneficial, longer duration of treatment to the infants could not substitute for longer treatment of the mother.<sup>16</sup>

Lallemant et al. used AZT from 28 weeks of pregnancy and combined this with sdNVP given to either the women during labour and delivery or to the newborn. The transmission rate at 6 months was as low as 1.1%.<sup>17</sup> Mandelbrot et al. using combination ARVs, AZT and lamivudine (3TC) reduced transmission to 1.6%.<sup>18</sup> In Thailand, a study starting AZT a little later (34-36 weeks) in pregnancy was less successful with a transmission of 4.6% at 4 months.<sup>19</sup>

The Petra study was a randomised, double-blind, placebo-controlled trial that examined the efficacy of three short-course regimens of AZT and 3TC in Tanzania, South Africa, and Uganda. Here the long term benefits were lost due to the increased risk of transmission from breastfeeding.<sup>20</sup>

The South African Intrapartum Nevirapine Trial (SAINT) study had a successful outcome. It used a simple, inexpensive regimen of NVP, given at the onset of labour, and demonstrated an efficacy similar to a combination of AZT and 3TC.<sup>21</sup>

The landmark HIVNET 012 study in 1999 established that a short intrapartum and neonatal regimen of sdNVP to the mother at onset of labour, and to the infants within 72 hours of birth, reduced the risk of perinatal HIV transmission among breastfeeding women in Uganda by 47% at 14-16 weeks and by 41% at 18 months compared to a short intrapartum/neonatal regimen of AZT.<sup>22, 23</sup> This trial was hailed as a boon to most of the affected countries in the third world because of simplicity, safety, affordability and effectiveness of the regimen.

However, subsequent problems arise in that the regimen renders the women or infants more susceptible to the development of NVP resistant strains of HIV. Factors found to relate to the development of resistance are: NVP's long half-life, high maternal viral load, low CD4

counts, HIV subtype (Clade C>A>D), more maternal doses of NVP with shorter intervals between administration of the drug.<sup>4, 24</sup>

Trials which have continued using combination ARVS, after the above studies had been done, showed improved efficacies. It has been reported that in West Africa, a combination of AZT from 36 weeks and sdNVP obtained a transmission rate of 6.5% at 4-6 weeks, and 4.7% with the addition of 3TC from 36 weeks. With AZT alone the transmission was 14.7% at 4-6 weeks.<sup>4, 8</sup>

In summary, shorter courses of ARVs do reduce perinatal MTCT and are appropriate for developing countries. However, longer ARV prophylaxis (from about 28 weeks) through labour and delivery, and into the postpartum period, is more effective than shorter antepartum courses. Combination ARVs improved outcome over single ARVs.

As reported by Coovadia, a 2004 review of PMTCT trials in developing countries by the Ghent Group concluded that the most frequently used ARVs were AZT, AZT and 3TC, and NVP. They also concluded that with ARV the MTCT rates fell from 30-45% to 16-23%.<sup>8</sup>

Because of its simplicity and efficacy, sdNVP was initially adopted as the standard of care in resource-limited countries worldwide and had been endorsed by UNAIDS and many other international health organizations. NVP still has a role in PMTCT programmes in poor countries where complex regimens may be unavailable.<sup>4</sup>

Many less developed countries are having difficulty in implementing even these simpler regimens. Challenges include inadequate basic maternal child healthcare infrastructure, lack of prenatal HIV counselling and testing programmes, attitudes of healthcare workers and severely limited resources.

The World Health Organization (WHO) first issued recommendations for the use of ARV drugs for PMTCT in 2000. In 2006, the guidelines were updated to incorporate new evidence and were aligned with the global commitment to universal access; integration of

PMTCT into general health care delivery, the use of highly effective regimens to reduce HIV, and prioritizing women's health in decisions about ARV treatment during pregnancy.<sup>25</sup>

The criteria for commencing pregnant women on ARV treatment recommends that women in stage 3, or with a CD4 count of 350, should be initiated on ARV treatment. A prophylactic regimen that includes maternal AZT (from 28 weeks of pregnancy or as soon as possible thereafter) plus sdNVP, and a 7-day tail of AZT and 3TC is recommended. The infant regimen includes a one-week course of AZT.

### **1.3 PMTCT in South Africa**

#### **1.3.1 The Public Healthcare Sector**

South Africa has an estimated one million deliveries annually. Working on an average 25% HIV prevalence rate, this translates to almost a quarter of a million HIV positive pregnant women.<sup>3,7</sup> South Africa has considerably more resources than other sub-Saharan countries, but the government has been extremely resistant to implementing a programme to prevent MTCT of HIV.

In the early 2000s the country had been shrouded in a veil of controversy sparked by ex President Thabo Mbeki's flirtation with the denialist view that HIV might not cause AIDS, and that AIDS medications were toxic and inviting foreign AIDS denialist to advise his government.<sup>26</sup> Although the successful outcome of the SAINT study had been supported by the drug manufacturer's offer of free NVP for the PMTCT in developing countries there was a delay in implementation of such policy in South Africa. AIDS experts criticized the health ministry for this delay. The Treatment Action Campaign, a non governmental AIDS activist group, confronted the South African government in court in 2002 for not making MTCT prevention available to pregnant women.<sup>27</sup> It won this case on the basis of the South African constitutional guarantee of the right to health care, and the government was ordered to provide MTCT programs in public clinics.

South African National Department of Health has, over the past few years, phased in a comprehensive package for PMTCT. KZN implemented its programme in 2002. The main regimen used for PMTCT in the public sector had been sdNVP which is given during labour and a single dose to the baby within 72 hours of birth. Recently, the Department of Health revised its PMTCT guidelines to dual therapy as follows: AZT is given to the women from 28 weeks and sdNVP and AZT is administered at onset of labour. The infants are offered sdNVP and AZT for 7 days. If the maternal CD4 < 200 or there is suboptimal maternal ARV then the infant gets AZT for 1 month in addition to the sdNVP. If the maternal CD4 < 200 then HAART is initiated for her treatment.<sup>28</sup>

A few studies have described the operational effectiveness of PMTCT programmes in South Africa. The 2002 evaluation of South Africa's PMTCT of HIV reported that of 50% of HIV exposed infants followed up, 18% tested positive for HIV.<sup>29</sup> In Johannesburg a lower vertical transmission rate of 8.7% was reported in 2002.<sup>30</sup> A study in KZN in 2006 estimated a vertical transmission rate of HIV at 20.8% (CI:18.2%-23.6%) despite the availability of NVP.<sup>31</sup>

The Western Cape, which implemented the dual drug therapy of short-course AZT and sdNVP, reported a MTCT rate of 8.8% in 2003.<sup>32,33</sup> Thus far the most promising reduction in vertical transmission to 2.9% has come from the McCord PMTCT programme, a smaller, non-governmental project in KZN.<sup>34</sup> Some 44% of these women had had low enough CD4 cell counts to receive HAART while pregnant. Ninety eight percent of the infants had received NVP and 75% AZT as well.

### 1.3.2 The Private Healthcare Sector

South Africa spends a relatively large amount (8.4%) of its gross domestic product (GDP) on healthcare, compared to other developing countries.<sup>35</sup> In South Africa, around 61.4% of health expenditure occurs in the private sector which caters for a minority of the population. In May 2006, the General Household Survey, conducted by Statistics SA, revealed that 96% of people who obtain health services in the private sector are satisfied as opposed to 82% in the public sector.

The greater per capita expenditure in the private sector results in better standards of care, more sophisticated methods of management and more luxurious facilities than in the public sector.<sup>36</sup> The private healthcare industry has also increasingly become the main driver of innovation in healthcare. One such example is the Aid for AIDS (AfA) programme which very ably demonstrated the very early response to the HIV epidemic. This programme has been involved with changing the life of many of the HIV/AIDS patients.<sup>37</sup>

AfA is a private sector disease management programme, available to beneficiaries and employees of contracted medical funds and companies in Africa, who are living with HIV/AIDS. Since its inception in 1998 (a few years before the public sector response) AfA has made comprehensive HIV care available to over 80 000 people. The elements of the programme include encouraging voluntary counselling and testing (VCT) of its members; ART for adults and children; post exposure prophylaxis and PMTCT.

Usage of ARV for PMTCT in the program has gone through various phases. In 1998 AZT 250mg was given twice a day from 34 weeks gestational age (mono-therapy). In 1999-2001 some women received AZT and 3TC from 34 weeks gestational age (dual therapy). In 2002 HAART-triple therapy was given from the 2nd trimester onward. This comprised of AZT and 3TC (Combivir®) and either NVP or lopinavir and ritonavir (Kaletra®).

Pregnant women attend private obstetricians where HIV testing is almost routinely performed. HIV positive women are enrolled in the PMTCT program. AfA facilitates the clinical and financial management of each patient by the responsible medical practitioner, within the framework of a comprehensive and confidential disease management programme.

In summary HAART is given to the women, elective Caesarean section is performed, AZT is given to the neonate and formula feeding is supplied for six months. HAART is provided regardless of the CD4 count, but patients with high CD4 counts are counselled about stopping therapy after delivery (in order to limit toxicity and preserve future options). The CD4 count is monitored post delivery until the CD4 count is  $< 350$  then HAART is indicated.

Combivir® and Kaletra® are recommended to HIV positive pregnant women with a CD4 count  $>250$ . Combivir® and NVP are used if CD4 count  $< 250$ .<sup>37</sup> It has been recommended that NVP should not be prescribed in women with CD4 count  $>250$  due to the increased risk of toxicity such as hepatitis and rash. The use of dual nucleoside therapy alone (e.g. Combivir®) for PMTCT is discouraged because of the risk of developing 3TC resistance.<sup>37</sup> In all cases infants receive AZT suspension for 6 weeks (4mg/kg/dose twice a day starting 8–12 hours after birth). Full blood counts are recommended at 2 to 3 weeks to exclude anaemia or neutropaenia. Formula feeds are authorized for six months (2kg/month).

A qualitative HIV Polymerase Chain Reaction test (PCR) should be performed on the infants at 4-6 weeks to determine if infection has occurred. PCR is the preferred virological method for diagnosing HIV at less than 18 months of age. This is a qualitative HIV DNA PCR that is 40% sensitive within 48 hours, 90% sensitive within days and 99.9% sensitive by 6 months. Detection of HIV antibodies via the relatively inexpensive Enzyme Linked Immunosorbent Assay (ELISA) after 18 months confirms infection.

A study conducted by AfA concluded that HAART for 1 month is more effective than HAART for <1 month, or mono- or dual-therapy for PMTCT.<sup>38</sup> The data supported the use of HAART for a minimum of 2 months for effective PMTCT. It also revealed that transmission in “low risk” settings (plasma viral load <log 10<sup>4</sup> or CD4 >500) is still significant and HAART should be considered for all pregnant women. The Caesarean section rate was >84%. The respective HIV transmission rates were similar for mono (5.2%), and dual therapy (6.3%), but tended to be lower for HAART (1.5%). AfA is in the process of reviewing their results, but preliminary data suggests a transmission rate of <1% in those women who are fully compliant. (Regensberg, L. Specialist physician. Personal communication. 9<sup>th</sup> February 2009.)

Practitioners in the private sector may opt to use different treatment regimens depending on the cost factor. There are many independent practitioners. There are no enforced rules and regulations. There are no peer review programmes and neither is there any audit of clinical practice. Not much data is available of the outcome of infants born to HIV positive mothers managed in private practice. In view of this, the present study aimed to assess success or otherwise of PMTCT in private paediatric practice in South Africa.

Aim: To assess the PMTCT outcome in a group of infants attending paediatric practices in Central Durban.

Research Hypothesis: The outcome of infants receiving PMTCT in the private sector is comparable with that in the developed world.

Objectives: To describe in this group:

- HIV transmission from HIV positive mother to child
- Any relationships between outcome and maternal or paediatric characteristics such as:
  - Viral loads
  - CD4 counts
  - Antiretroviral regime
  - Mode of delivery

# CHAPTER 2

## METHODS

## **2.1 Ethics**

Ethical approval was obtained from the Biomedical Research Ethics Committee of the Nelson R Mandela School of Medicine South Africa (Reference number BEO47/47) (Appendix 1). No individual patient consent was deemed necessary as this was an anonymous chart review. Personal information remained confidential and personal practices were not identified

## **2.2 Study Design**

This was a retrospective descriptive study.

## **2.3 Setting**

In order to achieve the objectives of the study a suitable private sector population was chosen. The setting for the study was private paediatric practices in the Central region of Ethekeweni Metro area of KwaZulu Natal.

All the service providers were in the clusters of the planning area as follows. Durdoc Centre; Durban Medical Centre; Maxwell Centre (Durban CBD and Warwick area); Parklands Hospital and Nu-Shifa Hospital (Umgeni South including Springfield, Sydenham, Sparks Estate, Clare Estate); St Augustine's Hospital and Entabeni Hospital (Berea North including Musgrave, Morningside, Essenwood) (Singh, V. Department of Planning, Ethekeweni Municipality. Personal communication. 20<sup>th</sup> November 2008).

There are approximately 20 paediatric practitioners in this geographic area. Letters were sent to all paediatricians practicing in this region asking them to participate (Appendix 2). Many of the patients who attend the private health sector belong to private medical schemes and there are a few that can afford out of pocket payment for medical care. Many belong to a large group administration called AfA.

## **2.4 PMTCT Program in Private Sector**

This was as per the AfA recommendation for PMTCT as outlined in 1.3.2.

## **2.5 Study Population**

The Study Population was all infants (HIV exposed) born to HIV positive mothers who attended the paediatricians who agreed to participate.

## **2.6 Selection of Study Population**

There was no sampling method as the charts of all the infants born to HIV positive mothers for the study period in the practices of the paediatricians who agreed to participate were reviewed. The inclusion criteria were all HIV exposed infants. Records of infants born between January 2004 and June 2005 were reviewed.

## **2.7 Data Collection**

Data was collected by means of a questionnaire that was sent to those paediatricians who agreed to participate. This questionnaire was structured in two parts:

The maternal data, (Appendix 3a) consisted of questions regarding demographics, the diagnosis and treatment of HIV, mode of delivery, viral load and CD4 count. This data was accessed by the paediatrician from the maternal records obtained from the obstetrician.

The baby data, (Appendix 3b) consisted of questions regarding the condition of the baby. The outcome of baby was their HIV status. This had been determined either by PCR or ELISA.

The study was piloted with three paediatricians who, between them, completed five questionnaires. From the responses received the questionnaire was deemed feasible. In discussion with a statistician it was estimated that a sample size of 98 would be appropriate and would satisfactorily represent a subset of a larger population at any given time.

## **2.8 Data Analysis**

All responses per question on the questionnaire were given a numeric value that was used for coding (Appendix 4). The coded data was then entered as a dataset into a Microsoft Excel Spreadsheet. The data entry was checked and errors were corrected.

## **2.9 Statistical Analysis**

Consultation with a statistician revealed that a sample size of 98 was acceptable to get a 95% confidence interval of 0-4.7% around an estimated true population prevalence of transmission of 2% with an estimated population size of 2000 HIV-infected women in the 18 month period.<sup>39</sup> The final sample size was increased to 101 infants. Data were captured and analysed using SPSS 15 (SPSS Inc., Chicago, Ill). EpiCalc 1.32 was used to calculate 95% confidence intervals. Data were presented in frequency tables, histograms, bar charts/pie charts, and variables were summarized using mean, median and range.

# **CHAPTER 3**

## **RESULTS**

### **3.1 Participating paediatric practices**

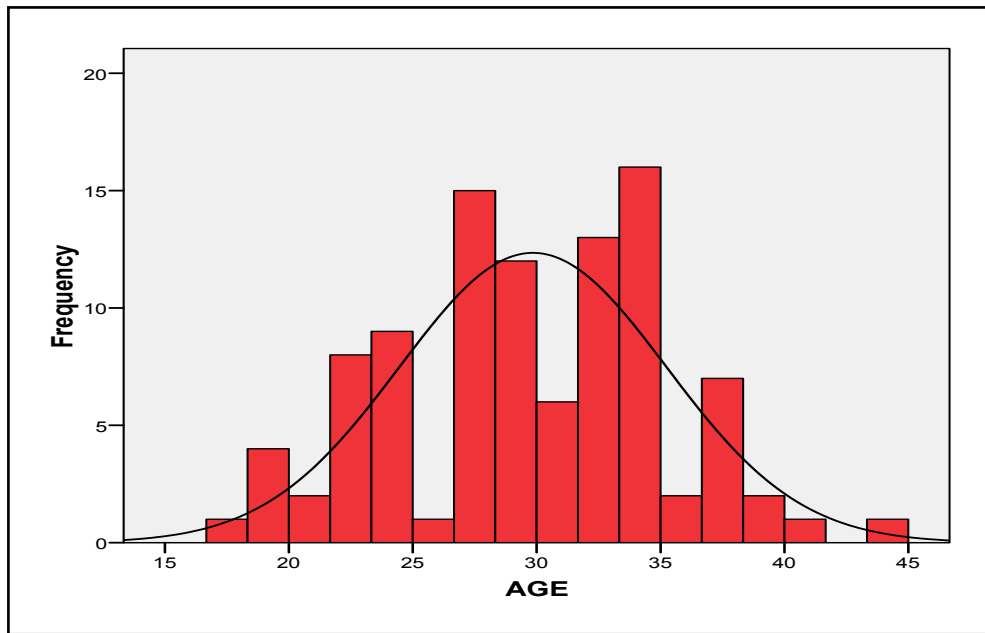
Of the total of 20 paediatricians in the Durban Central Area, four (20 %) did not respond to the request. Eight (40%) agreed to participate. The main reason given by those who did not wish to participate (40%) was the fact that they did not do relevant neonatal work and would therefore not be able to contribute patients. Three were sub-specialists paediatric cardiologist (1) neurology (1) haematology (1) respectively, two were in limited private practice and three were scaling down their practices.

One hundred and one charts were made available by the paediatricians in these eight practices. The paediatrician, when necessary accessed maternal records from the obstetrician to extract the relevant maternal data. Fifty of these came from a single practice due to fact that this particular practitioner was a referral centre for pregnant HIV positive women and paediatric HIV patients. The balance of the charts was contributed approximately equally by the remaining practitioners, providing an average of seven patients per practitioner.

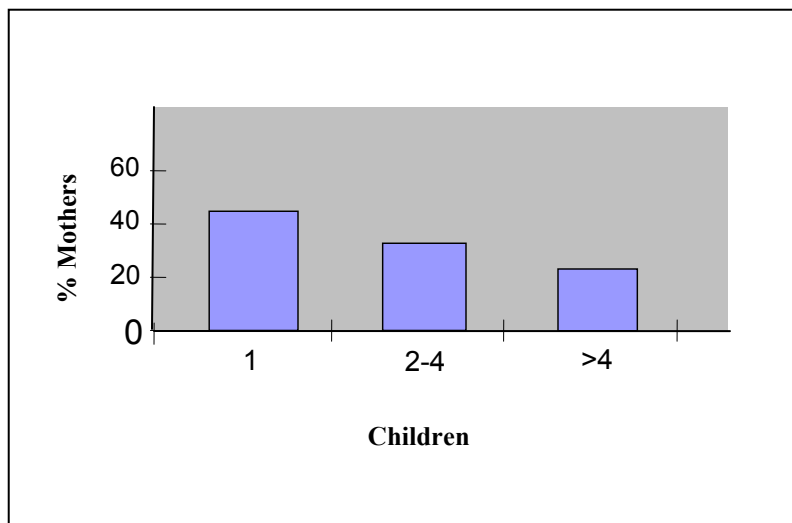
### **3.2 Details of women**

#### **3.2.1 Demographic and clinical details**

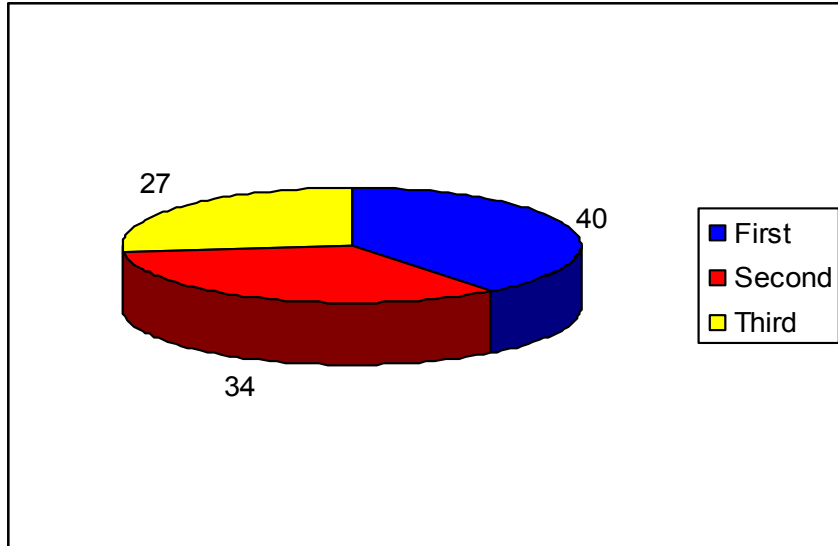
The 101 infants were delivered of 100 Black African HIV positive women (one woman had a set of twins). Infants were delivered as follows in the respective hospitals: 26 at City Hospital, 67 at St Augustine's Hospital and 8 at Parklands Hospital. Ninety-seven patients were on medical aid of which 86 were contracted to AfA. The mean age of the women was 29.85 years (SD 5.38; range 18-44 years) and more details are shown in Fig.1. The mean parity of the women was 1 child (range 1-4 children) and more details are given in Fig.2. The trimester at first presentation and at which antenatal care was initiated is shown in Fig.3. The mean gestational age at presentation and antenatal care initiation was the first trimester. Diagnosis of HIV infection was made in the current pregnancy in 75 cases. Prior knowledge of their status was known in the rest.



**Fig.1 Age distribution of mothers (n=100)**



**Fig.2 Parity of mothers (n=100)**



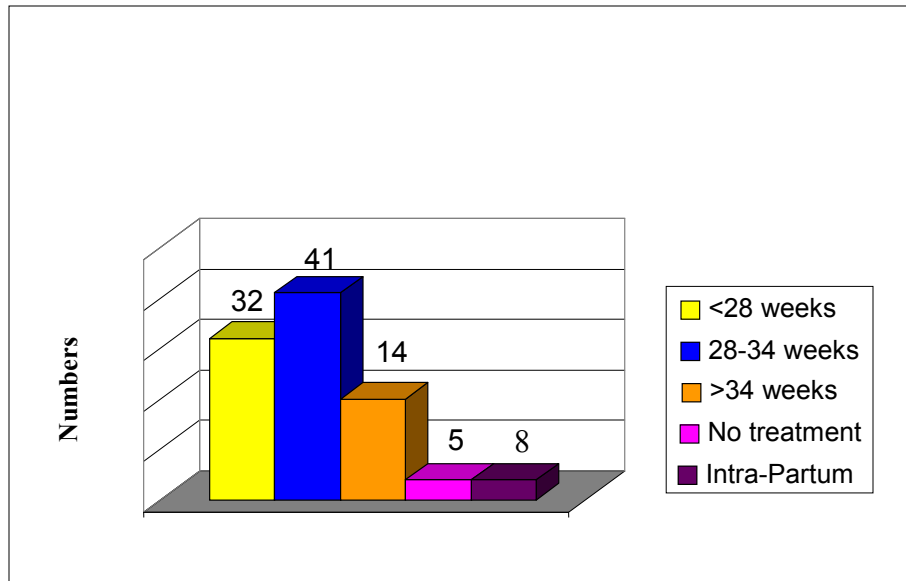
**Fig.3 Trimester in which antenatal care initiated in HIV positive mothers (n=100)**

### **3.2.2 Viral load and CD4 counts**

Eighty six and 91 of the women had recorded viral load and CD4 count measurements, in their antenatal records, respectively. The median CD4 count was 426 (IQR 244-613). Only 13% of the women had CD4 counts less than 200. The median viral load at first presentation was 3.97 logs (IQR 1.6-5.8) or 11 391 copies/ml (IQR 2 013-41 502).

### **3.2.3 Prophylactic regimen**

Only five women had no prophylactic treatment at all. Of the remaining 95, 86 women (90.5%) had HAART and in all cases this regimen included intrapartum intravenous AZT. Nine women did not receive HAART but had other prophylaxis: seven received only intrapartum intravenous AZT, one had only NVP at delivery and one had dual therapy with Combivir®. In 73 women treatment had been initiated at less than 34 weeks of gestation, 72 of these were women who received HAART and one was the patient who had Combivir® and her particular treatment started at 33 weeks (Fig.4 and Fig.5).

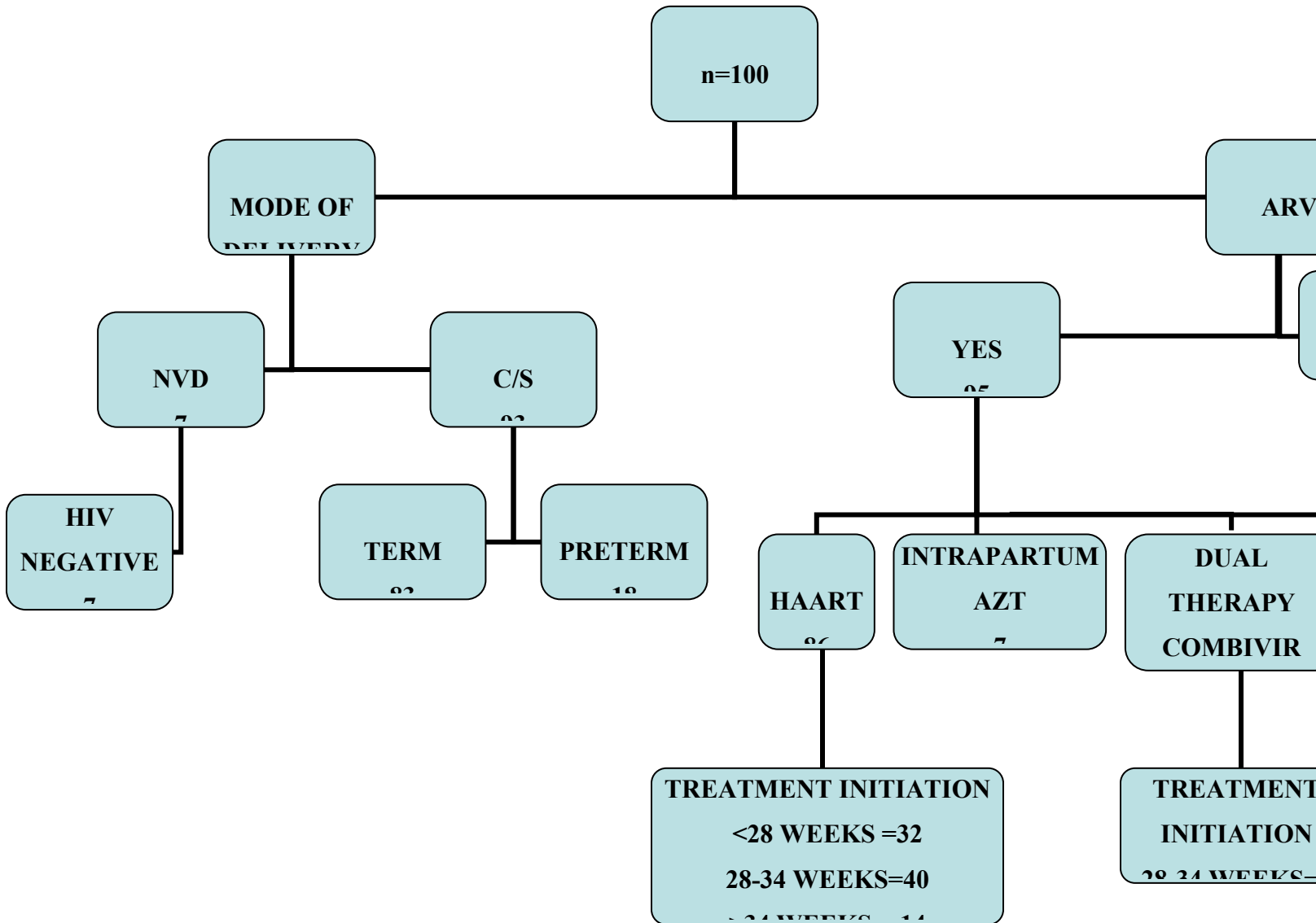


**Fig.4 ARV treatment initiation in pregnant mothers (n=100)**

### 3.2.4 Mode of Delivery

Ninety three and seven mothers had deliveries by caesarean section and normal vaginal delivery respectively (Fig.5). The reasons for the normal vaginal delivery were as follows: one was too sick for caesarean section, one opted for a vaginal delivery, and five presented in established labour and it was therefore too late for caesarean section.

Fig.5 Summary of Maternal Results



### **3.2.5 Maternal disease during pregnancy and post-delivery complications**

Although 14 patients had some associated problems as detailed below, none of these mothers delivered HIV-infected infants.

- One had severe anemia (Haemoglobin (Hb) 6g/dl) and was transfused prior to delivery.
- Two had postnatal depression (one of whom already had pre-existing bilateral amputation of lower limb due to prior car accident).
- Three had tuberculosis diagnosed during pregnancy (two pulmonary, and one abdominal).
- One had severe pregnancy induced hypertension (PIH) and delivered a preterm baby.
- Two had wound sepsis (one poor wound healing associated with syphilis; the other needed secondary suturing of dehiscence of the wound).
- Four incidental findings of grade 3 cervical intraepithelial neoplasia at six weeks post natal check up.
- One maternal death at 6 weeks due to pneumonia and diarrhoea. Although she had been on HAART since 2002 her viral load was 80 594 and CD4 count was 423. Her baby was HIV negative.

### **3.3 Details of infants**

#### **3.3.1 Demographic details**

The study group comprised 101 Black African infants, half of whom were boys. Seventy nine were average birth weight (2.5-4kg), 20 were low birth weight (< 2.5kg) and two were large for gestational age (> 4kg). Eighty three were born at term and 18 were born preterm.

#### **3.3.2 Clinical and medication details**

All infants had been formula fed and had received AZT syrup for 6 weeks as per the AfA protocol. Hb had been measured at six weeks in 98 of the patients and 18 had anaemia (Hb <10 g/dl) of whom only 4 were preterm. Cotrimoxazole for PCP prophylaxis was recorded in 79. Thirteen had no records and nine were not given any prophylaxis.

Fifteen infants were unwell at birth. Three of these were term infants: one had transient tachpnoea of the newborn, which resolved, and the other two were intrauterine grow retarded infants (IUGR) .One of these IUGR infants died before HIV testing and the other did not return for PCR or ELISA testing. No cause for the IUGR was found in the charts

Twelve were preterm (average birth weight 1.5kg and average gestational age 34 weeks) and presented with common problems frequently encountered in prematurity such as respiratory distress, hypoglycaemia etc. Of these only one was HIV positive.

### 3.4 Outcome of infants

Of the 101 baby charts, information about HIV diagnosis was unknown in nine. Eight did not return for testing. One died at 5 weeks, before testing. This was the unexplained intrauterine growth retardation (IUGR 1.9kg) term baby. The cause of the neonatal death remains unknown but on verbal autopsy the mother reported that the baby had been well post discharge and had died from a bleeding cord 5 weeks post delivery. No autopsy was performed. This infant was born to a 29 year old P1G2 who initiated HAART therapy under 28 weeks and whose viral load and CD4 count were 1109 copies/ml and 242 respectively. A summary of the paediatric outcomes is given in Fig.6.

Ninety two infants were tested, 61 at the first PCR, five of whom had a second PCR. Fifty six were tested by ELISA at 18 months (some of whom had already had a first PCR) (Fig.7). Two infants were diagnosed positive. The transmission rate excluding the 9 missing infants was 2.17% (95% CI: 0.38-8.38). The transmission rate including the 9 missing infants was 1.98 (95% CI: 0.34-7.66) (Table 1).

The two positive infants were both diagnosed at six weeks on the initial PCR test (Fig.8). HAART was subsequently initiated in both cases. The first positive infant was born to a 28 year old Primip who was diagnosed two years prior to pregnancy but presented very late for antenatal care. She did not have any antenatal component of PMTCT but had a preterm caesarean delivery at 33 weeks, intrapartum AZT intravenously and the preterm AGA 2.2kg (who had congenital pneumonia and anaemia) baby was given 6 weeks of AZT. No viral load and CD4 were available at the time of delivery. The other positive infant was born to a 37 year Para 2 Gravida 2 who confirmed pregnancy and was tested early but did not return timeously for management. She had only one week of HAART prior to a term caesarean delivery, intrapartum AZT intravenously and the term AGA baby was given 6 weeks of AZT. The maternal viral load was 50 000 and CD4 was 327. A summary of the HIV positive infants is given in Fig.8.

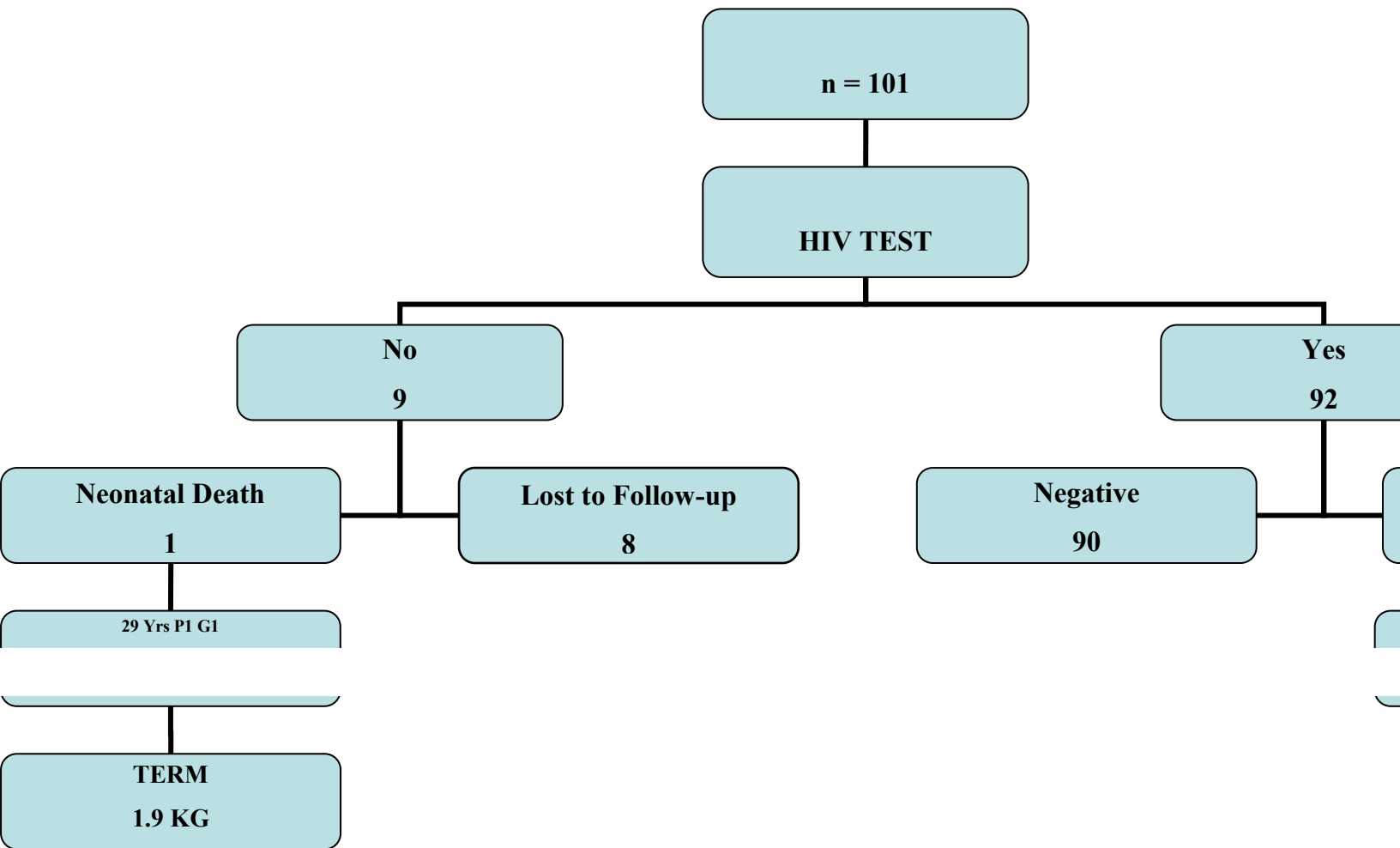
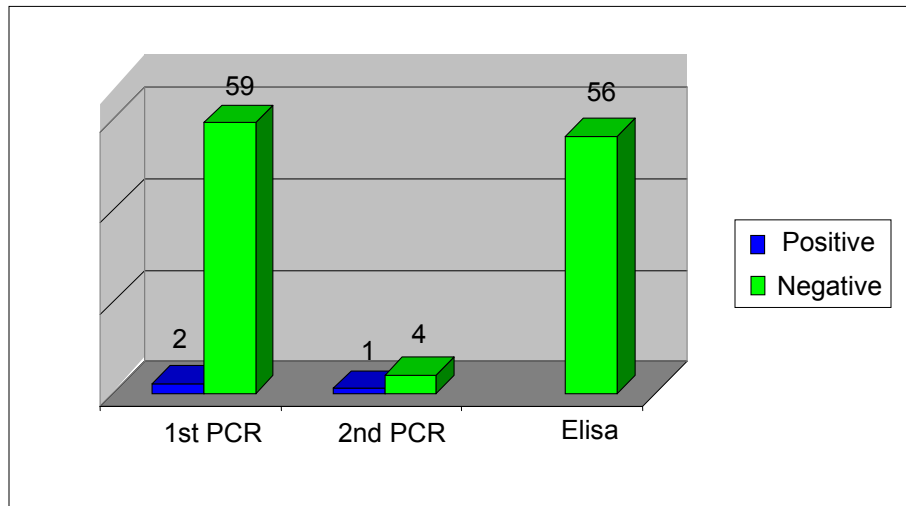


Fig 6 Summary of paediatric results



**Fig.7 Test Results of Infants**

	Frequency	Percent	Valid Percent
Positive	2	1.98	2.17
Negative	90	89.11	97.83
Total	92		100
Missing	9	8.91	
Total sample	101	100	

**Table 1. Transmission rates**

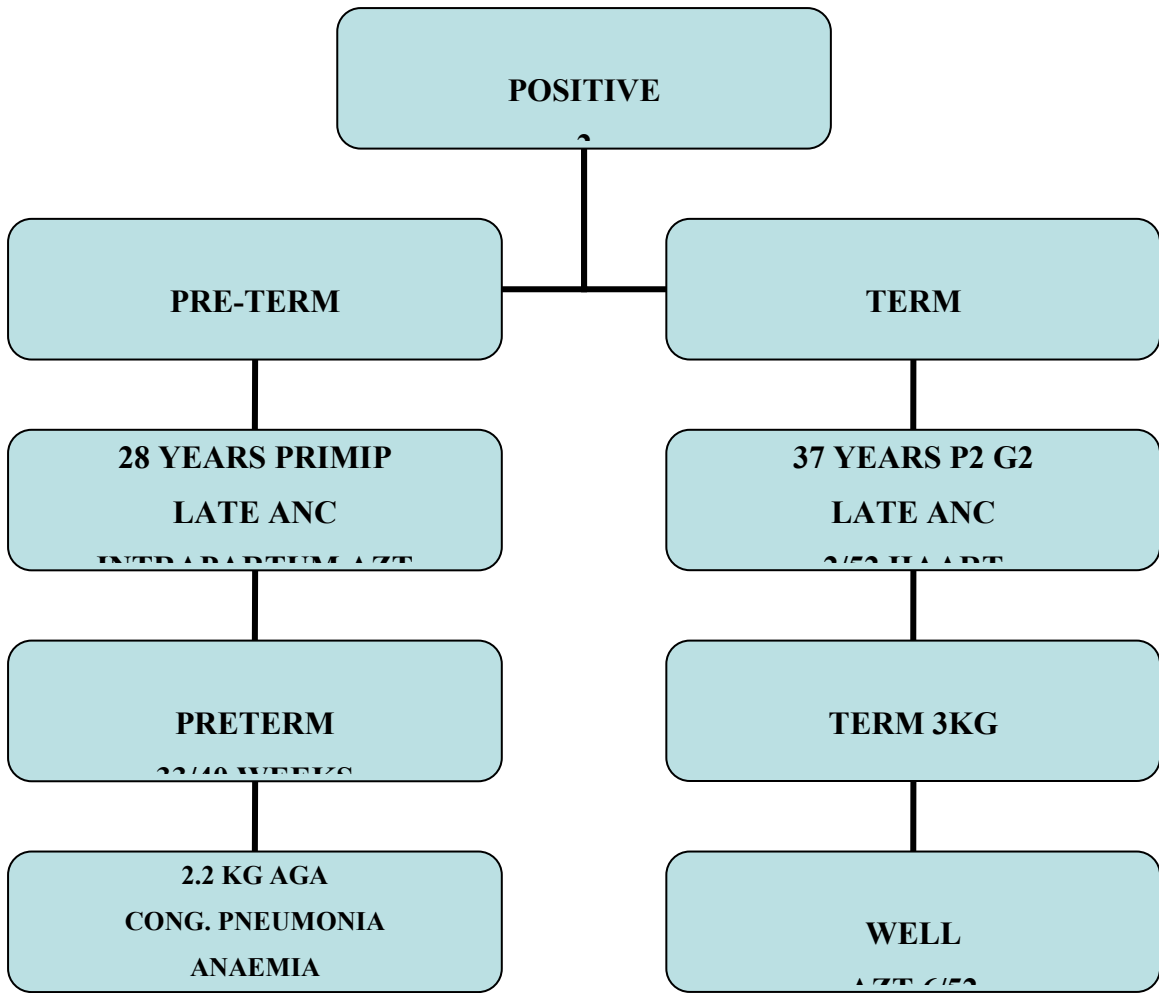


Fig.8 Summary of HIV Positive Infants

# CHAPTER 4

## DISCUSSION

The results of the present study indicate that the PMTCT programme in the private sector in central Durban from January 2004 and June 2005 achieved a positive outcome in that there was a low rate of vertical transmission of HIV. The transmission rate of 2.17 % would increase to 3.2% if the single neonatal death is included. This compares very favourably with the result 8.8% for the Western Cape (dual therapy)<sup>32, 33</sup> and does exceptionally well compared to the 20.8% for the KwaZulu Natal public sector (monotherapy).<sup>29</sup> Other countries in Africa still fare very badly, transmission is still as high as 37 % in Lesotho and in Zimbabwe 100 infants become HIV infected every day.<sup>40</sup>

Prevention of MTCT programs have succeeded in other developing countries e.g. Thailand, Brazil and Cameroon<sup>4, 8</sup> and now, more recently, in Botswana.<sup>40</sup> A country with strong political commitment, Botswana has shown the way forward for other countries in Africa. It has lowered MTCT to less than 4%. Botswana was one of the first countries in Africa to establish a national antiretroviral therapy programme in 2002. This programme includes routine HIV testing; AZT at 28 weeks and sdNVP in labour and the infant is given four weeks of AZT and sdNVP. Only recently did South Africa amend the PMTCT schedule to follow a similar dual therapy protocol as recommended by the amended WHO PMTCT guidelines.<sup>28</sup>

The cause of the neonatal death (unexplained IUGR infant ) remains unknown, but on verbal autopsy the mother reported that the baby had been well post discharge and died from a bleeding cord 5 weeks post delivery. Although the findings from the South African, Children with HIV Early Antiretroviral Therapy (CHER) Study Team demonstrated that HIV infection contributed significantly to infant mortality,<sup>41</sup> it would seem unlikely that this infant was HIV infected given the fact that the mother had a low viral load and had initiated HAART at less than 28 weeks of gestation.

If this neonatal death is excluded then the rate (2.17 %) compares favourably with the 2.9% from the McCord experience. Thus far the most promising reduction in vertical transmission rate in South Africa has come from the McCord PMTCT programme, a smaller, non-governmental project in Kwa Zulu Natal.<sup>34</sup> However, as discussed later, the

McCord study group had double the number of women with low CD4 counts and half the number receiving HAART. When this is considered, our outcome is actually less favourable than theirs.

The result of 2.17 % transmission in this study is in line with Europe and the USA, where fewer than 2% of babies born to HIV positive mothers are infected.<sup>12</sup> However, this figure is still slightly higher than the transmission rate of less than 1% expected according to the AfA preliminary data in women who are fully compliant (Regensberg, L. Specialist physician. Personal communication. 9<sup>th</sup> February 2009). The two infected infants in the present study were as a result of poor maternal compliance. If these two are excluded then the transmission rate is actually less than 1%. This then, will be consistent with the expected transmission rate of less than 1% according to the AfA. The numbers are small in the present study but they lead one to the hope that with appropriate compliance one could approach the virtual elimination of paediatric HIV as has been demonstrated in the developed nations.<sup>1, 14</sup>

The number that did not return for testing (9%) is a problem consistent with other studies. Although high, this is slightly less than the 11% in the McCord's study.<sup>34</sup> Another PMTCT study, involving a number of different resource limited countries, also reported a significant loss to follow-up (although the exact percentage was not stated).<sup>42</sup> If the loss to follow up are all considered positive then the transmission rate would rise to an unacceptable high 10%. However, in studies of this nature the loss to follow up are considered negative (Esterhuizen, T. Statistician. Personal communication. 9<sup>th</sup> March 2009). In addition, there is only a 30-45% possibility of overall vertical transmission in the absence of any preventative strategy.<sup>4</sup>

The loss to follow up in the present study could be attributed to the following factors: another paediatrician may attend to the newborn post discharge; the infant may not be registered on the medical aid scheme and there is reluctance to pay out of pocket for services; fear of the outcome and, in some instances, there is non-disclosure of the HIV-

infected status to partners; and poor counselling during and post delivery, regarding infant testing.

Follow up could be greatly improved, in the private sector, if all infants were automatically registered on the medical aid as soon as they were born. Counselling of mothers, regarding the necessity of early testing of their infants, also needs to be improved.

Maternal viral loads and CD4 counts are often used as markers for the prediction of risk of MTCT. The CD4 count is often used as a guide to the health status of the women. The majority of patients had viral load and CD4 count results, because most medical aids paid for these tests. Although the numbers were small, the median CD4 count 426 (IQR 244-613), was higher than the median CD4 count 293 (IQR 195-451) of the McCord study.<sup>34</sup> Also fewer of the patients (13%) in this study compared to McCord (26%) had CD4 < 200. This suggests that the women in our study had better preservation of immune function although the median viral load was slightly higher. The median viral load here was 3.97 logs (IQR 1.6-5.8) or 11 391 copies/ml (IQR 2 013-41 502) compared to the median viral load at McCord 3.9 logs (IQR 3.1-4.6) or 7 787 copies/ml (IQR 1 403-39 856).

It thus appears, that the present study patients were more advantaged than the McCord group and yet did not fare as well. In this study neither the viral load nor CD4 count result was related to the outcome of the infant and HAART was used in pregnancy irrespective of their values. A larger number of patients (87%) in the present study received HAART compared to 44% of the McCord group. This high percentage of HIV positive pregnant women receiving HAART is in line with the USA, where the proportion of women receiving HAART has increased over time.<sup>43</sup>

Almost all the women were on private medical aid schemes, many of which are affiliated to the AfA programme. Their recommendations are derived from those of the developed countries. The following factors greatly influenced the positive outcome: early antenatal care, almost routine HIV testing, early initiation of HAART, elective caesarean delivery, avoidance of breastfeeding and a long course of ARV given to the infants.

These are similar reasons which have led to the falling perinatal transmission rates in the developed world.<sup>11</sup> Often the medical aid administration reminds patients of investigations and encourages drug adherence. This approach helps to ensure adherence and good follow-up.

The fact that almost all of the patients were on private medical aid (having access to HAART) is indicative of a higher socioeconomic population than the rural areas where the majority of the pregnant women are unemployed and poor.<sup>44</sup> The average age of the pregnant women was 30 years and most were primigravid. This is in line with the situation seen in the developed world where an increasing proportion of births occur in women of advanced maternal age unlike developing countries where teenage pregnancy is still a problem.<sup>44, 45</sup>

Antenatal care is aimed at improving the general health status of pregnant women and also serves as an entry point for early VCT and is crucial for the provision of PMTCT strategies. Almost half of the women confirmed pregnancy and initiated antenatal care in the first trimester as opposed to public sector where local surveys of antenatal patients in Gauteng and in KwaZulu-Natal further demonstrated that the majority of women commence antenatal care in late pregnancy.<sup>44</sup>

Most of the women were diagnosed with HIV in the current pregnancy (76%). This supports the contention that PMTCT is an effective tool for determining one's status. However, it must be noted that HIV testing is almost routine in the private health care sector, although patients do have the option to decline unlike the public health care sector where there is VCT.

Counselling in the private sector is done by the health practitioner. Patients are not usually referred to a psychologist or an HIV counsellor in the private setting unless there is a specific indication to do so. This may be seen as a deficiency in the private sector.<sup>46, 47</sup> The Centres for Disease Control and Prevention (CDC), in April 2003, recommended a strategy where all women are tested in the antenatal period for HIV as a means to increase testing

rates unless they decline i.e. “opt-out”. The intention is to streamline HIV testing so that the extensive requirement for pre-test counselling is reduced.

Under the CDC interpretation of opt-out, pre-test counselling should be replaced by written information on HIV transmission and prevention. In addition, testing for HIV in pregnant women should be a part of the routine battery of prenatal blood tests. Refusal is to be documented in the woman's medical record, in lieu of signed informed consent. This is a recommendation that should be considered in South Africa. On the other hand, this may not be in keeping with the trend and guidelines to have trained counsellors, with the skills to manage the situation. Such trained counsellors would ensure confidentiality and build rapport with the clients enabling them to follow up and register behaviour change.<sup>47</sup>

In this study the Caesarean section rate (94%) was higher than in the McCord Hospital (70%) PMTCT programme. There were hardly any operative or post operative complications. The safety of the private health sector is demonstrated. This is in line with trends elsewhere; such as in USA and in Europe.<sup>11, 48</sup> It was also noted that only two of the women who had a caesarean section had wound sepsis.

A study in the public sector, found women who were HIV positive were at risk from dying following a normal vaginal delivery (even in the absence of AIDS defining features) and this risk was increased following caesarean section.<sup>49</sup> Although one maternal death occurred in the study group, this was at 6 weeks and was thus unrelated to postoperative complications; her baby was HIV negative.

Fourteen patients had viral loads less than 1000 copies/ml and still had deliveries via caesarean section. Earlier studies have shown that no transmission occurred where the maternal plasma viral load was less than 1 000 copies/ml and less than 500 copies/ml irrespective of the mode of delivery.<sup>11</sup> Currently in the USA, caesarean section is only recommended for women with a viral load of greater than 1000 copies/ml. However current plasma viral loads have lower limit of detection (as low as 50 copies/ml). The UK guideline would support a trial of labour where viral load < 50 copies/ml.<sup>50</sup>

However, a more recent meta-analysis of seven prospective studies demonstrated 44 cases of perinatal HIV transmission among 1202 women with plasma viral loads of less than 1000 copies/ml at or near the time of delivery.<sup>50</sup> At present the data suggest, there is insufficient evidence to define a plasma viral load threshold below which transmission never occurs.

HIV infection has been reported to have little effect on pregnancy outcome in the developed world, however early studies from sub-Saharan Africa suggest that infants of HIV-infected women may be at increased risk of adverse pregnancy outcomes such as lower birth weight, prematurity and perinatal and neonatal death.<sup>51</sup> A study of HIV-infected pregnant women in rural and urban South Africa found that maternal HIV infection was associated with an approximately 45% increased risk of having low birth weight infants. Low birth weight has been suggested as a surrogate for prematurity in infants of HIV-infected women.<sup>52</sup>

The present study found that the majority of the infants (79%) were of average birth weight and that 18% were preterm. Considering that the women in the present study came from a well resourced population, this percentage of prematurity is considerably higher, and inconsistent with that expected for developed countries (7%). It is rather more consistent with the 16.5% reported for developing countries.<sup>53</sup> The South Africa prematurity rate may be as high as 25% in the public sector.<sup>54</sup>

It has been suggested that the use of combination ART regimens before or early in pregnancy may slightly increase the risk of prematurity and that there is a significantly increased risk of premature delivery with protease inhibitor containing versus non- protease inhibitor containing combination therapy.<sup>55</sup> In the present study a large percentage did start ARV including protease inhibitor early in the pregnancy. However, a recent meta-analysis of published data concluded that, overall, the use of ART in pregnant HIV-infected women was not associated with a risk of premature delivery.<sup>56</sup>

There is an increased risk of HIV transmission with prematurity.<sup>7</sup> In the present study only one of the 18 premature infants was HIV infected and in that particular instance the woman had suboptimal prophylaxis. However the numbers here are far too small to say whether prematurity is or is not associated with an increased risk for HIV transmission.

Although the WHO/UNICEF/UNAIDS guidelines recommend exclusive breastfeeding for HIV-infected women for the first six months of life, all the infants in this study were formula fed as this was already approved by the medical aid as part of the protocol. This is in line with the further recommendation that where replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected women is recommended.<sup>57</sup> All these factors were present to make replacement feeding acceptable in this study.

Avoidance of breastfeeding for some women is difficult and may be considered a sign to others of the mother's HIV status. The possibility, that some women receiving HAART, could breastfeed safely has been raised. The DREAM study in Mozambique demonstrated that breastfeeding among HIV-infected mothers receiving HAART posed no additional risk of late postnatal HIV transmission to the infant by 6 months of age.<sup>58</sup> Another study provided good data that replacement feeding can be a safe option to consider for HIV-infected mothers in urban African settings when appropriate support is provided and clean water is available.<sup>59</sup>

Eighteen infants had anaemia of whom four were preterm. This was expected as all the infants were given AZT. Studies have shown that the only short-term toxic effect directly attributable to AZT is anaemia, which is mild and reversible.<sup>10</sup>

The current CDC guidelines for reasonable exclusion of HIV in an infant require two negative PCR tests, one of which should be performed at 1 month of age or older, and the other at 4 months of age or older. A positive PCR at any time requires a repeat test on a second blood sample as soon as possible for confirmation.<sup>60</sup>

Sixty percent had only the first PCR and some opted only for the cheaper ELISA test at eighteen months. This reluctance was due to concerns, of both practitioner and patient, that the costly PCR would deplete the medical aid funds earlier. In addition, this study was in the early stages of the PMTCT programme when mothers were reluctant to have their infants tested and practitioners did not appreciate the need for early testing and thus did not influence their patients accordingly. Subsequently there was a lag in diagnosis.

The WHO recommends that PCP prophylaxis in HIV exposed children continue to the age of 15 months, but suggests it be stopped earlier if HIV infection has been ruled out by PCR.<sup>61</sup> Studies by McNally et al.<sup>62</sup> and Jeena et al.<sup>63</sup> have suggested that besides HIV-infected children, the HIV exposed, but uninfected child, also seem to be at risk of acquiring PCP. Thus, they suggested that the WHO guidelines be reviewed and that PCP prophylaxis be continued in all HIV exposed infants. However, despite this recommendation, of the 32 cases of proven PCP in the McNally study only three were HIV exposed uninfected, while five of 52 identified PCP were HIV exposed uninfected in the Jeena study.

A previous study in KZN suggested that the HIV status of infants be determined as early as six weeks in order to prevent unnecessary exposure of uninfected infants to PCP prophylaxis because of a possible association between cotrimoxazole and an increased risk of diarrhoea.<sup>64</sup> There is the additional public health risk that unnecessary treatment in this much larger group of HIV exposed children will increase resistance to the drug. In the present study cotrimoxazole was given to a large number (78%) of infants to prevent PCP. Therefore many infants were given cotrimoxazole who did not actually need the prophylaxis. Another study in Abidjan demonstrated that the cost benefit of early testing and stopping cotrimoxazole early provides a huge saving.<sup>65</sup>

Of the two patients who tested HIV positive, the mother of the first was diagnosed two years prior to the pregnancy but presented very late for antenatal care. The mother of the second baby tested early but did not return for results. In both cases effective treatment could not be instituted timeously.

Had both these mothers taken their condition more seriously and sought appropriate treatment and been better counselled, the outcome for their babies may well have been different. There is thus evidence of denial and lack of insight into the condition. Non adherence is a risk factor in perinatal transmission but this is a problem that even a developed country like the UK is grappling with.<sup>66</sup>

## **BIAS AND LIMITATIONS**

This study may have been subject to selection bias. A large number of the completed questionnaires came from one particular practitioner because this was a referral centre. In fact, all the health care providers who participated were probably more aware and knowledgeable of the PMTCT protocol than average practitioners due to special interest in the field. Thus the results may not be extrapolated to the whole of the private sector.

Furthermore, almost all (97%) of these patients were on a private medical aid and therefore may be socio-economically and educationally better off. This may influence health and compliance and may therefore not be extrapolated to the general antenatal population who may attend the private sector.

This study relied on data collected from records of all infants of HIV positive mothers who presented at the paediatrician's practice for follow up. Infants of pregnant women who did not know their HIV status, and also some pregnant women who were offered VCT and may have opted out, were excluded.

There may have been errors in written records. Such a possibility always exists when collecting retrospective data.

Another limitation of this study is that the sample size was small and therefore it may not be possible to extrapolate to the whole of the private sector.

# **CHAPTER 5**

## **CONCLUSION AND RECOMMENDATIONS**

Children are the innocent victims of this deadly epidemic. By decreasing vertical transmission, the incidence and suffering of many children will be ameliorated. The results of the present study indicate that the PMTC program of the private sector in central Durban from January 2004 and June 2005 achieved a positive outcome with regards the reduction of vertical transmission of HIV. It must be noted that the two women whose infants were HIV infected did not have optimal PMTCT as recommended.

Thus the transmission rate was actually less than 1% in those women who were fully compliant. This is in line with the transmission rate of less than 1% expected according to the AfA preliminary data in fully compliant women. It is also similar to the developed world, where the transmission is down to about 1% or 2%. Although the study sample was small, the results indicate the possibility of the virtual elimination of MTCT of HIV in the private sector provided the recommendations are followed. Early antenatal initiation and adherence to HAART could have averted these two cases that were infected.

The PMTCT protocol recommended by the medical aids are guidelines based on the recommendations of the developed world. The excellent results are also indicative of resources available. The private healthcare sector may be seen by some as elitist and only caring for the “haves”, at the expense of the “have nots”. However, lessons can be learnt from each sector, as expounded in the Health Charter which promotes a partnership between both the public and the private sector. The present research finding is indirectly a means of sharing such information and building partnerships.

The success of decreasing perinatal HIV would be a huge boost to overall infant and child mortality and morbidity. However, there is no room for complacency as the number of HIV positive women having babies continues to increase. Worldwide and country level efforts are needed to scale-up HIV prevention, care and treatment for all strata of society: men, women and children, rich and poor alike. This can be achieved by effective leadership, commitment, partnership and ownership.

Recommendation as a result of the study findings are as follows:

- All pregnant women should have HIV testing and realise the necessity of early prophylaxis and adherence to protocols in PMTCT.

Further recommendations for the success of PMTCT based on personal experience and from the literature are as follows:

- PCP prophylaxis could be stopped as soon as possible in HIV exposed but uninfected infants.
- Testing for HIV in pregnancy should be a part of the routine battery of antenatal blood tests.
- The extensive requirement for pretest counselling should be reduced.
- Doctors should be trained with basic counselling skills.
- Efforts to increase PMTCT should be scaled up.
- Pretest counselling could be replaced by written information on HIV.
- Refusal of an HIV test is to be documented in the woman's medical record, in lieu of signed informed consent.
- All women who receive antiretroviral therapy in pregnancy should be registered prospectively into a register like the Antiretroviral Pregnancy Registry in the UK.
- Women should be advised to continue follow up and monitoring.
- Other cheaper tests should be developed to allow early diagnosis.
- The private sector should replace the whole blood PCR testing with heel prick dried blood spot test as done in the public sector. Although not cheaper, the advantages of this test include the following: that it does not need the expertise required for venesection, there is reduced biohazard status once dry, and there is no need for further processing in the field which thus eliminates the need for refrigeration.

# **APPENDICES**

## Appendix 1



UNIVERSITY OF  
KWAZULU-NATAL

### Research Office

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15 October 2007

Dr SM Cassim  
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PROTOCOL: A Descriptive study of Prevention of Mother-to-Child Transmission (PMTCT) of HIV in Private Practice in Central Durban. Dr. Shakira Mahomed Cassim. Dept. of Public Health. Ref: BE047/07.

Dear Dr Cassim

## EXPEDITED APPLICATION - RATIFICATION

This letter serves to notify you that at a full sitting of the Biomedical Research Ethics Committee meeting held on **09 October 2007**, the Committee **RATIFIED** the sub-committee's decision to approve the above study.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Suraiya Buccas', written in a cursive style.

**SURAIYA BUCCAS**  
Ethics Research Administrator  
SB/pn

## Appendix 2

### 1 INFORMATION DOCUMENT

Study title: A Descriptive study of Prevention of mother-to-child transmission (PMTCT) of HIV in Private Practice in Central Durban

1.1. Dear Dr .....

Introduction:

I, Dr Shakira Cassim (Paediatrician), am doing a research study as part of my requirement towards a Masters in Public Health with the University of KwaZulu Natal. (School of Family and Public Health Medicine, Nelson Mandela School of Medicine). In this study we want document the outcome of infants born to HIV positive mothers managed in private practice in Central Durban.

The objectives are to describe:

- Trends of transmission rate from HIV positive women to baby
- Trends between maternal CD4, viral loads and outcome
- Trends of antiretroviral regime
- Trends in mode of delivery
- Trends in feeding practices

1.1.2 Not much is known about what happens in private practice with the regards the above topic.

Invitation to participate: We are asking / inviting you to participate in this research study.

What is involved in the study?

There are approximately 20 paediatric practitioners in this geographic area. The area is as follows: Durdoc Centre (Smith Street); Durban Medical Centre and Maxwell Centre (Beatrice and Lorne Street area); Parklands Hospital and Nu-Shifa Hospital (Overport); and St Augustine Hospital and Entabeni Hospital (Glenwood).

This will be a retrospective descriptive study of patient records from participating paediatricians between January 2004 to June 2005. The birth period has been chosen such as to ensure that all infants during the data collection period (May – October 2007) will be between 15 - 18 months old.

The inclusion criteria will be all HIV exposed infants. The outcome of infants will be their HIV status. This will have been determined by PCR or Elisa test. Certain other demographic and clinical data regarding the infant will be sought from the paediatric records.

The paediatrician will also be asked to collect certain corresponding maternal demographic and clinical data. The study may entail a data collector collecting data (Should you be too busy).

Data collection: May to July 2007

Collation and analysis: August to October 2007

Submission: November 2007

There are no risks of being involved in the study,

The benefits of being in the study include the collection and analysis of information which might be advantageous to you and others.

You will be given pertinent information on the study while being involved in the project and after the results are available.

Participation is voluntary, that refusal to participate will involve no penalty or loss of benefits

Confidentiality: Efforts will be made to keep personal information confidential. Personal practices will not be identified.

Contact details of researcher/s – for further information please contact:

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- Supervisor: Prof Julia Botha, Department of Therapeutics and Medicine Management, University of Kwa Zulu Natal, Telephone (031)260 4333

Contact details of administrator – for reporting of complaints / problems:

- Department of Therapeutics and Medicines Management  
School of Family and Public Health Medicine,  
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### Appendix 3

#### QUESTIONNAIRE

##### (a) MATERNAL DATA

1. Health care : Medical aid                      Private
2. Date of birth : \_\_\_\_\_
3. Place of Delivery : \_\_\_\_\_
4. Gestational Age  
When pregnancy confirmed : \_\_\_\_\_  
When antenatal care initiated : \_\_\_\_\_
5. Parity : \_\_\_\_\_
6. Date of HIV Diagnosis : \_\_\_\_\_  
(If actual date not known approximate) \_\_\_\_\_
7. Drug History : ARV Medication and Duration  
\_\_\_\_\_  
: Monotherapy  
: Dual  
: HAART  
Any other treatment : \_\_\_\_\_  
Initiation of Treatment  
When : \_\_\_\_\_
8. Mode of Delivery : NVD                      C/S                      Assisted
9. Investigation  
Results : Viral Load                      CD4  
Date : \_\_\_\_\_
11. Post Delivery Complication : \_\_\_\_\_

**(b) BABY DATA**

1.	<u>Date of birth</u>	:	_____	
2.	<u>Race</u>	:	_____	
3.	<u>Sex</u>	:	Male	Female
4.	<u>Birth Weight</u>	:	_____	
5.	<u>Gestational</u>	:	Term	Preterm
			AGA	SGA
6.	<u>Condition @ birth</u>	:	Well	Sick (details)
7.	<u>Feeds</u>	:	Breast	Formula
	Duration	:	_____	
8.	<u>ARV prophylaxis</u>			
	Drug	:	_____	
	Duration	:	_____	
	Adherence	:	_____	
9.	<u>FBC</u>			
	Result	:	_____	
	Date	:	_____	
10.	<u>PCP Prophylaxis</u>			
	Duration	:	_____	
	Adherence	:	_____	
11.	<u>Outcome @ 18mnths</u>			
	1 <sup>st</sup> PCR	:	Positive	Negative
	2 <sup>nd</sup> PCR	:	Positive	Negative

## Appendix 4

### PRELIMINARY ANALYSIS OF RAW DATA

#### (a) MATERNAL DATA

1.	Age	:	<input type="text" value="15yrs"/>	<input type="text" value="15-25yrs"/>	<input type="text" value="25-35yrs"/>	<input type="text" value="&gt;35yrs"/>
2.	Parity	:	<input type="text" value="0-1 child"/>	<input type="text" value="2-4 children"/>	<input type="text" value=" &gt; 4 children"/>	
3.	Diagnosis confirmed	:	<input type="text" value="Previously"/>	<input type="text" value="Current Pregnancy"/>		
4.	ARV regime	:	<input type="text" value="Dual Therapy"/>	<input type="text" value="HAART"/>		
5.	Initiation of Treatment	:	<input type="text" value=" &lt; 28 weeks"/>	<input type="text" value="28 – 34 weeks"/>	<input type="text" value=" &gt;34 weeks"/>	
6.	Mode of Delivery	:	<input type="text" value="NVD"/>	<input type="text" value="C/S"/>		
7.	Viral Load	:	<input type="text" value=" &lt; 1 000"/>	<input type="text" value="1 000 – 5 000"/>	<input type="text" value=" &gt; 5 000"/>	
	CD4	:	<input type="text" value=" &lt; 200"/>	<input type="text" value="200 – 500"/>	<input type="text" value=" &gt; 500"/>	
8.	Post Delivery Complications	:	<input type="text" value="Absent"/>	<input type="text" value="Present"/>		

#### (b) BABY DATA

1.	Birth Weight	:	<input type="text" value=" &lt; 2.5kg"/>	<input type="text" value="2.5kg – 4kg"/>	<input type="text" value=" &gt; 4kg"/>	
2.	Condition @ birth	:	<input type="text" value="Well"/>	<input type="text" value="Sick"/>		
3.	Feeds	:	<input type="text" value="Breast"/>	<input type="text" value="Formula"/>		
4.	ARV - AZT @ 6 weeks	:	<input type="text" value="Yes"/>	<input type="text" value="No"/>		
5.	Anaemia	:	<input type="text" value="Yes"/>	<input type="text" value="No"/>		
6.	PCP Prophylaxis	:	<input type="text" value="Yes"/>	<input type="text" value="No"/>		
7.	Outcome @ 15 months					
	1 <sup>st</sup> PCR	:	<input type="text" value="Positive"/>	<input type="text" value="Negative"/>		
	2 <sup>nd</sup> PCR	:	<input type="text" value="Positive"/>	<input type="text" value="Negative"/>		
	Elisa > !8 months	:	<input type="text" value="Positive"/>	<input type="text" value="Negative"/>		
8.	If seroconvert	:	<input type="text" value="ARV"/>	<input type="text" value="No ARV"/>		

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