PREVALENCE OF PRETERM DELIVERIES IN WOMEN LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS AT MANKWENG HOSPITAL, LIMPOPO

by

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DEDICATION

This study is dedicated in memory of Prof N Shipalana who inspired the topic during her wisdom-packed ward rounds. To her exemplary dedication and leadership to the Paediatrics and Child Health Department at Polokwane and Mankweng hospitals and the Limpopo Province in general. May the great work that she has done in the department and the Limpopo province live on!

D E C L A R A T I ON

I declare that: Prevalence of preterm deliveries in women living with human immunodeficiency virus at Mankweng hospital is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other degree at any other institution.

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Glenrose Rikhotso Date

ACKNOWLEDGEMENTS

I thank God for providing this opportunity for me to be able to go through this journey.

To my husband, it has been a very long road for me. Thank you for your patience and for never allowing me to give up.

To my parents, thank you for equipping me, and grooming me to be able to stand on my own.

Kati, thank you for the daily inspiration.

To my Supervisor, Prof Sutton, thank you for taking me on, may I one day learn to be as effective as you are. I am truly inspired by your work ethic.

To the statistician Mr Peter Mphekgwana, thank you.

To Mr Fannie, thank you for helping with the retrieval of the patient records. It would have been a disaster, but you made sure that I got the files I needed.

ABSTRACT

Objectives:

To determine the prevalence of preterm deliveries amongst HIV-positive women, to describe the demographic characteristics of HIV-positive women delivering preterm babies and to determine the possible risk factors that may be associated with preterm delivery amongst HIV-positive women delivering in Mankweng hospital.

Materials and Methods:

A retrospective cross-sectional study was conducted at Mankweng hospital labour ward and neonatal unit over twelve months, from January 2019 to December 2019. The maternity register was used to identify patients' medical records which were then retrieved and used for the study.

Results: The prevalence of preterm delivery amongst HIV-positive women was found to be 34.1%. This was very high compared to the global prevalence. Maternal age was not associated with preterm delivery. Factors that were found to be significantly associated with preterm delivery in our setting are hypertension, fibroid uterus, urinary tract infection and chorioamnionitis.

Conclusion: The prevalence of preterm delivery in our setting is very high. The risk factors that contribute to preterm delivery among HIV-positive women are like that of the general population. Further studies need to be done to determine if these factors are increased among HIHIV-positiveomen.

KEY CONCEPTS

Prevalence, preterm delivery, human immunodeficiency virus, risk factors.

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DEFINITION OF KEY CONCEPTS

Antenatal steroids: Steroids given to a pregnant woman in whom preterm delivery is inevitable to improve the outcome of the preterm baby. Usually given to women with a gestational age between 24 weeks and 34 weeks.

In his study, the regimen used at Mankweng hospital is 2 doses of dexamethasone 12mg 24 hours apart.

Prevalence: The proportion or percentage of people affected at a point in time (Indrayan 2013)

In this study it refers to the number of preterm babies born to mothers with HIV in a 1-year period. The population at risk is all viable babies delivered to HIV-positive women in Mankweng hospital.

Preterm: Birth occurring before 37 completed weeks of gestation (WHO 2012).

In this study, it refers to all babies born between 24 completed weeks of gestation and 37 completed weeks of gestation.

Delivery: Passage of the foetus and placenta from the genital canal into the external world (Stedman's Medical Dictionary 2005).

In this study, it refers to all viable deliveries amongst HIV-positive women that took place in Mankweng hospital during the study period. These will include normal vaginal deliveries, assisted vacuum or forceps vaginal deliveries, and caesarean sections.

Human Immunodeficiency Virus: The Human Immunodeficiency Virus (HIV) is a type of virus that infects cells of the immune system (CD4 cells), destroying or impairing their function. Infection with the virus results in progressive deterioration of

the immune system, leading to acquired immunodeficiency syndrome (AIDS) (WHO 2017).

In this study, it refers to all women with a positive confirmatory laboratory test for HIV infection in their patient records who delivered babies during the study period.

Women: Adult female human beings (Cambridge Dictionary 2020).

In this study, it refers to all pregnant women who were diagnosed with HIV before pregnancy, during pregnancy or after giving birth as reflected on the Maternal record. Most diagnose through a rapid HIV test.

Viability: The ability of the foetus to survive independently of a pregnant woman's womb (Romanis 2020). A viable foetus is defined as a foetus that has achieved at least 24 weeks of gestation in utero according to the World Health Organization (Ikechebelu, Eleje, Ugwochukwu and Edokwe 2014).

South African legislature does not define viability. It is different in different countries. In this study 24 weeks as described by the WHO will be used.

ABBREVIATIONS AND ACRONYMS

AIDS - Acquired Immunodeficiency Syndrome

ANOVA – Analysis of Variance

ACOG – The American College of Obstetricians and Gynaecologists

ANC – Antenatal Care

C/Section – Caesarean Section

ART - Anti-Retroviral Treatment

EFV – Efavirenz

HAART – Highly Active Anti-Retroviral Treatment

HIV – Human Immunodeficiency Virus

IUFD – Intra Uterine Foetal Death

LPV/r – Lopinavir / Ritonavir

NVD – Normal Vaginal Delivery

PI – Protease Inhibitors

PMTCT – Prevention of Mother-to-Child Transmission

WHO – World Health Organisation

CHAPTER 1

INTRODUCTION AND BACKGROUND

1.1 Introduction

Preterm delivery is known to cause significant child mortality and morbidity worldwide (Slyker, Patterson, Ambler, Richardson, Maleche-Obimbo, et al. 2014). There are studies to show that women with HIV are at an increased risk for preterm delivery (Coley, Msimanga, Smith Fawzi, Kaaya, Hertzmark, et al. 2008). This is important in countries like South Africa with a high prevalence of HIV of about 13,5% (Stats SA, 2019). The possible increased risk of preterm delivery in women with HIV may perpetuate the burden of prematurity on the healthcare system, especially in resource-limited developing countries. This study aims to determine the prevalence of preterm delivery among HHIV-positivewomen. This may help in determining possible preventable factors within this population.

Term birth is birth occurring after 37 full weeks of gestation, with further characterisation into early-term, full-term, late-term, and post-term (ACOG Committee 2013). Preterm birth is defined by WHO (2015) as birth before 37 full weeks of gestation. Preterm birth is the leading cause of perinatal and neonatal mortality and morbidity. According to the global action report on preterm birth, preterm birth rates are increasing each year (WHO 2012). Several risk factors associated with preterm birth have been identified and knowing these risk factors may help in preventing preterm birth. Preterm birth rates range from 8% to 18% in low- and middle-income countries and 5% to 7% of live births in some developed countries (Beck, Wojdyla, Say, Betran, Merialdi et al. 2010).

Most preterm births occur spontaneously, but some are due to early induction of labour or caesarean birth (WHO 2018). Factors that have been associated with preterm labour can be classified into maternal factors, placental factors, foetal factors, and socio-economic factors. Common maternal factors that have been associated with preterm labour include the following: multiple pregnancies, infections, and chronic

conditions such as diabetes and high blood pressure, but often the cause is not known (WHO, 2018). The aforesaid infection leads to chorioamnionitis, which is inflammation of the membranes and placenta. Intrauterine inflammation is one of the most common antecedents of premature births (Galisky, Polglase, Hooper, Black and Moss 2013). Other risk factors associated with preterm delivery include pyrexia of any aetiology other than chorioamnionitis. This includes infections such as malaria, pyelonephritis, HIV, and many other infections (Wagura, Wasunna, Laving Wamalwa, and Ng'ang'a 2018). It was also shown in the same study that maternal parity of more than 4 increased the risk of preterm delivery. This was attributed to possible uterus changes due to myometrial stretching in previous pregnancies. The factors that directly affect the integrity of the uterus and cervix are as follows: history of caesarean section, history of trauma, history of surgery to the uterus, uterine abnormalities, placental insufficiency, placenta praevia, abruptio placenta, amniotic fluid leak, rupture of membranes, cervical insufficiency.

Foetal factors are multiple pregnancies or polyhydramnios, oligohydramnios, and congenital foetal abnormalities (Halimi-asl, Safari & Parvareshi-Hamrah 2017). Sexually transmitted diseases, alcohol use, drug abuse, poor socio-economic circumstances and harmful work conditions have been identified as the socio-economic factors that contribute to preterm labour (Das, Panda, Ahanthem, Sourabh and Bhanu 2015).

Preterm labour is a major obstetric and paediatric challenge because it is a common, persistent, and often devastating condition with considerable medical, economic, emotional, and social impact (Halimi-asl et al 2017). In resource-limited settings, the care of premature infants poses a significant challenge to the existing healthcare infrastructure (Koss *et al.,* 2014). Those infants who live beyond the neonatal period are at increased risk of morbidities which are: developmental delay, lower educational attainment, and increased lifetime risk of non-communicable disease (Slyker *et al.,* 2014).

With the increase in the implementation of the PMTCT programme, there is a reported decline in HIV transmission from mother to child. Even with this decrease, it has been

noted in the literature that there is a reported increase in the number of preterm babies born HIVpositive time mothers.

1.2 Problem statement

Preterm labour is a problem with serious consequences for both the mother and the baby. It has been reported in the literature that there is an increase in the proportion of preterm babies born to HIV-positive mothers. Anecdotally this seems to be the case at Mankweng hospital but there has been no formal evaluation of preterm deliveries in HIV-positive mothers. Caring for preterm babies makes considerable demands on the health system both financially and in terms of resources. The impact of this is particularly noticeable in Mankweng hospital where facilities for the care of preterm babies are limited. Prematurity also poses a risk to the future general health of the preterm newborn because it is associated with many acute and long-term co-morbidities. Therefore, it is important to evaluate the association between HIV-infected mothers and premature deliveries as this might have positive implications in establishing preventative measures to mitigate the problem. This may help to decrease some of the burdens on the health system, the patients, and the patient's families.

1.3 Purpose of the study

1.3.1 Aim

To determine the prevalence of preterm delivery in women who are HIV positive delivering in Mankweng hospital, Limpopo.

1.3.2. Objectives

To determine the prevalence of preterm deliveries amongst HIV-positive women in Mankweng hospital, Limpopo.

To describe the demographic characteristics of HIV-positive women delivering preterm babies at Mankweng hospital, Limpopo.

To determine the risk factors that may be associated with preterm delivery amongst HIV-positive women delivering in Mankweng hospital, Limpopo.

1.3.3. Research questions

What is the prevalence of preterm delivery amongst HIV-positive women at Mankweng hospital, Limpopo?

What are the demographic characteristics of HIV-positive women delivering preterm babies in Mankweng hospital?

What are the risk factors that may be associated with preterm delivery amongst HIV-positive women delivering in Mankweng hospital, Limpopo?

1.4. Significance of the study

It has been shown that preterm deliveries among HIV-positive mothers are a growing problem globally. Babies born prematurely are at a considerably higher risk for multiple pathologies during the neonatal period and throughout their lives. Within the Limpopo province, research on this topic has not been conducted. It would be interesting to define this problem accurately and to compare the findings of this study to outcomes from previous studies that were conducted in other settings. It is therefore on this background that the researcher seeks to discover the severity of this problem in Mankweng hospital. The relationship between the mothers' demographics and preterm labour will also be evaluated. Furthermore, the study will be able to reveal factors associated with preterm delivery among HIV-positive women. At the end of the study, recommendations on strategies to decrease preterm labour in HIV-positive patients will be considered. Systems for the identification and management of dependent risk factors will also be recommended if the problem is found to be significant.

The provincial DOH, Capricorn District and managers from Mankweng hospitals will be deemed as the relevant stakeholders in the development of preventative and therapeutic modalities in addressing this problem.

1.5 Conclusion

Many preterm babies are born and managed in Mankweng hospital. From observation, while working in Mankweng hospital it seems that there are more preterm babies born to HIV-positive women than those born to HIV-negative women. This was the motivation for this study since no study like this conducted in Mankweng hospital or the province has been published so far. Knowing what is happening locally in our setting will help us manage our patients better.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Preterm labour has become a major obstetric and paediatric challenge globally (Halimi asl et al 2017). In high-income countries, up to 95% of infant deaths occur in infants who are delivered before the 32nd week of pregnancy or who have a birth weight of less than 1500g (Parekh, Ribaudo, Souda, Chen, Mmalane, et al. 2011). The relationship between mortality rate and gestational age is inversely proportional in that there is an increase in mortality with decreasing gestational age and birth weight. The HIV epidemic is also a major challenge to global health. According to WHO about 34 million people were living with HIV (Byrne, Fakoya and Harding 2012). Literature addressing HIV infection in women has provided conflicting reports on the association between HIV infection and pregnancy outcomes (Coley et al 2001).

Some studies show that maternal HIV infection has been associated with an increase in preterm birth but mechanisms underlying this association have not been clearly defined (Slyker et al 2014). It is unknown if preterm birth results from a direct effect of the virus, the immunosuppression, the associated co-morbidities or from non-HIV associated factors (Dos Reis et al 2015).

In a study that was done in Kwa-Zulu Natal, a significant association between preterm delivery and the HIV status of a woman was found (Naidoo, Sartorius and Tshimanga-Tshikala 2011). According to the study, there was a fourfold risk of HIV-positive mothers having a preterm delivery than those who were HIV-negative. It was also demonstrated that babies born prematurely to HIV-positive mothers had more neonatal complications than those born to HIV-negative women. Another study which was done in Cape Town showed that there was an overall higher level of preterm delivery and low birth weight among HIV-positive women compared to HIV-negative women. The authors reported that there seemed to be no association between the timing of ART initiation (before or during pregnancy) and adverse birth outcomes

(Malaba, Phillips, Le Roux, Brittain, Zerbe, et al. 2017). A study done across 6 hospitals in Botswana indicated that HIV infection is associated with both preterm delivery and low birth weight (Parekh *et al*, 2011).

A strong relationship between ARV treatment and preterm delivery has been consistently reported in European cohorts and an American study but was not found in most American studies (Sibiude, Warszawski, Tubiana, Dollfus, Faye, et al. 2012). Most cohort studies done in Switzerland, the United Kingdom, Germany and Australia failed to adjust for premature birth risk factors, such as socioeconomic conditions, access to care, obstetrical history, infertility treatments, body mass index, or smoking. The relationship between antiretroviral treatment use and preterm delivery has been reported in some observational studies (Powis et al, 2011). The use of antiretroviral therapy in pregnancy substantially reduces the risk of mother-to-child HIV transmission. Despite the benefits of antiretroviral treatment, evidence suggesting an association with preterm delivery has emerged, and concerns about other adverse effects in pregnancy and early life have been raised (Townsend, Tookey, Newell, and Cortina-Borja 2010).

A cross-sectional study was done using secondary analysis of the WHO multicountry survey on maternal and newborn health (Morisaki, Togoobaatar, Vogel, Souza, Rowland Hogue, et al. 2014). In this study countries were categorised into very high, high, medium, and low-developed countries, using the human development index. The study looked at the risk factors for spontaneous preterm birth and provider-initiated preterm birth. They found that AIDS did not have a significant effect on overall preterm birth. But the effect on preterm birth was higher in countries with a high human development index. They found a similar effect in the United States of America. This was thought to be explained by the behavioural, and socioeconomic characteristics associated with having HIV in a setting where there is low prevalence.

In another study performed in a tertiary public university hospital in South-eastern Brazil, the preterm birth rates in HIV-positive women were found to be higher than in the general population. In the same study a non-significant trend for a higher proportion of preterm birth in AIDS cases, compared with HIV-only cases was observed (Dos Reis, Araujo, Ribeiro, Da Rocha, et al. 2015). Also, for those babies

that were born to HIV-infected women, the proportion of small for gestational age was higher, showing foetal growth restriction

2.2 African perspective

More than 60% of preterm births occur in Africa and South Asia (WHO 2018). Studies related to HIV and preterm birth are emerging. A study done in Malawi found no evidence suggesting HIV infection as a cause of preterm birth in patients who are unexposed to anti-retroviral treatment (Van den Broek, Jean-Baptise & Neilson 2014). The study was done during a time when the patients did not have free access to anti-retroviral treatment.

A study was done in Tanzania to determine the risk factors for preterm birth among HIV-positive Tanzanian women (Zack, Golan & Aboud 2014). It was found that an HIV stage of more than 2 increased the risk of preterm delivery. They did not find any further association between prematurity and either CD4 cell count or viral load Lack of weight gain during pregnancy was found to be associated with preterm delivery as well. It was also found that younger maternal age (less than 20 years) was a risk factor for preterm delivery among HIV-positive women. This concurred with a study that was done in Cameroon which referenced ve study. A study done in Nigeria, showed the incidence of spontaneous preterm delivery in HIV post-positive is 11,1 or 100 births (Ezechi, Gab-Okafor, Oladele, Ohwodo, Adu, et al. 2013). It also showed that HIV post-HIV-positive with multiple pregnancies, symptomatic HIV infection at delivery and first-trimester foetal exposure to PI-based triple therapy were at risk of spontaneous preterm delivery.

Many theories remain regarding the potential adverse effects of Highly Active Antiretroviral Therapy (HAART) use in pregnancy, including the association between PI-based HAART regimens and preterm births. Some studies reported an increased risk of preterm delivery with PI's while others did not find this association (Powis, Kitch, Ogwu, Hughes, Lockman, et al. 2011). In another study LPV/r when compared to EFV is not associated with an increased risk of preterm birth (Koss et al 1999)

2.3 South African perspective

South Africa, as a low-to-middle-income country has preterm birth and low birth weight prevalence rates as high as 14.17% (Fouche, Kritzinger, and Leroux 2018). The prevalence of HIV among South African females of reproductive age(20 to 34 years) has been estimated to be 31.6%(Clouse, Malope-Kgokong, Bor, Nattey, Mudau et al. 2020). This is a very high burden of disease. The true national burden of preterm birth in South Africa is unknown. The prevalence of congenital HIV in neonates born in a South African hospital(Charlotte Maxeke hospital) was found to be 2.5%(Benali, Ramdin and Ballot. 2019). This shows that despite the EMTCT guidelines the rate of transmission remains high. In the same study most of the infants had low birth weights and were born prematurely). The current estimates of preterm birth in South Africa rely on hospital mortality data and projections (Ramoko, Malaba, Rhoda, Kauchali, and Goga 2019). Some studies have been done in South Africa regarding HIV and preterm delivery. A study done in Kwa-Zulu Natal showed that there was a significant association between preterm delivery and maternal HIV infection (Naidoo et al 2011). In the same study a trend of more complications in HIV-exposed preterm neonates, than in HIV-unexposed preterm neonates was demonstrated.

A study looking at the factors associated with delivering premature and/or low birth weight infants among pregnant HIV women on antiretroviral treatment was done in Dr George Mukhari hospital. It was found that HIV-positive pregnant women not on ART were at risk of delivering preterm babies with a gestational age of fewer than 28 weeks or a birth weight of less than 1000g (Gibango, Mda and Ntuli 2018). This is in contrast with a study that was done in rural Kwa-Zulu Natal where maternal HIV infection was found to increase the risk of small for gestational age babies, but not preterm birth (Ndirangu, Newell & Bland 2015). This latter study was conducted at a time when antiretroviral treatment was not available, but mothers were given nevirapine to prevent transmission during delivery.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Introduction

The methodology of the study will be discussed in this chapter. The chapter will discuss the study design, the setting of the study, the study population, and the sampling method. The data collection tool and data analysis will be described. The chapter will also address the reliability and validity of the study. The ethical considerations for this study will also be discussed.

3.2 Study design

A study design is a structured approach followed by a researcher to answer a research question (Joubert and Ehlrich 2007). A retrospective cross-sectional study was done at Mankweng hospital, labour ward and neonatal unit over twelve months, from January 2019 to December 2019.

3.3 Study area

Mankweng hospital is a tertiary hospital situated in Mankweng, Polokwane, Limpopo Province South Africa. The province consists of five districts. Mankweng hospital is situated in the Capricorn district. Patients needing tertiary care especially those at risk of preterm delivery are referred to Mankweng Hospital. The only other tertiary institution available in the whole province is Pietersburg hospital. The Mankweng labour ward consists of 7 delivery rooms and 1 maternity theatre. There are usually four professional nurses who are trained in midwifery and neonatal resuscitation during the day and the night. There are also medical interns, medical officers, and obstetricians (consultants) available every day.

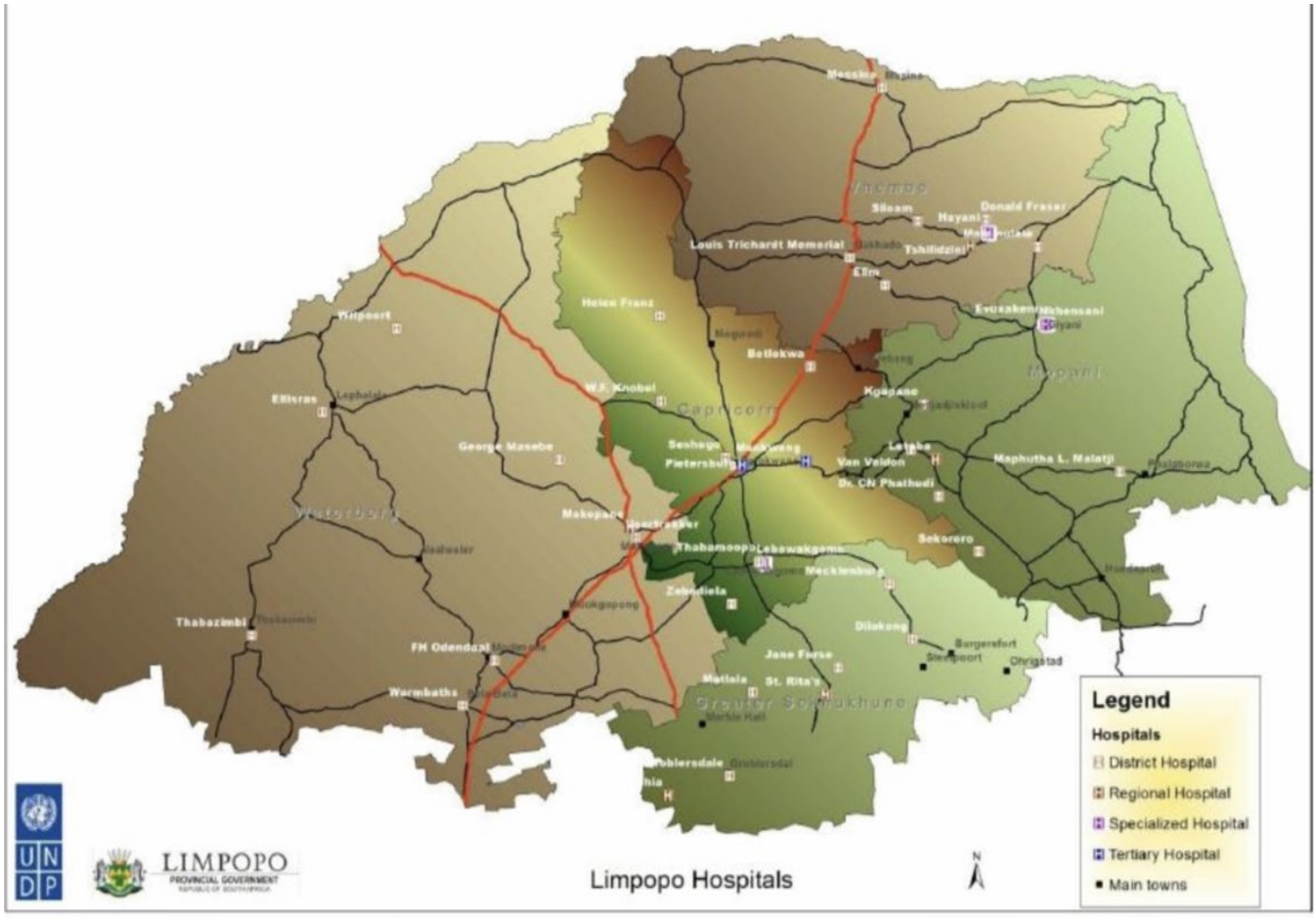

Figure 1: Map of Limpopo province also showing the study site. source: Limpopo department of health, health market inquiry. From: http://www.compcom.co.za/wp-content/uploads/2016/05/Presentation-by-Limpopo-DoH-18052016.pdf (accessed 08/11/2018)

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3.4 Study population

The study population is the group from which information is gathered to conclude (Joubert and Ehlrich 2007). The study population for this study was all HIV-positive women who delivered in the Mankweng labour ward in one year. The annual deliveries by HIV-positive women in Mankweng are about 1284. This includes both premature and term deliveries. To differentiate between preterm delivery and intrauterine growth restriction, the gestational age by sure dates, by early sonar (as documented in the patient file), and/or by Ballard score was used.

3.5 Sampling

The sample size was calculated using previous hospital statistics. The average annual delivery by women living with HIV in the Mankweng maternity ward is about 1284 per year. Everyone meeting the study criteria was selected. The Yamane formula (Yamane 1967) was used to calculate the sample size. Considering we accept a sample error of 5% with a confidence interval of 95%.

Calculation of Sample Size

$$n = \frac{N}{1 + N(e)^2}$$

$$= \frac{1284}{1 + 1284(0.05)^2}$$

$$= 305 \text{ (calculated sample size)}$$

n = Sample size
N = Population size . N = 1284
e = margin of error. e = 0.05

As per the sample size calculated above a minimum number of 305 patients' files was needed for the study to be representative of the study population. Systematic probability sampling was used. The population was selected according to a random starting point but with a fixed periodic interval. The periodic interval was calculated by dividing the population size by the desired sample size. The periodic interval was then used on the maternity register to pick out the desired file numbers. That information was then used to retrieve the files from the shelves at records. In this case, the periodic interval was every fourth file as they appeared on the maternity record.

3.5.1 Inclusion criteria

All HIV-positive mothers delivering in the Mankweng hospital labour ward from January 2019 to December 2019.

3.5.2 Exclusion criteria

HIV status not clearly stated on maternity record.

Mothers admitted to Mankweng hospital after delivery in another unit or at home.

Patients delivering outside the specified period.

Patients delivering before the defined age of viability.

3.6 Data collection

Data was collected from the maternity delivery register of women giving birth in Mankweng during the 2019 calendar year. The patient's name, surname, file numbers and HIV status were retrieved from the maternity register. Patient files were retrieved from records using the information obtained from the maternity delivery register. The patient files were used to obtain information that was needed to fill in the data collection tool as below.

3.7 Data collection tool

A data collection tool was used to collect the required information from the file. The data collection tool was composed of 2 sections. Section A consists of the maternal demographic details that are: maternal age, gravidity, parity, gestational age at booking, HIV status, date of initiation of ART, ART regimen, CD4 count (most recent available results), recent viral load and maternal co-morbidities during pregnancy. The co-morbidities were regarded as present if they were documented in the patient record. Section B contained labour and neonatal data, namely, date of delivery, mode of delivery, gestational age at delivery, perinatal steroid administration, birth weight, Apgar scores, birth PCR, the outcome at birth and prematurity-related problems.

3.8 Data analysis

Data was captured in a Microsoft Excel spreadsheet, cleaned, and transferred to SPSS version 25 for analysis. Normally distributed continuous variables were presented as mean ± standard deviation. Non-normally distributed continuous variables were presented as median ± Interquartile range. Categorical variables were presented as frequency, percentages, and charts. Demographic and clinical parameters were compared between preterm and normal delivery using Pearson's chi-square test. The prevalence of prematurity was calculated by dividing the number of preterm babies (numerator) by the total number of deliveries to HIV-positive women and expressing it to one decimal point as a percentage. This was compared with the known prevalence of all preterm deliveries.

3.9 Reliability and validity

Reliability is the consistency and dependability of a research instrument to measure a variable (Brink, 1996). The systematic probability sampling method was used to obtain the data. This introduces some fairness in the selection process. The list from the register was taken as it appears and was not compiled in any biased way. The study was done using patient records which are legal documents and the information contained is presumed to be credible. Some of the information was not documented which created some gaps in the information obtained.

Validity is the ability of an instrument to measure the variable that it is intended to measure (Brink, 1996). The assessment of prematurity was based on records made during the pregnancy or at the assessment of the newborn. Gestational age by sure dates, early sonar or by a Ballard score was used. Sure dates followed by early sonar were considered to be the most reliable estimates of gestational age. HIV status was based on antenatal records, maternity records, and neonatal records. All patients with no clear HIV status were excluded from the study.

3.10 Bias

3.10.1 Selection Bias

Selection bias occurs when there are systematic or directional errors in how participants are sampled in a study, which leads the study sample to be systematically different from the population of interest (Joubert and Ehlrich 2007). The systematic probability sampling method of patients was done, and the sample size was calculated for the sample to be representative of the population of interest.

3.10.2 Information Bias

Information bias occurs when there is a systematic or directional error in how measurements are taken on participants within the study (Joubert and Ehlrich 2007). Some of the files could not be located in records and therefore could not be included in the study. Some files had some missing information and depending on the missing information they had also to be excluded. This was unavoidable.

The use of the Ballard score is accurate only within plus or minus 2 weeks. Therefore, the gestational age could be incorrectly determined by two weeks.

3.11. Ethical considerations

Ethical clearance

Ethical clearance was obtained from the Turfloop Research and Ethics Committee (TREC).

Permissions

Permission to access the patient records was obtained from the Limpopo provincial Department of Health and Mankweng Hospital Management.

Informed consent

A consent waiver was requested since this was a retrospective study, and it would have been difficult to get in contact with the participants. The risk to the patient was minimal and was avoided by making sure that the files were dealt with confidentially and anonymised. Only the researcher was using the files and returned them as soon as the information was collected. The study did not in any way influence patient care.

Protection from harm

No harm occurred to patients during this study as there was no form of contact with the patients.

Privacy and confidentiality

The right to privacy is a fundamental human right in the Bill of Rights of the constitution. During the study patients' records were reviewed and patients' names were replaced by codes. Therefore, the collected information could not be immediately associated with the patient except by the researcher.

CHAPTER 4
RESULTS AND INTERPRETATION OF RESULTS

4.1 Introduction

In this chapter, the findings of the study will be presented. The chapter will be subdivided into:

1. The prevalence of preterm delivery in the study population.
2. The demographics of the study population.
3. The risk factors associated with preterm delivery.

4.2 The prevalence of preterm delivery

For 20 of the 305 patients in the sample, hospital record files could not be found. A total of 285 patient records were analysed. The total number of preterm births was 89 and there were 172 term births (Figure 2). In 24 files there was no record as to whether the baby was preterm or term.

The highest number of preterm infants were born to mothers in the age group 26 – 35 years. This age group also had the highest total number of births (Table 1). In the age group 18 to 25 years there were 19 (41.3%) women who delivered preterm babies and 27 (58.7%) women who delivered term babies. In the age group 26 to 35 years there were 50 (33.1%) women who delivered preterm babies and 101 (66.9%) women who delivered term babies. In the age group 36 to 45 there were 19 (30.2%) women who delivered preterm babies and 44 (69.8) who delivered term babies. The p-value was 0.935 which means there was no significant difference between the age group categories in the proportion of preterm to term babies. Although there were proportionally more preterm babies born to mothers in the younger age groups this was not statistically significant.

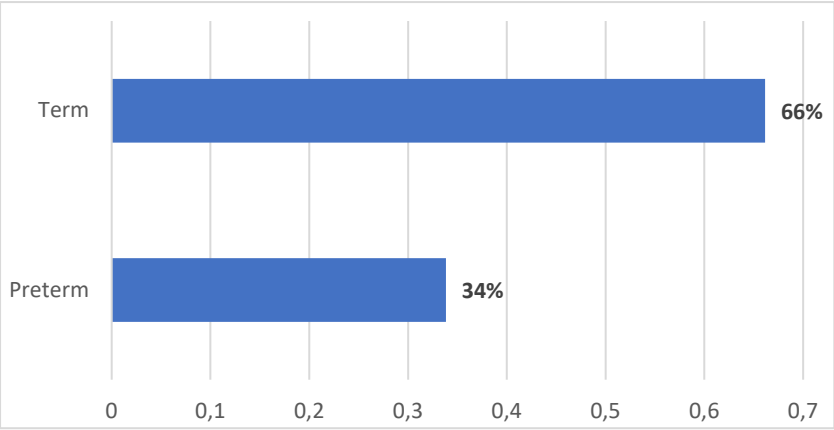

Figure 2. the percentage of Term infants and Preterm infants in the study population

Table 1. The number and percentage of Preterm and Term infants per maternal age group

	Preterm	Term	P-value
Age			
<18	1 (50%)	1 (50%)	
18-25	19 (41.3%)	27 (58.7%)	0.935
26-35	50 (33.1%)	101 (66.9%)	
36-45	19 (30.2%)	44 (69.8%)	

4.3 Mode of delivery and antenatal steroids

Out of 285 patients, 35% were delivered by caesarean section and 65% were delivered by normal vaginal delivery (Figure 3). Only 7.9% of the mothers who delivered preterm infants were recorded to have received antenatal steroids. Of the 7.9% who received antenatal steroids 27.8% of them (2.2 % of all the preterm babies) did not receive the complete course. For the rest of the mothers (92.1%) who delivered preterm infants, there was no record of receiving antenatal steroids.

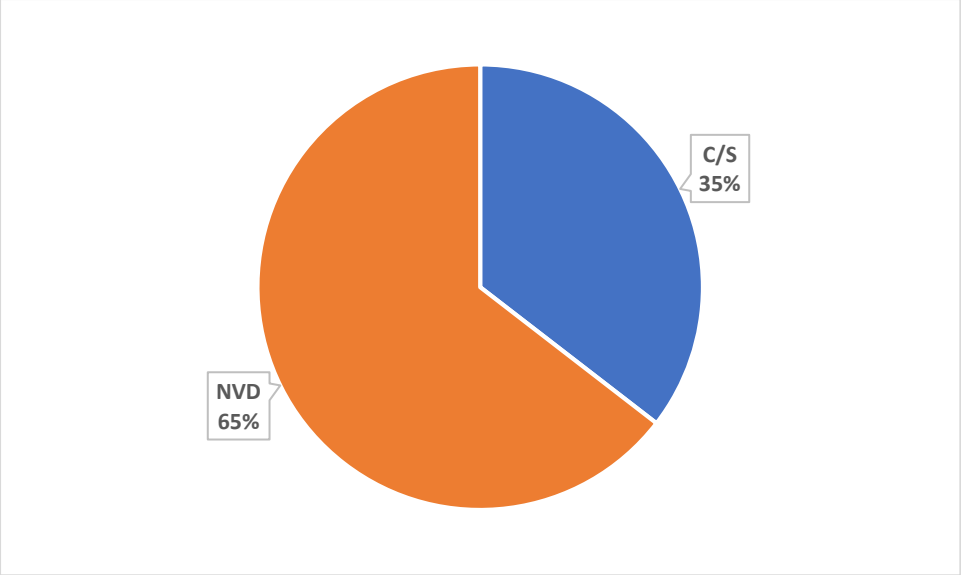

Figure 3. The Percentage of normal vaginal and caesarean section deliveries within the study population.

4.4 Demographics of the study population

Most of the mothers in the overall sample fell within the age group 26 to 35 years, that is 58 % (151/261) as seen in figure 4. This was followed by the age group 36 – 45 years with 24% (63/261). The group with the least births was the age group less than 18 years old. Within the age group less than 18 years, there was 1 woman who delivered a preterm baby and 1 woman who delivered a term baby.

The mean parity was 2 ±0.089 and the mean gravidity was 3.22 ±0.093. The mean number of miscarriages for these women was 1.53±0.174. The mean gestational age at booking was found to be 19 ±0.381 weeks (Table 2).

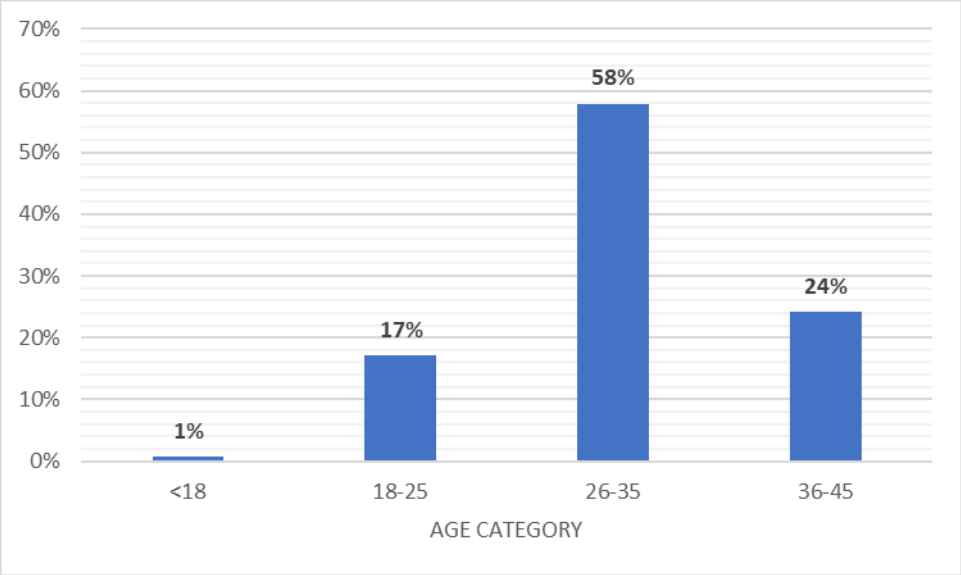

Figure 4. The number of deliveries (in %) per age group

Table 2a: Maternal demographic characteristics

Variables	**Mean (standard deviation)**
Gravidity	3.22 (0.093)
Parity	2 (0.089)
Gestational age at booking (weeks)	19.44 (0.381)
Miscarriage	1.53 (0.174)

When it comes to the social demographics of the women, quite a big number of the patient records 1 or more of the variables were not recorded (Table 2). Of the 167 patients with recorded information on employment 48 (29%) were employed and 119 (71%) were not employed. Smoking and alcohol consumption was reported in 244 patient records. Of the 244 patients, 3 (1%) smoked cigarettes and 241 (99%) did not smoke. Regarding alcohol consumption during pregnancy, of the 244 patients, 12 (5%) did consume alcohol and 232 (95%) did not consume alcohol.

Table 2b: Maternal characteristics

Variables	**Frequency (%)**
Employment: Yes	48 (29)
No	119 (71)
Smoking: Yes	3 (1)
No	241 (99)
Alcohol: Yes	12 (5)
No	232 (95)

4.5 Maternal CD4 and viral load status

Most of the women (99%) were on first-line ARV treatment. There was 1 woman who refused treatment and 2 that were on second-line ARV treatment. The mean CD4 count was 514 ±23.7 cells/mm^3. In the group of women who had a CD4 count that was less than 200 cells,/mm^3 7 (46.7%) gave birth to preterm babies, and 8 (53.3%) gave birth to term babies (Table 3). In the group of women with a CD4 count that was more than 200 cell/mm^3 47 (33.3%) women gave birth to preterm babies and 94 (66.7%) gave birth to term babies. The rest of the women had either an unknown CD4 or an unknown gestational age at birth. The P-value was 0.392. The CD4 count was not significantly associated with preterm birth.

Table 3: Association of CD4 count per preterm and term groups

CD4 Count (cells/mm^3)	Preterm Frequency(%)	Term Frequency(%)	Total n=156	Fisher's exact test
≤ 200	7(46.7)	8(53.3)	15	0.392
>200	47(33.3)	94(66.7)	141	0.392

The viral load was found to be lower than the detectable limit in 111 of the women, not suppressed in 86 of the women and was undocumented in the rest of the 87 of the women (Table 4). In the group which had a viral load which was lower than detectable

33 (32.4 %) delivered preterm babies, 69 (67.6%) delivered term babies and the gestational at the birth of the remaining 9 (8.1%) babies were not recorded. For the group of women with a viral load that was not suppressed 27 (33.8.0%) gave birth to preterm babies, 53 (66.2%) gave birth to term babies and in 7 (8.0%) the gestational age was not recorded. The distribution of births in the group of mothers with an unknown viral load was similar. The P-value was 0.995 which is not significant. Some of the women with an unknown viral load were recently diagnosed with HIV and had therefore only started treatment less than 3 months before delivery but for most of them a viral load result was just not available on both the file and the laboratory system and was therefore possibly not done.

Table 4: Association of viral load per preterm and term groups

Viral load	Preterm Frequency(%)	Term Frequency(%)	Total n =182	Fisher's exact test
Suppressed	33(32.4)	69(67.6)	102	0.875
Not Suppressed	27(33.8)	53(66.2)	80	0.875

4.6 Maternal co-morbidities

Most of the women (65.3%) did not have any other comorbidities except for HIV according to the records. Of those with recorded co-morbidities, 9.8% had hypertension, 5% had urinary tract infection, 2.9% had fibroid uterus, 0.8% had chorioamnionitis, 0.4% had gestational diabetes mellitus and 16.5% had other co-morbidities like anaemia, renal failure, etc (Figure 5). In the group of women who had no co-morbidities 44 (23.7%) delivered preterm babies. 130 (70.0%) of these women delivered term babies while for 12 (6.5%) the gestational age at delivery was unrecorded. In the group of women who had hypertension 18 (64.3%) delivered preterm babies. Seven (25%) of them delivered term babies and 3 (10.7%) had an unreported gestational age at delivery. In the group with urinary tract infections, 2 (14.3%) of the women delivered preterm babies, 10 (71.4%) delivered term babies and 2 (14.3%) had an unrecorded gestational age at delivery. In the group of women with fibroid uterus, 7 (87.5%) babies were born preterm, none were born at term and

1 (12.5%) baby had an unreported gestational age. In the group of women with other co-morbidities, 16 (34.0%) babies were delivered preterm, 26 (55.3%) were delivered at term and 5 (10.6%) had an unrecorded gestational age. The p-value was less than 0.001 demonstrating a significant association between co-morbidities and preterm birth.

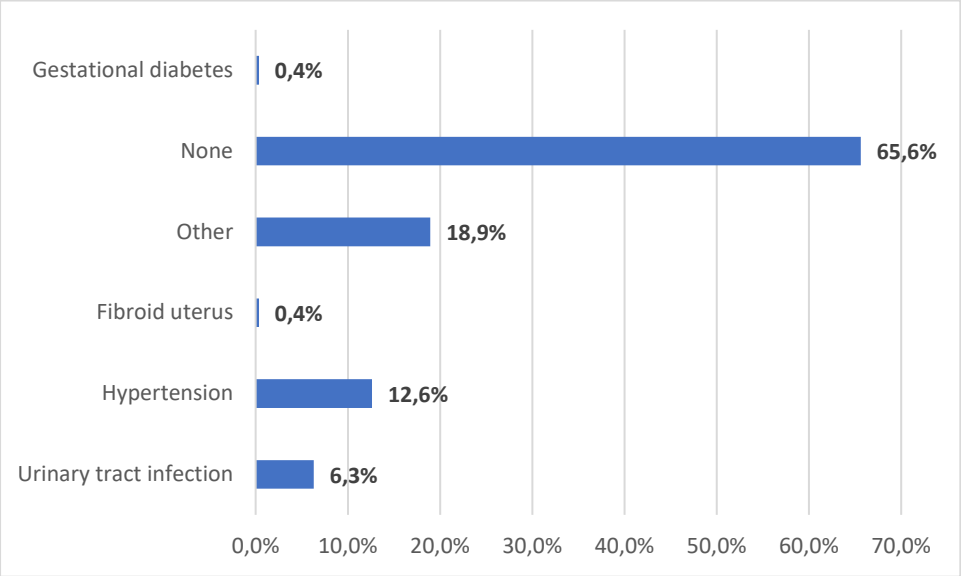

Figure 5: Maternal Co-morbidities

Table 5: Maternal Co-morbidities vs maturity at birth

Variable	Preterm Frequency(%)	Term Frequency(%)	Gestational unknown Frequency(%)	Total n = 285	p-value
Urinary tract infection	2(14.3)	10(71.4)	2(14.3)	14	0.000
Chorio-amnionitis	2(100)	0(0)	0(0)	2	0.000
Hypertension	18(64.3)	7(25.0)	3(10.7)	28	0.000
Fibroid Uterus	7(87.5)	0(0)	1(12.5)	8	0.000
Gestational diabetes mellitus	1(100)	0(0)	(0)	1	
Other	16(34.0)	26(55.3)	5(10.6)	47	0.000
None	44(23.7)	130(70.0)	12(6.5)	186	0.000

4.7 Infant characteristics and outcome at birth

The average gestational age at delivery was found to be 36.43 ± 0.24 and the average birth weight was found to be 2118 grams (g) and ranged from 400g to 4770g (Table 6). The average Apgar scores were 8.22 ± 0.10 and 9.47± 0.09 at 1 minute and 5 minutes respectively. Acquiring the results for the birth PCR for the infants proved to be very challenging. Only 9 (3%) of the maternal records had lab reference numbers to trace the results for the birth PCR (Table 7). It was difficult for the rest of the infants as the infants possibly had a different file number from the mothers and therefore could not be traced from the lab system using the mother's details.

Table 6. Infant characteristics

Variables	**Mean (standard deviation)**
gestational age at delivery (weeks)	36.43 (0.237)
1 minute Apgar /10	8.22 (0.104)
1 minute Apgar twin /10	7.64 (0.498)
5 minutes Apgar /10	9.47 (0.093)
5 minutes Apgar twin /10	9.36 (0.269)
Birth weight (g)	2118

Table 7. Birth PCR

Variables		Frequency (%)
Birth PCR	Negative	9 (3)
	Unknown	276 (97)

Most of the babies (75%) had a good outcome at birth and were sent to their mothers after birth. Twenty-three per cent of the babies were admitted to the neonatal unit for

different reasons. About 2% of the babies had an outcome of death. Some were macerated stillbirths; others fresh stillbirths and others were failed resuscitation resulting in early neonatal death. Only the outcome at birth was assessed, the babies were not followed to the neonatal unit or the postnatal unit to assess the outcome beyond birth.

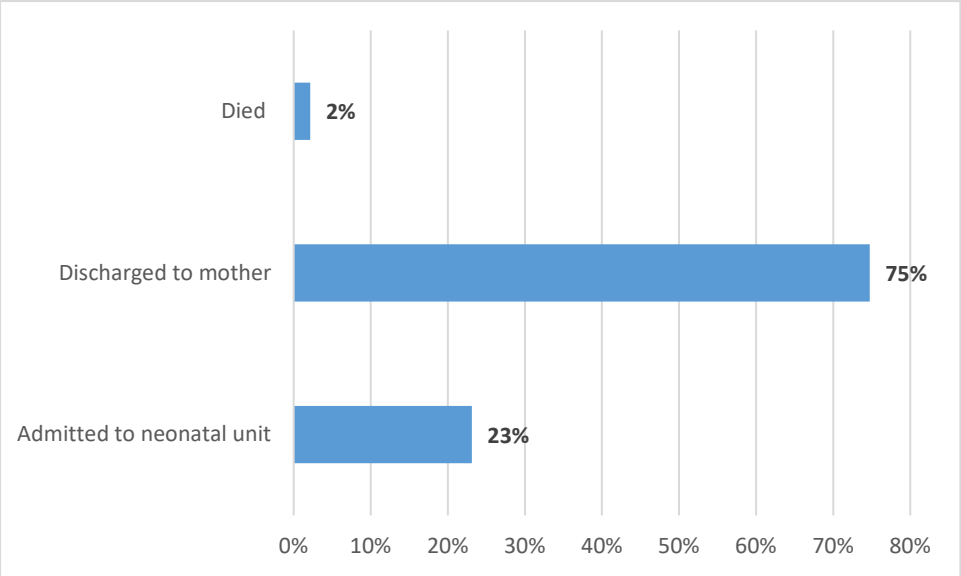

Figure 6: neonatal outcome at birth

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Introduction

In this chapter, the findings of the study will be discussed and compared to similar studies in other settings. There was no study like this, done in Mankweng hospital, that could be found in the literature. This chapter will be separated into 3 sections. Firstly the prevalence of preterm deliveries amongst HIV-positive women in Mankweng hospital, next the demographic characteristics of HIV-positive women delivering preterm babies at Mankweng hospital and finally risk factors that may be associated with preterm delivery amongst HIV-positive women delivering in Mankweng hospital.

5.2 The prevalence of preterm deliveries

In a study that was done worldwide on preterm births, it was found that 15 million babies are born prematurely (Gulland, 2012). In the study, the world's average rate of preterm birth was 11%, and the country with the highest prevalence was found to be Malawi with 18%. In this study, the prevalence of preterm delivery among HIV-positive women was found to be 34%, which is 3 times higher than the world average in the general population. This is comparable to a study that was done in Dr George Mukhari hospital where the prevalence of preterm delivery amongst HIV-positive women was found to be 34% (Gibango et. al. 2018). The other setting that may be closest to ours was a study done in Durban in which the prevalence among HIV-positive women was found to be 14% compared to 6% in HIV-negative women (Naidoo et al. 2011). Compared to a study done in Tanzania looking at the risk factors for preterm birth among HIV-Infected Tanzanian women, the prevalence was found to be 24% (Zack et al. 2014). This was higher than that of their general population which was said to be about 11% in their setting. No study has been done thus far in our setting to determine the prevalence of preterm delivery among HIV-positive women to compare this.

Different reasons may be driving the high prevalence of preterm deliveries in our setting. Mankweng hospital is the only hospital in Limpopo province that provides both obstetrics and neonatal tertiary services. Patients get referred from the district and regional hospitals for complications such as uncontrolled hypertension, pre-eclampsia etcetera, in which most cases preterm delivery is anticipated. The other hospital that provides tertiary obstetrics services is Pietersburg hospital, which does not have a neonatal ICU. For this reason, most of the complicated obstetric cases will be preferentially referred to Mankweng hospital. This will clearly drive up the number of preterm babies being delivered in Mankweng hospital.

5.3 The demographic characteristics of the study population

Extremes of age have been associated with preterm delivery (Ross, 2021). In this study, there was no statistically significant difference between the different age groups in the likelihood of delivering a preterm baby (the p-value was 0.935). For other social demographic variables like employment, smoking and alcohol consumption, there was a lot of missing information. This made it very difficult to draw any meaningful conclusions from the findings. Other socio-demographic characteristics of the study population were not explored because they are not routinely recorded in maternal records and therefore would be very difficult to explore in a retrospective study.

5.4 Risk Factors that may be associated with preterm delivery

Different risk factors are known to be associated with preterm delivery. Some of those factors were also looked at as a cause of preterm delivery in these women. Some studies have shown an association between immunosuppression and preterm delivery (Van der Merwe et. al. 2017). The preterm delivery rate was compared between the women with a CD4 of less than 200 and the women with a CD4 count of more than 200. The prevalence in the group of women with a CD4 of not less than 200 was 46.7% and in the group of women with a CD4 count, of more than 200 was 33.3%. The group with a CD4 count that is less than 200 had a higher prevalence of prematurity. This difference was however not statistically significant with a p-value of 0.392. When

looking at the viral load, the group of women with a viral load that is lower than detectable (suppressed) had a prevalence of preterm delivery of 32.4% and the group of women with a viral load that is not suppressed had a prevalence of preterm delivery of 33.8%. There was no statistical difference between the 2 groups (p-value of 0.875).

In this study, women who had hypertension, UTI, chorioamnionitis, and fibroid uterus had more likelihood of delivering preterm babies compared to those HIV-positive women with no other co-morbidities. This was statistically significant with a p-value of <0.001. These are known risk factors of preterm delivery for the general population as well. There was only 1 woman who had gestational diabetes, who also delivered a preterm baby. This was not enough to be able to conclude the contribution of Gestational diabetes to preterm delivery among HIV positive women premature babies compared to those women without hypertension. This was primarily due to uncontrolled hypertension and the need to do an emergency caesarean section to save both the mother and the unborn child.

The question that might arise from this is: since the prevalence of preterm delivery amongst HIV positive women in Mankweng hospital is so high, are these risk factors higher in HIV positive compared to the general population? Another study comparing the risk factors for preterm delivery amongst HIV positive patients and HIV negative patient needs to be done. In this study, compared to the general population, UTI's did not seem to be a big risk factor for preterm delivery. Possible reasons for this may be that they were picked up early and treated or that some were not picked up at all and therefore not recorded in the maternal records.

Another finding was that of poor administration of antenatal steroids in eligible patients. Only 7.9% of the women who delivered preterm babies were recorded to have received steroids. Some of them did not receive a full course. It was quite surprising to see such a low number of patients receiving antenatal steroids. The question is: are these women presenting to the hospital in advanced labour such that there is no chance to give antenatal steroids? These parameters were not clearly stated in the patient records. This is worrying since antenatal steroids have been shown to decrease neonatal morbidity and mortality. An additional study could explore the

uptake of antenatal steroids and find out reasons why some women who are eligible for steroids do not receive them.

5.5 Conclusion

The prevalence of preterm delivery amongst HIV positive women delivering in Mankweng hospital is very high compared to other settings. The CD4 count and the viral load seem to not have an impact on the likelihood of delivering a preterm baby amongst HIV positive women. Factors such as hypertension, chorioamnionitis and fibroid uterus seem to contribute to this occurrence as in the general population.

Recommendations:

Antenatal management and control of maternal co-morbidities during antenatal care is also very important to decrease preterm delivery.

The proper management of HIV is very important to decrease the prevalence of prematurity amongst HIV positive women.

Better record keeping is needed to get good quality, representative data to conduct further studies that are representative of the general population.

Further research needs to be done in our setting to determine the overall incidence of preterm delivery in both HIV-positive and HIV-negative patients.

And research needs to be done looking specifically as to whether the known risk factors of preterm delivery are increased in HIV positive women compared to HIV-negative women.

5.6 The Study Limitations

This was a retrospective study, therefore some of the patient records could not be located and therefore the calculated sample size could not be reached. Because of this, the study may not be representative of the study population and the findings may not be generalised to the general HIV positive population.

In some of the patient records that were retrieved, a lot of data was missing causing challenges with data interpretation. Although all babies born to HIV-positive mothers in Mankweng hospital are done a birth PCR, most of the babies did not have an HIV

PCR result because it was difficult tracing the results because the maternal record and newborn record had different hospital numbers. These children are usually followed up at the local clinic.

This was a single-centre study, and the sample size was small

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ANNEXURE 2: **DATA COLLECTION TOOL**
Prevalence of preterm deliveries in women living with human immune deficiency virus at Mankweng hospital, Limpopo.

Designated number ☐

SECTION A: Demographic data

1. Maternal age <18 ☐
   18 – 25 ☐
   26 – 35 ☐
   36 – 45 ☐
   > 45 ☐
2. Gravidity ☐
3. Parity ☐
4. Gestational age at booking ☐
5. HIV Screening
   5.1 First HIV test ☐
   5.2 Second HIV test ☐
   5.3 Date of initiation of ART ☐
   5.4 ART regimen(current) ☐
   1.
   2.
   3.
   5.5 CD4 Count ☐
   5.6 Viral load ☐

6. Co-morbidities

1. Urinary tract infection
2. Chorio-amnionitis
3. Cervical insufficiency
4. Gestational diabetes
5. Hypertension
6. Fibroid uterus
7. Obesity
8. Other
9. None

SECTION B: Labour and neonatal data

1. Date of delivery
2. Mode of delivery

C/Section	NVD	Assisted

3. Employment: Yes No
4. Smoking: Yes No
5. Alcohol use: Yes No
6. Gestational age at delivery
7. Perinatal steroid administration

No		Yes	
	If yes, how many doses		

8. Birth weight
9. Apgar

1min		5min		score

10. Birth PCR

11. Outcome at birth: admitted to the neonatal unit. ☐

Discharged to mother. ☐

Died ☐

12. Prematurity-relatedated problems

1.
2.
3.
4.
5.

ANNEXURE 3:APPROVAL LETTER FROM TREC

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email:anastasia.ngobe@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: **27 July 2021**

PROJECT NUMBER: **TREC/102/2021: PG**

PROJECT:

Title:	Prevalence of preterm deliveries in women living with Human Immunodeficiency Virus at Mankweng Hospital, Limpopo
Researcher:	G Rikhotso
Supervisor:	Dr CJ Sutton
Co-Supervisor/s:	Dr MI Hlahla
School:	Medicine
Degree:	Master of Medicine in Paediatrics and Child Health

PROF P MASOKO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE
The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

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ANNEXURE 4: APPROVAL LETTER FROM THE DEPARTMENT OF HEALTH

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Department of Health

Ref : LP_2021-08-003
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

Glenrose Rikhotso

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

Prevalence of preterm deliveries in women living with human immunodeficiency virus at Mankweng hospital, Limpopo

1. Permission to conduct research study as per your research proposal is hereby Granted.
2. Kindly note the following:
   a. Present this letter of permission to the institution supervisor/s a week before the study is conducted.
   b. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
   c. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   d. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   e. The approval is only valid for a 1-year period.
   f. If the proposal has been amended, a new approval should be sought from the Department of Health
   g. Kindly note that, the Department can withdraw the approval at any time.

   Your cooperation will be highly appreciated

PP **Head of Department** **Date** 13/09/2021

Private Bag X9302 Polokwane
Fidel Castro Ruz House, 18 College Street. Polokwane 0700. Tel: 015 293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

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ANNEXURE 5: PERMISSION LETTER FROM MANKWENG HOSPITAL

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

MANKWENG HOSPITAL

Dear Dr G Rikhotso,

RE: REQUEST TO CONDUCT RESEARCH AT MANKWENG HOSPITAL

1. Permission is hereby granted for your research titled: Prevalence of preterm deliveries in women living with Human Immunodeficiency Virus at Mankweng Hospital, Limpopo.
2. Permission is granted provided that the conditions set out in the permission letter issued by the Limpopo Department of Health (Ref: LP_2021-08-003) are abided by in entirety.
3. Please provide the Office of the Clinical Executive Director with an updated timeline of when the data will be collected at least one week prior to planned collection.
4. Permission may be withdrawn at any time.

Dr TM Ndou
Public Health Medicine
Acting Clinical Executive Director

27 September 2021
Date

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