VERTICAL TRANSMISSION OF HIV AMONG HIV INFECTED MOTHERS WITH TERM PRE-LABOUR RUPTURE OF MEMBRANES IN MULAGO HOSPITAL

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MAY 2010
DECLARATION

I declare that the work done in this book was personally done by the author in Labour ward of New Mulago Hospital, Kampala District, Uganda and has never been presented to any institution of learning for any academic award.

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DEDICATION

I dedicate this work to my Beloved parents, Mr. John J. Umoren (late) and Mrs. Christiana J. Umoren; great lovers of education who gave all their children the best education they could afford as a second gift, the first being the knowledge, Love & respected fear of God.

Prompted by my curiosity, my father taught me ALL I needed to know in primary one and much more before I could set my tiny feet in school!
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<table>
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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency syndrome</td>
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<tr>
<td>ANC</td>
<td>Antenatal care</td>
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<td>ALARM</td>
<td>Advances in Labour and Risk Management</td>
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<td>ARV</td>
<td>Antiretroviral drugs</td>
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<td>AZT</td>
<td>Zidovudine (ZDV)</td>
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<td>ECS</td>
<td>Elective Caesarean Section</td>
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<td>GA</td>
<td>Gestational age</td>
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<td>HAART</td>
<td>Highly active antiretroviral therapy</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>IDI</td>
<td>Infectious disease Institute</td>
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<tr>
<td>LNMP</td>
<td>Last normal menstrual period</td>
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<tr>
<td>MB.Bch</td>
<td>Bachelor of Medicine and Bachelor of Surgery</td>
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<tr>
<td>MB.ChB</td>
<td>Bachelor of Medicine and Bachelor of Surgery</td>
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<tr>
<td>MJAP</td>
<td>Mulago – Mbarara Teaching Hospitals’ Joint AIDS Program</td>
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<tr>
<td>M. Med</td>
<td>Master of Medicine.</td>
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<td>MOH</td>
<td>Ministry of health</td>
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<td>MTCT</td>
<td>Mother to Child Transmission of HIV</td>
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<tr>
<td>NVP</td>
<td>Nevirapine</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>PMTCT</td>
<td>Prevention of mother to child transmission of HIV</td>
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<td>PROM</td>
<td>Pre-labour rupture of membranes.</td>
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<tr>
<td>RA</td>
<td>Research Assistant</td>
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<tr>
<td>SD NVP</td>
<td>Single dose Nevirapine</td>
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<td>SVD</td>
<td>Spontaneous vertex delivery</td>
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<tr>
<td>TASO</td>
<td>The AIDS Support Organisation</td>
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<tr>
<td>UNAIDS</td>
<td>United Nations Agency for Acquired Immunodeficiency syndrome.</td>
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<td>VT</td>
<td>Vertical Transmission of HIV</td>
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OPERATIONAL DEFINITIONS

HIV positive
A person tested for HIV infection using highly sensitive test – determine HIV1/2, HIV 1/2 stat Pak & Uni-Gold test and found to be having antibodies to HIV 1 and 2.

HIV Negative
A person tested for HIV infection using highly sensitive test – determine HIV1/2, HIV 1/2 stat Pak & Uni-Gold test and found not to be having antibodies to HIV 1 and 2.

A case of PROM
A pregnant woman at 37 or more weeks of amenorrhoea with no vesico-vaginal fistula having history of draining fluid vaginally and found actively draining liquor on speculum examination with positive litmus paper test.

Vertical Transmission of HIV
Transfer of HIV infection from an infected mother to her child.
ABSTRACT

**Background**

The risk of an infected mother transmitting human immuno-deficiency virus (HIV) to her baby ranges from less than 2% in United Kingdom (UK) and North America to 45% in sub-Saharan Africa. Pre-labour rupture of membranes (PROM) is the spontaneous rupture of chorioamniotic membranes of the fetus anytime after 37 weeks but before onset of labour. HIV is one of the risk factors for PROM. Antiretroviral drugs (ARV) given to HIV infected pregnant mothers have been shown to reduce the risk of vertical transmission (VT). There are many HIV infected mothers whose pregnancies are complicated by PROM in Mulago hospital - 4.2% in 2009 with an average of 7 HIV infected mothers with PROM per week. We did not know how much PROM had contributed to VT in Mulago hospital in this era of ARV.

**General Objective.** To determine the risk of vertical transmission of HIV among HIV infected mothers whose pregnancies were complicated by PROM in Mulago hospital.

**Methodology.** A prospective cohort study was conducted in Mulago labour ward. Fifty one HIV infected pregnant mothers whose pregnancies were complicated by PROM and 51 HIV infected mothers without PROM were recruited for the study. Their babies’ blood sample were collected at six weeks and subjected to a DNA/PCR test.

**Data Management.** Data was collected using a pre tested interviewer administered questionnaire after seeking informed consent. CD4 count and DNC/PCR data were obtained from medical records after test was done. The data collected were entered into the computer using Epi data double entry, cleaned and exported to stata version 10 for analysis.

**Result:** There was an increased risk of HIV transmission in babies born to HIV infected mothers whose pregnancies were complicated by PROM though the significance could not be statistically established at logistic regression analysis. HIV infected mothers who had taken combination ARV therapy had reduced rate of VT of HIV to their babies compared to those who took single dose nevirapine. The study also re-affirmed the protective effect of exclusive breastfeeding in reduction of HIV transmission to babies.
CHAPTER ONE

1.1 INTRODUCTION

Pre – labour rupture of membranes is the spontaneous rupture of membrane anytime beyond 28th week of pregnancy but before the onset of labour. There are two types:

a) Preterm pre - labour rupture of membranes (PPROM) which is the rupture of membranes before 37 completed weeks of gestation.

b) Pre-labour rupture of membranes (PROM) which occurs after 37 completed weeks but before onset of labour.

Both of these types are common complications of pregnancies seen often in Labour ward of Mulago hospital. The prevalence of PROM in Mulago hospital over three years, 2007 – 2009 ranges between 3.4 - 4.2% with an average of 7 HIV infected mothers whose pregnancies were complicated by PROM per week. The emphasis of this study was on PROM.

HIV infected mothers had a 25 – 35% chance of transmitting the virus to their babies before the introduction of antiretroviral drugs. The risk of vertical transmission before the advent of ARV has been documented to increase if there is pre-labour rupture of membrane by 2% for every hour of PROM after the first 4 hrs from onset of PROM. How much PROM has contributed to the incidence of VT of HIV in HIV infected mothers in this era of antiretroviral therapy (ARV) had not been documented in Mulago hospital. This study was conducted in the Mulago setting to address this gap in knowledge.
1.2 LITERATURE REVIEW

Human immuno-deficiency virus prevalence among pregnant women attending antenatal clinics in Uganda is 6.2 % with spikes observed in selected sites\textsuperscript{5} while the prevalence among pregnant women attending antenatal clinic in Mulago hospital is 10\%\textsuperscript{6} being higher in women than men and children. Overall, it is estimated that 59\% of HIV infection in Uganda is among women of 15 – 49 years old \textsuperscript{7}. This demonstrates the significance of mother to child transmission of HIV in the Mulago setting.

Term pre-labour rupture of membrane (PROM) occurs in 2 – 10\% of pregnancies while preterm pre-labour rupture of membrane (PPROM) occurs in 2 -3\% of pregnancies. The risk of infection to mother and fetus is increased after occurrence of PROM, whether at or before term \textsuperscript{8}.

The fetal membrane contains progelatinase, progelatinase activator and progelatinase activator inhibitor. Progelatinase activator activates progelatinase into an active enzyme gelatinase that breaks down gelatin in collagen of amniotic membrane leading to membrane weakness. Progelatinase activator inhibitor inhibits excessive activity of progelatinase activator until late in labour so that the membranes rupture only when labour is near \textsuperscript{9}. It is pathological then, when membranes rupture before term or before onset of labour.

The cause of PROM is not known in majority of cases. Some of the risk factors associated with PROM include polyhydramnious, cervical incompetence, uterine abnormality, previous cervical surgery (conization or cone biopsy), following cervical cerclage or amniocentesis, trauma including motor vehicle accident or domestic violence.
Other risk factors include past obstetrical history of PROM, race – black race more at risk than white race, smoking, use of drugs and stress \(^8\).

It is reported that coitus and repeated vaginal examinations increase the risk of PROM \(^{10}\). Anaemia, previous abortion, previous caesarean section, hypertension are also risk factors for PROM \(^{11}\).

Other risk factors are maternal age at delivery of 35 years and above, primigravida, premature contractions, vaginal bleeding in first trimester \(^{12}\). Infections like chorioamnionitis, urinary tract infection, bacterial vaginosis, lower genital tract infection, HIV infection among others are known risk factors associated with PROM. The prevalence of bacterial vaginosis among women in labour at term in Mulago hospital has been documented as 69% and it had a positive association with PROM \(^{13}\). Infections cause more progelatinase activator activity resulting in more progelatinase being converted into gelatinase. This breaks down the collagen in amniotic membrane leading to weakness of the membrane. Also the inflammatory process of infection and bacteria produce proteases which breakdown protein of the chorioamniotic membrane decreasing its tensile strength. As stated by Buga, it is not known whether the infection of HIV does the same, but it could be that the same process of weakening of the membrane is caused by HIV infection on the membrane or it could be that the high viral load of bacterial vaginosis in HIV infected mothers is the contributing factor \(^{14}\).

1.2. **PMTCT IN UGANDA**

The prevention of mother-to-child transmission (PMTCT) programme in Uganda began in 2000 to address the heavy burden arising from association between HIV/AIDS and pregnancy and the potential benefits of averting VT of HIV \(^{15}\). The programme provides
comprehensive package of care including administration of prophylactic ARVs to the pregnant women living with HIV during pregnancy, labour and immediate post partum period. Records show that by December 2005, the PMTCT programme had provided counseling to about 35% of all pregnant women; test about 20%, identified about 15% of pregnant women living with HIV of which 10% of them were able to access prophylactic ARVs.\(^{15}\)

### 1.2 PMTCT IN MULAGO HOSPITAL

The PMTCT programme in Mulago hospital started in 2001 after the programme was initiated at the National level by the Ministry of health in 2000. The objectives include:

- Increase access to HIV counseling and testing among new antenatal attendees (plus labor & delivery).
- Increase the proportion of HIV infected women who enroll into PMTCT and who receive the intervention up through delivery & return for postnatal care.
- Increase follow up of both mothers and infants postnatally through:
  - Provision of early diagnosis for HIV exposed infants born to HIV infected women in the PMTCT
  - Linkage for ARV treatment at paediatric clinics offering treatment
  - Provide follow up & post partum linkage to care and treatment for infected women and their partners identified through the PMTCT program.
- Expand PMTCT core program services to include greater access to:
  a) PMTCT ARV prophylaxis as indicated by Ministry of Health (MOH) policy
  b) Infant feeding counseling
  c) Peer psychosocial support
d) Uptake of family planning

e) Couple counseling

f) Male and community involvement in PMTCT services including HIV testing and referral.

Mulago hospital PMTCT activities are carried out in three antenatal care (ANC) clinics – upper Mulago, lower Mulago and private outpatient department (OPD); three labour wards – upper Mulago, lower Mulago & private wards (6D&E); three postnatal clinics – upper Mulago, lower Mulago & private OPD and one ART clinic (the PMTCT follow-up clinic). It has an average daily attendance of ANC (new clients) – 90 in upper mulago, 60 in lower mulago & 10 in private OPD; labor & delivery – 3 in upper mulago, 7 in lower Mulago & 1 in private ward; post natal (1st visit) – 5 upper mulago, 3 in lower mulago & <1 in private OPD and PMTCT follow-up of 70 6. In 2008, new attendees were 3000 women & all of them accepted HIV test and were given results. HIV prevalence in 2008 among pregnant women attending ANC in Mulago hospital was 10% 6. ARV regimens available for PMTCT are SD NVP, AZT + SD NVP, AZT/3TC + SD NVP and HAART for low CD4 (<250/WHO stage III & IV) for mothers and NVP and AZT syrup for babies. In addition, PMTCT in Mulago offer septrin prophylaxis for all women, support for infant feeding, home visiting for women on HAART, weekly men’s access evening clinic, children’s club among others. Infant follow-up (8weeks & below) of 2008 had 1113 infants, 1020 were tested and 49 (4.8%) were positive 6. Postnatal women are referred for treatment when babies are 6 months to MJAP, IDI, TASO, Mildmay and other treatment sites close to patients’ homes.
1.2.3 MOTHER TO CHILD TRANSMISSION OF HIV

Mother-to-child transmission (MTCT) of HIV is the commonest etiology of paediatric HIV infection throughout the world. MTCT accounts for 90% of HIV infection in children. Transmission of HIV can occur at any point in pregnancy as well as after birth while mother is breastfeeding. In non-breastfeeding populations, most transmission (50–75%) is believed to occur near or during the time of delivery when membranes have ruptured and the infant is exposed to fluids in the maternal genital tract. The infant at this point may ingest maternal secretions from the cervix or vagina through the nose or mouth. A study in Thailand showed a very strong association between the presence of HIV in infant nasal/oral secretions and mother-to-child transmission. In utero infection through the placenta accounts for 25%; intrapartum accounts for 60% and postnatal transmission through breastfeeding accounts for 15%. Possible mechanisms include transfusion of the mother’s blood to the fetus during labour contractions, infection after rupture of membranes and direct contact of fetus with infected secretion or blood from maternal genital tract. High levels of plasma Human immunodeficiency virus – 1 as evidenced by low CD4 count is associated with high risk of vertical transmission.

1.2. VERTICAL TRANSMISSION OF HIV AND MODE OF DELIVERY

Several interventions for reducing vertical transmission of HIV have been tried. Elective caesarean section (ECS), that is Caesarean section before onset of labour or rupture of membrane in HIV infected mothers has been found to reduce MTCT of HIV as against other mode of delivery. In a meta analysis of twenty six studies by the Cochrane collaboration, ECS in mothers not taking ARV or those on only Zidovudine was found to reduce MTCT. Post partum morbidity was seen to be generally higher in HIV infected
mothers who had ECS than those who had spontaneous vaginal delivery (SVD). These include febrile morbidity, urinary tract infection, endometritis, thromboembolism. Emergency CS carries higher post partum morbidity than ECS. SVD is safer than operative deliveries in terms of morbidity to the mother. As stated by the Cochrane collaborative analysis, the magnitude of the effect of ECS in decreasing MTCT is larger than the risk of post partum morbidity, the chosen mode of delivery of HIV infected mothers should be assessed in terms of risks as well as benefits.

1.2 PROM AND VERTICAL TRANSMISSION OF HIV

PROM is one of the risk factors for VT of HIV in pregnancy. Prolonged rupture of membranes has been shown to double the risk of VT of HIV. It increases more if membranes have been ruptured for more than 4 hrs. The risk of MTCT is said to increase approximately 2% for every hour of membrane rupture up to 24 hrs. A meta-analysis of fifteen cohort studies indicated that the VT in pregnancy complicated by PROM is 8 – 31% at 2 hrs & 24 hrs respectively. In Mulago hospital, it has been found that the proportion of HIV infection was higher in mothers with PROM than mothers without PROM who were in active labour but there is no documentation of the risk of VT in Mulago. There may be greater risk of VT in PROM mothers than non PROM mothers with HIV infection in Mulago hospital.

1.3 ANTIRETROVIRAL DRUGS AND VERTICAL TRANSMISSION OF HIV

WHO estimates that VT is responsible for over 1.5 million HIV infected children annually world wide. The risk of an infected mother transmitting HIV to her baby ranges from less than 2% in UK & North America to 45% in sub-Saharan Africa. ARV reduce
the viral replication and can reduce MTCT of HIV either by lowering plasma viral load in pregnant women or through post exposure prophylaxis in their newborn. Based on thirteen cohort studies, the risk of VT of HIV without ARV was estimated to be about 15 – 20% in Europe, 15 – 30% in the USA and 25 – 30% in Africa. A meta-analysis of the efficacy of ARV in reducing MTCT of HIV in Africa has shown that VT is 10.6% (95% CI: 8.6 – 13.1) at 4 – 6 weeks and 21.0% (95% CI: 15.5 – 27.7) transmission for placebo. No documentation is available on the contribution of PROM to the incidence of VT with ARV treatment among HIV positive mothers whose pregnancies are complicated by PROM in Mulago hospital. This study aimed at addressing this gap in Mulago hospital.

1.4 PROBLEM STATEMENT

There are many HIV infected mothers whose pregnancies are complicated by PROM in our setting, 4.2 % in 2009 with an average of 7 HIV infected mothers with PROM per week. Most mothers with PROM report in labour ward after many hours of rupture of membrane. Even when they are admitted, the active management of labour they require, mainly induction of labour in favourable conditions may not be possible due to high number of patients in labour at the same time and inadequate staff. This leads to further delay before delivery. There is need therefore to document how much PROM contributes to the incidence of VT in HIV infected pregnant mothers on antiretroviral therapy in our setting.
1.5 Study Justification

The contribution of PROM to the incidence of vertical transmission of HIV in HIV infected mothers in Mulago hospital was not known. Before the introduction of ARV and the PMTCT programme, the risk of VT of HIV was 25 – 35% among HIV infected pregnant women. PROM had been documented before advent of ARV to be one of the risk factors of VT and the risk thought to be higher if the duration of PROM is more than 4 hrs. VT had been found to be directly proportional to the duration of PROM with a 2% risk increase for every hour of membrane rupture after 4 hrs. Every HIV infected pregnant mother in Mulago hospital has access to at least one type of ARV. There is still limited research about VT of HIV among mothers whose pregnancies are complicated by PROM on ARV treatment.

The findings of the study might be helpful in formulating policy for the management of HIV infected mothers whose pregnancies are complicated by PROM in our setting. It may help to enhance education of women of reproductive age about HIV and encourage testing of women pre pregnancy or in early pregnancy to improve the quality of care of pregnant mothers with HIV infection. The study may also provide baseline information for further studies.
The variables in the conceptual framework above are some of the risk factors likely to influence VT of HIV. ARV taken before conception or early in pregnancy may reduce the risk of VT and raise the CD4 count of the mother. Knowledge of the CD4 count of the mother influences the choice of ARV\(^6\). CD4 count has effect on Clinical stage of HIV which in turn affect VT of HIV\(^{19}\). Clinical stage 3 (moderate disease) and 4 (severe disease) have low CD4 counts\(^{27}\). Clinical stage of HIV may also affect breastfeeding. A mother with severe disease (stage 4) may not be able to breastfeed. There is a possibility of high risk of VT if she breastfeeds her baby. History of other infection like genito-
urinary tract infection in a HIV infected pregnant mother increases the risk of VT \(^{28}\). This may affect CD4 count. A low CD4 count provides opportunity for other infections. Duration of PROM affects VT. It has been documented that the risk of VT is higher after 4 hrs \(^4\). There is HIV transmission in - utero. It is one of the known means of VT of HIV. It has been shown that mode of delivery affect the risk of VT. ECS has been documented to reduce VT by at least 20% as compared to other modes of delivery \(^{29}\).

1.6 **RESEARCH QUESTION.**
What is the risk of vertical transmission of HIV in babies born to HIV infected mothers whose pregnancies are complicated by PROM?

1.7 **RESEARCH OBJECTIVES.**

**GENERAL OBJECTIVE**
To determine the contribution of PROM to vertical transmission of HIV among HIV infected mothers whose pregnancies are complicated by PROM in Mulago hospital.

**SPECIFIC OBJECTIVE**
1. To compare the risk of vertical transmission of HIV in babies born to HIV infected mothers whose pregnancies are complicated by PROM and those without PROM in Mulago hospital.

2. To compare the efficacy of combination therapy versus single dose nevirapine in reduction of VT of HIV in babies born to HIV infected mothers whose pregnancies are complicated by PROM and those without PROM.

1.8 **RESEARCH HYPOTHESIS.**
**Null Hypothesis:**
PROM does not increase the risk of vertical transmission of HIV in babies born to HIV infected mothers in Mulago hospital.
Alternative Hypothesis:

PROM increases the risk of vertical transmission of HIV in babies born to HIV infected mothers in Mulago hospital.
CHAPTER TWO

2.0 METHODOLOGY

2.1 Study Design.
This was a prospective cohort study.

2.2 Study setting.
This work was done at Mulago Hospital complex which is the national referral hospital and one of the teaching hospitals in Uganda. It is situated in Kampala, the capital city and is approximately two kilometres north-east of the city centre. The hospital consists of two parts; the Old Mulago (now known as Upper Mulago) and New Mulago (now known as Lower Mulago). The New Mulago Hospital is a 1200 bed hospital. It was opened on the 16th October 1962 by her Royal Highness the Duchess of Kent.

Mulago hospital complex is divided into various specialized departments namely; Medicine, Paediatrics, Surgery, Directorate of Obstetrics and Gynaecology and their subspecialties, Ear Nose and Throat, Anaesthesia, Public Health, Orthopaedics, Psychiatry, Radiology and Imaging, Radiotherapy and Physiotherapy. There are several research centres within the hospital complex such as Baylor College of Medicine – Uganda, Infectious Disease Institute (IDI), Makerere University – John Hopkins University (MU-JHU) research collaboration and several others.

Mulago hospital offers training for Makerere University Medical students at both undergraduate and postgraduate levels; nursing, midwifery and paramedical training.

The Directorate of Obstetrics and Gynaecology
This directorate occupies the whole fifth floor of New Mulago with three general wards housing the different units; general gynaecological/reproductive medicine unit, materno – fetal unit, gynaecological unit. There is also a labour ward, an emergency gynaecological
ward (5A- Annex), an operating theatre, a neonatal intensive care ward (special care unit) and an Ultrasound scan unit on the floor. The private patients’ wards (6D & E) and private patient’s operating theatre are located on the sixth floor, while private outpatient clinics are run on the second floor. The department also runs Upper Mulago Maternity Centre (UMMC) in ward 14 and Upper Mulago based family planning and voluntary surgical contraception (VSC) centre and the postnatal/ family planning clinic and urogynaecology ward 11.

The directorate is staffed by different cadres of professionals who include professors, senior consultant, senior lecturers, lecturers, registrars, senior house officers and junior house officer. Others are nurses/ midwives, social workers, theatres attendants, record assistant and other auxiliary staff.

**The labour ward**

This is situated directly opposite ward 5B. Duty coverage is undertaken following a monthly timetable for professors/senior consultants, consultants/registrar, senior house officers and junior house officers. The labour ward is divided into a registration area, admission room, first stage room, second stage (delivery rooms), postnatal room, neonatal resuscitation room, operating theatre and high dependency side – where complicated cases (pre-eclampsia, eclampsia, multiple pregnancy etc) are monitored. Mothers with unknown HIV status admitted into the labour ward are counseled and tested for HIV infection by the PMTCT team. Those found to be positive are given ARV treatment. Babies born to HIV infected mothers are given ARV within 24 hours of delivery. Mothers whose pregnancies are complicated by PROM and drained for less than twenty four hours but not in labour are given antibiotics cover and managed
conservatively. Those that have drained for more than twenty four hours with adequate pelvis are started on induction of labour and those with other indications undergo C/S.

2.3 Study Population.

All pregnant mothers who were HIV infected, fulfilled the selection criteria and were willing to participate in the study.

2.4 Selection criteria

Inclusion criteria

1. HIV infected mothers whose pregnancies were complicated by PROM admitted in labour ward that were willing to participate in the study.

2. HIV infected mothers without PROM admitted in labour ward that were willing to participate in the study.

Exclusion criteria

1. HIV infected mothers with and without PROM who were very sick and not able to answer questions.

2. HIV infected mothers with and without PROM with multiple pregnancy. The membranes of one twin might rupture while the other was intact. It was difficult to know which had ruptured by physical examination only.

3. HIV infected mothers with and without PROM with pre-eclampsia.

4. HIV infected mothers with and without PROM with ante partum haemorrhage (APH). Pre-eclampsia and APH are related with VT but it is not very clear how they are related. These mothers often remain very sick even after delivery.

5. HIV infected mothers with and without PROM with intrauterine fetal death (IUFD). The baby will not be there at six weeks’ follow up visit.
2.5 Sampling method
Consecutive sampling was done to get the required sample size. When a mother who was HIV infected and whose pregnancy was complicated by PROM was recruited, the next HIV infected mother without PROM in labour was selected.

2.6 Sample size estimation
The sample size was 102 participants using the formula for two incidence rates (two-sided test). The formula for sample size was obtained from the WHO sample size determination in health studies [30].

\[
\begin{align*}
\text{n} &= \text{Sample size} \\
\alpha &= \text{Level of significance ( % )} = 5 \\
1 - \beta &= \text{Power of the test ( % )} = 99 \\
\lambda_1 &= \text{Anticipated rate of VT in PROM} = 30^{24} \\
\lambda_2 &= \text{Anticipated rate of VT in non PROM} = 10^{26} \\
K &= \text{Population ratio (1)} \\
Z &= \text{Constant (1)}
\end{align*}
\]

The sample size \(n\) was obtained to be 42 participants in each arm of the study, making a total of 84 participants.

Twenty percent (20 %) loss to follow up was added to this.

\[20 \times 84 / 100 = 16.8 \sim 17\]

To get equal number on each arm, 18 was taken

\[84 + 18 = 102\] participants.
1.8 Data collection
Identification of HIV infected mothers was done by the Principal Investigator (PI) or research assistant (RA) at the admission desk of the labour ward. This was followed by mothers being adequately informed about the study. History taking and examination of the mother to confirm or rule out draining of liquor per vagina was done at admission room or in her bed after admission into labour ward. The examination procedure was explained to the mother – painless routine procedure for mothers with complaint of draining if liquor, with slight discomfort when the speculum is being passed. If active draining was found, it was tested with litmus paper. If it was liquor, it turned blue. Mother then gave her consent to participate in the study and was enrolled after she was stable in the ward. She was assigned a study number and the questionnaire was administered. CD4 of the mother was recorded or blood taken before she delivered for CD4 count test if she had none. A total of 102 HIV infected mothers were recruited in both groups.
Variables

The major predictor (Independent) variables collected were:

1). Presence or absence of PROM confirmed by examination of the mother using speculum and litmus paper (see data collection above).

2). Type of ARV medication was obtained from history taking.

Other predictor variables were:

3). CD4 count was obtained from ante natal record of the mother or blood was taken from the mother for test for those mothers without CD4 count.

4). The clinical stage of HIV was determined from examination of the mother using WHO criteria for clinical staging of HIV (see appendix III).

5). The mode of delivery was obtained from labour suite record after delivery of baby.

6). Breastfeeding option was obtained from history taking at follow up visit in six weeks.
7) History of genito-urinary tract infection at any time during the pregnancy was noted. The mother was followed up in labour until delivery. Baby was recruited for the study after delivery. Administration of ARV to the baby was noted in the data sheet. The babies born to mothers on HAART were given only single dose NVP within 24 hours of delivery while those born to mothers on SD NVP or combination therapy were given NVP and combivir syrup within 24 hrs of delivery and supply for 1 week post delivery.

Six weeks follow up:

The mother interviewed breastfeeding option. Blood was collected from the heel of baby for DNA/PCR. The collection of blood sample from the baby was done under aseptic procedure. The heel of the baby was cleaned with spirit swab. Using a sterile lancet, the heel was pricked to get small volume of blood (about 50-100 ul). This was collected on dry filter paper on five circled spots well marked for blood collection for each baby – (dry blood spots -DBS specimen). After collection, pressure was applied on the spot of collection for few seconds to prevent further bleeding. The filter paper was properly labeled and sent to Mildmay Centre laboratory. At least three of the five spots should have blood well centred in the circle \(^{31}\). The result from Mildmay centre was recorded in the follow up form at six weeks.

Mother and her baby were encouraged to continue care or referred to a programme if she had none. Mother was given transport money for coming for follow up visit at six weeks. A total of 84 HIV infected mothers turned up for follow up in both groups.

Outcome variable.

HIV status of baby at six weeks. Blood was taken from the heel of the baby by bloated paper and test for HIV using DNA PCR (see data collection above).
2.9 Data Analysis
The data was coded, double entered into the computer using EPI data 2.1b, cleaned and exported to stata version 10 for analysis.

Bivariate and multivariate analysis were done using generalized linear models (glm) yielding risk ratios and 95% confidence intervals for the different independent variables for the main outcome variable (baby HIV status at six weeks).

Only those variables which had significant p-value at bivariate analysis were fit in the multivariate model.

Attributable risk of PROM to VT of HIV was calculated.

2.10 Quality control
A pre-tested questionnaire was used to collect data. DNA/PCR kits from same manufacturer were used.

The research assistants were trained in the relevant fields pertaining to this study like approach to the mothers, translation of questions, quoting responses, examination of the mothers and others.

The questionnaires were tested to see if it would be able to extract all the needed relevant information. Adjustments were made as needed before the study period.

Accredited laboratories were used for the study. Double entry data was done.

2.11 Ethical consideration
The study had no major ethical issues. Permission to carry out this research was sought from: The Department of obstetric and Gynaecology, Mulago hospital; College of Health Sciences Ethics Research Committee & National Council for Science and Technology, Uganda.

The nature and purpose of the study was fully explained to the participants.
Consent to participate in the study was obtained from participants.

Participation in the study was free and voluntary.

Participants who wanted to withdraw from the study at any stage of questioning were free to do so.

Confidentiality was ensured by using only the study numbers on the questionnaire without participant’s identity.

There access to data was restricted only to the PI and the supervisors.

2.12 Study limitation

a) Lack of knowledge of the viral load during pregnancy in the HIV infected mothers whose pregnancies were complicated by PROM and those without PROM. A high viral load at any time during pregnancy would increase the risk of VT.

b) Inability to measure the vertical transmission rate of HIV in utero in the mothers whose pregnancies were complicated by PROM and those without PROM.

These limitations were circumvented on the assumption that the effect would be the same in both groups (PROM and non PROM).
CHAPTER THREE

3.0 RESULTS
This study aimed at determining the risk of vertical HIV transmission among HIV infected mothers whose pregnancies were complicated by PROM. 51 HIV infected mothers whose pregnancies were complicated by PROM and 51 HIV infected mothers without PROM, giving a total of 102 HIV infected mothers were recruited into the study. A total of 84 HIV infected mothers came back for follow up visit at six weeks post delivery (42 HIV infected mothers whose pregnancies were complicated by PROM and 42 HIV infected mothers without PROM). The following are the results.

Figure 4: Flow chart of recruitment and six weeks’ follow-up visit of study Participants

<table>
<thead>
<tr>
<th>PROM GROUP</th>
<th>NON PROM GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 HIV infected mothers recruited</td>
<td>51 HIV infected mothers recruited</td>
</tr>
<tr>
<td>Mothers delivered. 102 babies recruited within 6 hours of delivery</td>
<td></td>
</tr>
<tr>
<td>2 babies died before 6 weeks. 1 mother went back to the village. 4 mothers said they had check up in HC near their home. 2 could not be traced.</td>
<td>1 baby died before 6 weeks. 3 could not be traced. 2 mothers went back to the village. 3 mothers said they had check up in HC near their home.</td>
</tr>
<tr>
<td>6 weeks’ follow up visit 42 Mothers and Babies. (Included in the analysis)</td>
<td>6 weeks’ follow up visit 42 mothers and babies (Included in the analysis)</td>
</tr>
</tbody>
</table>
3.1 RESEARCH RESULTS

Table 1: Some characteristics of the study participants. N = 84

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>PROM n(%)</th>
<th>NON PROM n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 &amp; Less</td>
<td>12 (44.4)</td>
<td>15 (55.6)</td>
</tr>
<tr>
<td>25 +</td>
<td>20 (52.6)</td>
<td>27 (47.4)</td>
</tr>
<tr>
<td>**Educational Level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school &amp; None</td>
<td>22 (50.0)</td>
<td>22 (50.0)</td>
</tr>
<tr>
<td>Secondary school &amp; Tertiary</td>
<td>20 (50.0)</td>
<td>20 (50.0)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prime</td>
<td>8 (53.3)</td>
<td>7 (46.7)</td>
</tr>
<tr>
<td>2 – 4</td>
<td>27 (58.7)</td>
<td>19 (41.3)</td>
</tr>
<tr>
<td>5 +</td>
<td>7 (30.4)</td>
<td>16 (69.6)</td>
</tr>
<tr>
<td>Type of ARV taken</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‡ Combination therapy</td>
<td>29 (51.8)</td>
<td>27 (48.2)</td>
</tr>
<tr>
<td>SD NVP</td>
<td>13 (46.4)</td>
<td>15 (53.6)</td>
</tr>
<tr>
<td>Clinical stage of the disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>35 (50.7)</td>
<td>34 (49.3)</td>
</tr>
<tr>
<td>2</td>
<td>7 (42.7)</td>
<td>8 (57.3)</td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 350</td>
<td>19 (50.0)</td>
<td>19 (50.0)</td>
</tr>
<tr>
<td>351 +</td>
<td>23 (50.0)</td>
<td>23 (50.0)</td>
</tr>
<tr>
<td>Mean CD4 = 442</td>
<td></td>
<td></td>
</tr>
<tr>
<td>† History of vaginal discharge with pus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (50.0)</td>
<td>25 (50.0)</td>
</tr>
<tr>
<td>No</td>
<td>17 (50.0)</td>
<td>17 (50.0)</td>
</tr>
<tr>
<td>† History of vaginal itching</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28 (51.9)</td>
<td>26 (48.1)</td>
</tr>
<tr>
<td>No</td>
<td>14 (46.7)</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>† History of painful urination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (53.6)</td>
<td>13 (46.4)</td>
</tr>
<tr>
<td>No</td>
<td>27 (48.2)</td>
<td>29 (51.8)</td>
</tr>
<tr>
<td>Mode of Delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVD</td>
<td>26 (40.0)</td>
<td>39 (60.0)</td>
</tr>
<tr>
<td>C/S</td>
<td>16 (84.2)</td>
<td>3 (15.8)</td>
</tr>
<tr>
<td>Method of breastfeeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>28 (43.1)</td>
<td>37 (56.9)</td>
</tr>
<tr>
<td>Not exclusive breastfeeding</td>
<td>14 (73.7)</td>
<td>5 (26.3)</td>
</tr>
</tbody>
</table>

n= number of participants in each group; % = percent
Mean age = 26.9 (5.16)
Median age = 27.5
IQR = 23.5 – 30.0
*Age: The range was 15 – 40 years
**Educational level: No education (6) and tertiary education (5) participants
‡ Combination therapy = AZT/Combivir/NVP/HAART
† History of genito-urinary tract infection in present pregnancy
Majority of the mothers who delivered by C/S were in the PROM group, 16(84.2%) compared to 3(15.8%) in the non PROM group. Many of the mothers in the PROM group did not practice exclusive breastfeeding (73.7 cf 26.3%).

The basic characteristic of the study participants who were lost to follow up were:

Mean age = 25.1; median age = 26 and IQR = 24 – 31.0 years. Their mean CD4 count was 438. These were similar to those who came back for follow-up visit at six weeks.

### Table 2: Comparison of exposure variables with vertical transmission of HIV in babies at six weeks (a bivariate analysis)

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>Total no</th>
<th>POSITIVE n(%)</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROM</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>42</td>
<td>5 (11.9)</td>
<td>2.50</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>42</td>
<td>2 (4.8)</td>
<td>1</td>
<td>0.51 – 12.17</td>
</tr>
<tr>
<td><strong>ARV taken</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>25</td>
<td>6 (19.4)</td>
<td>1</td>
<td>0.012 –</td>
</tr>
<tr>
<td>NVP</td>
<td>52</td>
<td>1 (1.8)</td>
<td>0.09</td>
<td>0.773</td>
</tr>
<tr>
<td>Combination therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CD4 count</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 350</td>
<td>38</td>
<td>3 (7.9)</td>
<td>0.90</td>
<td>0.21 – 3.80</td>
</tr>
<tr>
<td>&gt; 350</td>
<td>46</td>
<td>4 (8.7)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>69</td>
<td>6 (8.7)</td>
<td>0.77</td>
<td>0.99 – 5.91</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>1 (6.7)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>History of genito-urinary tract infection in pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- vaginal discharge with pus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>50</td>
<td>4 (8.0)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>3 (8.8)</td>
<td>0.90</td>
<td>0.19 - 4.30</td>
</tr>
<tr>
<td>- Painful urination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28</td>
<td>2 (7.1)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>56</td>
<td>5 (8.9)</td>
<td>0.79</td>
<td>0.14 – 4.32</td>
</tr>
<tr>
<td><strong>Mode of deliver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVD</td>
<td>65</td>
<td>5 (7.7)</td>
<td>1.37</td>
<td>0.29 – 6.50</td>
</tr>
<tr>
<td>C/S</td>
<td>19</td>
<td>2 (10.5)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Exclusive Breastfeeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>65</td>
<td>3 (4.6)</td>
<td>0.22</td>
<td>0.05 – 0.89</td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>4 (21.1)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

n= number in each group; % = percent; RR = Risk Ratio; CI = Confidence interval

Mothers with PROM were more than two times likely to transmit HIV virus to their babies than mothers without PROM (RR = 2.50; 95% CI 0.51 – 12.17).
Exclusive breastfeeding is likely to be protective (RR = 0.22; 95% CI 0.05 – 0.89). Mothers receiving combination ARV therapy had a lesser chance of transmitting HIV virus to their babies (RR = 0.09; 95% CI 0.012 – 0.773) compared to mothers who got SD NVP.

Table 3: Comparison of adjusted relative risk for CD4 count, clinical stage, genito-urinary tract infection and mode of delivery with vertical transmission of HIV in babies at six weeks (a multivariate Analysis).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Crude RR (95% CI)</th>
<th>Adjusted RR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROM</td>
<td>2.5 (0.51 – 12.17)</td>
<td>1.92 (0.45 – 8.25)</td>
<td>0.377</td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>0.22 (0.05 – 0.89)</td>
<td>0.19 (0.54 – 0.72)</td>
<td>0.012</td>
</tr>
<tr>
<td>ARV taken</td>
<td>0.09 (0.01 – 0.77)</td>
<td>0.07 (0.01 – 0.58)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Generalised linear modeling was done for all variables whose p-value was significant at bivariate analysis. In this study that all HIV infected pregnant mothers had received some form of ARV before delivery, PROM did not statistically contribute to VT. Exclusive breastfeeding and combination ARV therapy reduce VT of HIV.

The risk of vertical transmission of HIV in babies born to HIV infected mothers whose pregnancies were complicated by PROM compared to babies born to mothers without PROM in this study is 1.92

**Attributable risk of PROM to VT of HIV in babies at six weeks**

\[
\text{Attributable risk} = \frac{\text{incidence in PROM group} - \text{incidence in the non PROM group}}{\text{incidence in PROM group}} \times 100\%
\]

\[
= \frac{5 - 2}{42} \times 100\% = 8.3\%
\]

The attributable risk of VT of HIV among HIV infected mothers whose pregnancies were complicated by PROM in this study is 8.3 %.
CHAPTER FOUR

4.0 DISCUSSION

There was no difference among HIV infected mothers in the PROM and non PROM groups in terms of age, educational level, parity, type of ARV taken, clinical stage, history of genito-urinary tract infection and CD4 count. The mean age of the participants was 26.9 (5.16); median age was 27.5 (IQR = 23.3 – 30.0 and range 15 – 40 years). This finding was similar to the mothers in a study done in Italy on MTCT in 1999 (Mean age 26 years, range 16–44) 33. Majority of the HIV infected mothers who were delivered by C/S were in the PROM group. This could be explained by the fact that PROM in itself is a risk factor for C/S even without HIV infection.

The result of this study suggests that the presence of PROM was a risk factor for vertical transmission of HIV ( RR = 2.5; 95% CI = 0.51 – 12.17) though we could not establish a statistical significance during logistic regression analysis due to small sample size. This positive trend of PROM increasing the risk of VT in HIV infected mothers whose pregnancies were complicated by PROM was also seen when comparing babies born to mothers in both groups and supported by the attributable risk of PROM to VT of 8.3%.

The current transmission rate in the advent of ARV for Uganda is 6.7% 34. Other studies in this area compared the duration of membrane rupture to the risk of VT. Prolonged rupture of membranes has been shown to double the risk of VT of HIV 21. It increases more if membranes have been ruptured for more than 4 hrs 4;22. The risk of MTCT is said to increase approximately 2% for every hour of membrane rupture up to 24 hrs 23. A meta-analysis of fifteen cohort studies indicated that the VT in pregnancy complicated by PROM was 8 – 31% at 2 hrs & 24 hours respectively 24.
In our study, the least duration of membranes rupture before delivery was 5 hrs. We found no vertical HIV transmission between 5 – 15 hrs of draining of liquor. Four (80%) of VT of HIV occurred in HIV infected mothers whose pregnancies were complicated by PROM that had drained for 16 – 24 hrs while one (20%) occurred after 24 hrs. We could not analyse for this due to the small number of vertical HIV transmission in this group.

In our studies, we found that HIV infected mothers who received combination ARV therapy had a lower risk rate of VT than mothers on SD NVP. It could be that most mothers who received SD NVP had no prior knowledge of their HIV status and had not been on any ARV until they came in labour and were tested. However, other studies have found that HAART is more effective than SD NVP in preventing MTCT of HIV [Vertical transmission risk decreased significantly from 18.2% without treatment to 8.6% with mono/dual therapy and 0.6% with HAART] 35, 22. Some other studies have found SD NVP to be associated with increased risk of VT. In a study done in South Africa on surveillance of mother – to – child transmission prevention programmes at immunization clinics, Rollins N et al stated “amongst mothers who reported that they had taken single dose nevirapine for PMTCT, VTR was 15%” 36.

In this study, CD4 count, mode of delivery and clinical stage of the disease were not significant in the risk of VT among HIV infected mothers whose pregnancies were complicated by PROM. This may probably be as a result of wide use of ARV which has been shown to improve CD4. Majority of the babies who were found to be HIV positive were born to mothers in clinical stage 1. It may be due to the fact that some of these mothers had been on ARV therapy long before they became pregnant and their clinical
stage did not deteriorate, or some were mothers who might have got the infection just before becoming pregnant. HIV positive mothers were not seen in clinical stage 3 or 4. May be advanced HIV infection may possibly reduce fertility, or these mothers may have had miscarriage earlier in pregnancy, making it impossible to have pregnant mothers in these stages.

Exclusive breastfeeding was observed to be protective against VT of HIV. This is in line with other studies. In a study in Kwa Zulu Natal, Coovadia et al found that breastfed infants who also received solids were significantly more likely to acquire infection than were exclusively breastfed children (HR 10.87, 1.51 – 78.00, p=0.018) \(^{37}\). In this study, the risk of VT of HIV was more in babies born to HIV infected mothers whose pregnancies were complicated by PROM compared to babies born to HIV infected mothers without PROM.
CHAPTER FIVE

5.0 CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSIONS
1. In this study, where all HIV infected mothers had taken some form of ARV before delivery, there was an increased risk of HIV transmission to babies born to HIV infected mothers whose pregnancies were complicated by PROM though the significance could not be statistically established at logistic regression analysis.

2. HIV infected mothers who had taken combination ARV therapy had reduced rate of VT of HIV to their babies compared to those who took single dose nevirapine.

3. The study re-affirmed the protective effect of exclusive breastfeeding in reduction of HIV transmission to babies.

5.2 RECOMMENDATIONS
1. The use of combination ARV therapy instead of SD NVP in pregnancy should be scaled up even in our environment to reduce risk of VT.

2. The practice of exclusive breastfeeding among HIV infected mothers in our setting needs more encouragement.

3. Larger studies on effect of duration of membrane rupture and the risk of vertical transmission in this era of ARV in our setting is needed.
REFERENCES.


24. Read J. Duration of ruptured membranes and vertical transmission of HIV-1: A meta-analysis from 15 prospective cohort studies. 7th conference on retroviruses & opportunistic infection. Jan 30 – Feb 2nd, 2000; 7:198


31. AMPLICOR HIV-1 DNA Test, Version 1.5 For Research use only. Roche Diagnostics. Roche Molecular Systems, Inc. 2006


35. Amparo Garcia-Tejedor; Vicente Maiques; Alfredo Perales;Jose Lpez-Aldeguer “Influence of highly active antiretroviral treatment (HAART) on risk factors for


APPENDICES

Appendix 1: Informed Consent Form

IA: Information to the patient.

Introduction

I am Dr. Magdalene Umoren, the Principal Investigator (PI), a master’s degree student in Obstetric/Gynaecology Department of Makerere University College of Health Science, Mulago hospital / I am…, a research Assistant (RA) collecting this data for Dr. Umoren. This study is being carried out with the aim of improving care and provide ways of reducing HIV infection in babies born to HIV infected mothers whose pregnancies are complicated by pre-labour rupture of membranes. It is also as a partial fulfillment for the award of Masters of Medicine degree in Obstetrics and Gynaecology of Makerere University. I am here to request you to participate in the study.

Title of the study:

Vertical transmission of HIV among HIV infected mothers with term pre-labour rupture of membranes in Mulago hospital.

Purpose of the study:

The study is aimed at determining how much the rupture of membranes before onset of labour in HIV infected mothers contributes to their babies getting HIV infection. This will be determined by comparing babies born to HIV infected mothers with PROM and those without PROM. You are chosen because you have fulfilled the criteria of being included in the study (that is, having HIV infection and having pre-labour rupture of membranes / not having pre-labour rupture of membranes).

Study procedure:

You are welcome to participate in this study. Your participation is very important to the success of this study. After your acceptance to participate in the study, you will be asked questions about yourself, the present pregnancy, your past delivery and the drug you are taking for your HIV infection. Your answers will be noted down and kept as confidential records. Some little blood will be collected from the heel of your baby by needle prick
and put on filter paper for the dry spot test. This procedure will be done at six weeks to enable us detect whether the baby has HIV virus.

**Risk:**
The study carries minimal risk to the baby because of the small prick on the heel to collect some little blood for the test. For you, there will be some discomfort by taking you away from the rest of the mothers for interview. The purpose for this is to ensure privacy during the interview.

**Rights:**
Participation in this study is voluntary. You have a right to decline to participate in the study or withdraw from it at any stage without interfering with various level of care on you and your baby. However, we appreciate your time if you accept to participate.

**Confidentiality:**
All information got from you shall be kept confidentially. Only study numbers are on the questionnaire without your identity and results will be produced without your identity.

**Benefits:**
You will benefit from the advice and explanation on your health status by the Principal Investigator and Research Assistants (RA). The knowledge of your baby’s HIV status and starting treatment early are also beneficial to you. The information gathered may help improve management care of other mothers in Uganda whose pregnancy may have similar complications.

**Contact / Enquiries:**
In case of enquiries about the study, feel free to contact the PI, Dr. Umoren on phone No. 0772 370 593. Questions about participant’s right should be addressed to Dr. Charles Ibingira, Chairperson, Research Committee, College of Health Sciences, Makerere University (0414 - 530020).
1B: Statement of consent

I, the undersigned acknowledge that the Principal Investigator / Research Assistant has fully explained to me the nature, purpose and procedure involved in this study. I appreciate that the participation is completely voluntary and that my refusal or withdrawal from the study will not in any way affect any medical service or medical advice I may need now or in future. I therefore sign here as a proof of my consent to participate in this study.

..........................
Signature / Thumbprint

Date..................

I have explained all the features of the study to the participant and to the best of my knowledge and conviction she has understood them.

..........................
Signature of PI / RA

Date ..............
ABANA OKUSIGIBWA OBA OKUFUNA AKAWUKA KA MUKHENYA
MUKISERA KYOKUZAALIBWA NGA KAVA KU BAMAMA BABWE ENGERI
ENSUMDWE GYEYABIKA NGA TEBANATANDIKA KULUMWA OBA
OKUFUNA EBISA MU DWALIRO LYE MULAGO

OKUKKIRIZA OKWETABA MU KUNOONYEREZA

1A: Ekiwandiiko eri akwetabyeemu

Ennyanjula oba Ebigendererwa ne by’afayo:

Nze Dr. Magdalene Umoren, omunoonyerza omukulu, nga nsoma diguli eyokubiri mu byokuzalisa, okujjanjaba nokulabirira endwadde zabakyaala e Makerere University College of Health Science, Mulago hospital/ Nze ………….., omuyambi w’omunoonyereza nga nkunganyirizaako Dr. Umoren amawulire mu kunoonyereza kuno. Omulamwa mu kunonyereza kuno kwe kulongoosa mu ndabirira no kukendeeza omuweendo gw’abaana abazalibwa okufuna akawuka ka mukhenya mukisera kyokuzaalibwa nga kava ku bamaama babwe engeri ensundwe gyeyabika nga tebanatandika kulumwa oba okufuna ebisa.

Okunonyereza kuno kwekumu ku musomo ogwetagisa okumaliriza nsobole okufuna oba okumaliriza deguli eno eyokubiri. Nkusaba okwetaba mukunonyereza kuno.

Omutwe gwokunonyereza kuno:
Abaana okufuna akawuka ka mukhenya mukisera kyokuzaalibwa nga kava ku bamaama babwe engeri ensundwe gyeyabika nga tebanatandika kulumwa oba okufuna ebisa.

Omulamwa oba ekigendererwa mu kunonyereza kuno

Mukunonyereza kuno, twagala okumanya okwaabika kwe nsundwe nga maama w’omwana tanatandika kulumwa oba okufuna ebisa gyekuretera omwana okukwatiswa akawuka ka mukhenya okuva kumaama we.

Kino kijja kusalibwaawo nga tuggerageranya abaana abazalidwa ba maama babwe nga balina akawuka ka mukhenya nga ate babunduka amazzi mu bitundu byabwe ebyekyaama nga bali mbuto nabo abalina akawuka ka mukhenya nga bo tebabunduka amazzi mu bitundu byabwe ebyekyaama nga bali mbuto. Olondedwa kubanga olina byona ebyetaagisa okwetaba mu kunoonyereza kuno. (okuigeza , olina akawuka kamukhenya, obunduka amazzi / tobunduka mazzi.)
Ebinagobererwa mu kunonyereza kuno
Oyanilizidwa mu kunonyerezebwa kuno era okwetaba kwo mukunonyereza kuno kukulu nyo mu mukunonyereza kuno. Bwono kiriza okwetaba mukunoyereza kuno, ojja kubuzibwa ebibuzo abikwaata ku bulamu bwo, olubuto lwo, nga bwo bade ozaala mu emabega ne ddagala lyobadde onywa. Byoonotudamu byona bijja kukumbibwa nga byakyaama nyo . Omwana wo ajjakujibwaako omusaayi gukeberebwe oba alina akawuka ka mukenenya, kino kijja kukolebwa emirundi ebiri, oluvanyuma lwa sabiti mukaaga.

Obuzibu n’obutewulira bulungi:
Wayinza okubaawo okusiyiibwa n’okulumizibwa mu kukujjako omwana omusaayi naye kino tekilina kyabulabe kyona kyekigenda kutoosa ku bulamu bwe. Nawe nga maama w’omwana oyiinza obutawulira bulungi nga tukujje mu bazadde bano. Naye kino kijjakukolebwa olwo kukuuma ebyama byo.

Ddembe lyo okugaana okwetaba mu kunoonyereza kuno:

Okukuuma ebyama ebikukwaatako:
Ebiwandiiko ebiriko ebikukwatako bigenda kukumbibwa bulungi mukifo ekyekusifu nga kyakyaama era elinya lyo lyu kuwebula e namba enakozesebwanga mu kunonyereza kuno.

Byono’ganyulwa mukunonyereza:
Omunonyere ajja kuwa amagozi ku bulamu bwo okumanya amwana wo bwayimiride, n’okutandika obujanjabi amangu kijja kukuyamba. Ebinaazulibwa mukunonyereza kuno bijja kuyamba bazadde bano mu Uganda abalina obuzibu obufanana nga buno.

Ebibuuzzo:
Bwoba olina ebibuzo byona ebikwatagana no kunonyereza kuno ekiseera kyona, labagana nakukuliira Dr. Umoren ku simu eno 0772 370 593. Buuuza ebibuuzzo byona ebikwatagana ne Ddembe lyo mukunoonyereza kuno Dr. Charles Ibingira Chairperson,
1B: Ekiwandiko eky’ okukiriza:
Mbulidwa ne ntegera bulungi ebikwatagana no’kunonyereza kuno abakukulira era nsazeewo okukwetaba mu kyeyagarire era manyi nti nsobola okukusazaamu ekisera kyona nga kino tekigenda kutabula bujjanjabi bwenina kufuna mu dwaliro lino.

Omukono oba ekinkumu kyange wamanga kiraga nti nzikiriza.

……………………………………………                  ……………………………

Erinya mu kyapa n’omukono oba ekinkumu                  Ennaku z’omwezi

……………………………………………                  ……………………………

Mbulide ne nyinyonyora byona ebigendererwa byokunonyereza kuno eri agengenda okukwetabamu bulungi okusinzira kukumanya kwange era nkakasa nti abitegedde bulungi.

……………………………………………                  ……………………………

Erinya mu kyapa n’omukono oba ekinkumu                  Ennaku z’omwezi
APPENDIX 11. STUDY INSTRUMENT

Study number .......... 

QUESTIONNAIRE / OBSERVATION / TEST RESULT CHECK LIST TO DETERMINE VERTICAL TRANSMISSON OF HIV AMONG HIV INFECTED MOTHERS WITH TERM PRE – LABOUR RUPTURE OF MEMBRANES IN MULAGO HOSPITAL.

Socio-demographic data:
1. Age at last birthday ................. years
2. Educational level ..........................
3. Address .................................

Reproductive history:
5. Gravidity .............. Parity ........

Present obstetric events:
6. LNMP ............ EDD ............ GA ....... Completed weeks
7. Estimated fundal height ............. weeks
8. Have you ever had abnormal vaginal discharge (bad smell, pus-like, frothy or curdled milk-like) with the current pregnancy? Yes No
9. Have you ever had vaginal itching in this pregnancy? Yes No
10. Have you ever had severe backache in this pregnancy? Yes No
11. Have you ever had painful micturition in this pregnancy? Yes No
12. Is there any drainage of liquor during this pregnancy? Yes No
13. Date and time of onset of PROM ..........................
14. Date and time of diagnosis of PROM ........................

Past obstetric events:
15. Did you have an abortion (miscarriage) previously? Yes No
16. Did you have a caesarean delivery previously? Yes No
17. Did you have PROM in any of the previous pregnancy? Yes No

HIV related events:
18. Have you been on any form of ARV treatment? Yes No
19. Which ARV are you taking? ..........................
20. How long have you been taking ARV?
      ...... hours  ...... days  ...... weeks  ...... months  ...... years

21. Clinical Stage of HIV / AIDS disease: .....(write the correct number e.g 1, 2, 3 or 4).

22. Date and time of starting induction (if induced) ...........................................

23. Date and time of delivery .................................................................

24. Mode of delivery:    SVD          C/S
   Baby’s weight ....................... kg      Apgar score ..............

25. Baby received ARV after delivery   Yes    No
LABORATORY FORM / SIX WEEKS FOLLOW-UP TO DETERMINE VERTICAL TRANSMISSION OF HIV AMONG HIV INFECTED MOTHERS WITH TERM PRE – LABOUR RUPTURE OF MEMBRANES IN MULAGO HOSPITAL.

Study Number ..............................................
Antenatal number of Patient .........................
Result of CD4 count ......................................
Date tested ................................................

Baby’s DNA PCR result .................................
Date tested ................................................

Practice method of breastfeeding:
   Exclusive breastfeeding
   Not exclusive breastfeeding.
Enamba eyakuwebwa mukunonyereza ……

Ekiwandiiiko ekiriko ebizuulidwa okuva mu kyuuma okusalaowo oba omwaana yafuna akawuka ka mukerenya mukisera ky’okuzalibwa nga kava ku maama we, engeri ensumdwe gyeyabika nga tanatandika kulumwa oba okufuna ebisa mu dwaliro e Mulago

Ebikwata ku muntu wabulijjo:
1. Emyaka emeka gyewasemba okuzaalirako………………
2. Obuyigirize bwo ………………………………………
3. Gy’ Obeera ………………………………………

Ebyafayo byobulamubwo:
5. Embuto meka ze wakafuna……………………… Wakazaala abaana bameka?…………

Ebikwata kubulamu bwo:
6. Olunaku lwe wasemba okulwaala omweezi ……….. Olunaku lwo suubira okuzaala ……….. Olubuto lwa bangka ki? ……… Olubuto lwa sabiti meka?
7. obunene oba obugazi bwa nabaana…………………… sabiti
8. . Wali ofunyeko okubundura amazzi mubifobyo ebyekyaama nga olusu olubi oba amasiira nga oli lubuto? Yee Nedda
9. Osiyibwa mu bitundu ebyekyaama? Yee Nedda
10. Olumizibwa omugongo ng’ olina olubuto luno? Yee Nedda
11. Owulira obulumi ng’ ofuka nga olina olubuto luno? Yee Nedda
12. Oлина amazzi agakuvamu mukisera kino nga olilubuto? Yee Nedda
13. Kyatandika ddi? ………………………………………
14. Wa keberebwa ddi omusawo okumanya nti olina amazi? ……………………………

Ebyafaayo byo ebyemabega:
15. Wali ovudemu ko ku lubuto? Yee Nedda
16. Wali olongoseddaamu omwana? Yee Nedda
17. Wali obunduseeko ku mazzi mu bitundu byo ebyekyaama mu mbuto zobadde nazo Emabega? Yee Nedda
18. Wali obadde ko kubujjanjabi bwamakerenda agaweweza obulwadde
   Bwamukenyana? Yee Nedda
19. Ddagala eriweze mukenenya lyakika ki yomira? ..............................
20. Olimiride banga ki?
   ...... sawa ...... naku ...... sabiiti ...... myezi ...... myaka
    enamba entuufuukojeza nga 1, 2, 3, oba 4)
22. Edagala iye bisa balitandise saawa meeka (Bwe baba nga balimuwasde) .......
23. Enaku z’omwezi omwana iwazalidwa ............................................
24. Engeri omwana gyazalidwa? Bulungi kulongosebwa
    Bakuwade okyupa yebisa  Bamugyeyo na byuma
    Omwana yabadde nobuzito bwenkana wa? ...... kg  Apgar score ........
26. Omwana yawereedwa eddagala eriweze akawuka kamukunenya oluvenyuma
    Iwo kuzalibwa Yee Nedda
## Appendix 111
**WHO clinical staging of HIV / AIDS disease:**

<table>
<thead>
<tr>
<th>WHO Clinical Stage 1</th>
<th>WHO Clinical Stage 2</th>
<th>WHO Clinical Stage 3</th>
<th>WHO Clinical Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Mild disease</td>
<td>Moderate disease</td>
<td>Severe disease (AIDS)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No weight loss</th>
<th>Weight loss 5 – 10%</th>
<th>Weight loss &gt; 10%</th>
<th>HIV wasting syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms or only persistent generalized lymphadenopathy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Sores or cracks around lips (angular cheilitis).</td>
<td>- Oral thrush (or hairy leukoplakia).</td>
<td>- Oesophageal thrush.</td>
<td></td>
</tr>
<tr>
<td>- Itching rash (seborrhea or prurigo).</td>
<td>- More than one month of: - Diarrhoea</td>
<td>- More than one month of: - Diarrhoea</td>
<td></td>
</tr>
<tr>
<td>- Herpes zoster within last 5 years.</td>
<td>Or -Vaginal candidiasis</td>
<td>Or - Unexplained fever.</td>
<td></td>
</tr>
<tr>
<td>- Recurrent upper respiratory tract infections such as sinusitis or otitis).</td>
<td>- Severe bacterial infections (pneumonia, muscle infection, etc).</td>
<td>- Pneumocystic carinii pneumonia (PCP).</td>
<td></td>
</tr>
<tr>
<td>- Recurrent mouth ulcers.</td>
<td>- Pulmonary Tb within last one year.</td>
<td>- Extrapulmonary Tb.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cryptococcal meningitis.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- HIV encephalitis.</td>
<td></td>
</tr>
</tbody>
</table>