KAMPALA INTERNATIONAL UNIVERSITY – WESTERN CAMPUS

FACULTY OF CLINICAL MEDICINE AND DENTISTRY

RISKFACTORS ASSOCIATED WITH PRETERM PREMATURE RUPTURE OF MEMBRANES AT MBARARA REGIONAL REFERRAL HOSPITAL

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DECLARATION

I Tezita Alex hereby declare that the work presented in this dissertation in partial fulfillment of the requirements of the award of the bachelors degree of Medicine and Bachelors degree of Surgery of Kampala International University western Campus is my original work and has never been submitted to any other academic institution before for any awards.

Signed …….. Date ……...

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This dissertation has been produced under my supervision and submitted for examination with my approval;

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Signed ……. Date ……

DEDICATION

I dedicate this work to my parents, Mr. Patrick Bongho and Mrs. Iddah Bongho who stood by me through thick and thin and has been my tower of strength through all my academic adventure, I love you mummy and daddy

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LIST OF ACRONYMS

ACOG	American Congress of Obstetricians and Gynecologists
ANC	Antenatal Care
APH	Antepartum Hemorrhage
BMI	Body Mass Index
EDD	Expected Date of Delivery
EGA	Estimated Gestational Age
FREC	Faculty Research and Ethics Committee
FTB	Full Term Birth
FSB	Fresh Stillbirth
HIMS	Health Information Management Systems
HVS	High Vaginal Swab
IPI	Inter pregnancy interval
LNMP	Last Normal Menstrual Period
MRRH	Mbarara Regional Referral Hospital
MSB	Macerated Stillbirth
MUST	Mbarara University of Science and Technology
PPROM	Preterm Premature Rupture of Membranes
PROM	Premature Rupture of Membranes
PTB	Preterm Birth
PVL	Periventricular Leukomalacia
ROM	Rupture of membranes
SGA	Small for Gestational Age
TWEAK	Tumor Necrosis factor- like Weak Inducer of Apoptosis
UTI	Urinary Tract Infection

OBS & GYN Obstetrics and Gynecology

OPERATIONAL DEFINITION

Preterm Premature Rupture of Membranes is the rupture of membranes between 28 to 37 completed weeks of gestation.

ABSTRACT

Background: Preterm Premature rupture of membranes (PPROM) is rupture of fetal membranes before37 completed weeks of amenorrhea; it increases the risk of prematurity and leads to a number of other perinatal morbidities, including respiratory distress syndrome and prematurity. It complicated about 5% of all pregnancies.

Main study objective: A study to determine the risk factors associated with PPROM and outcomes of deliveries complicated by PPROM in MRRH.

Methods: 274 mothers were recruited in a prospective un- matched case control study in a ratio of 1 case to 3 controls to determine the risk factors associated with PPROM, at MRRH. Social demographic variables, obstetric history and information on medical factors were collected. High vaginal swabs were collected and analysed for bacterial colonization. Univariate and mmultivariate analysis to determine associated factors with PPROM was done. A p –value of 0.05 was considered statistically significant.

Results: Primary outcomes included alcohol intake during pregnancy P=0.01 (OR) 3.8 1.3-11.2(95%CI, HIV infection) P=0.03 (OR) 2.5 1.1-5.6(95%CI, presence of symptomatic urinary tract infection P=0.02 (OR)2.6 1.2-5.9 (95%CI), short inter pregnancy interval P=0.01 (OR)0.2 0.1-0.5(95%CI), high parity greater than 4 P=0.01 (OR)14.9 4-54.9(95%CI) and poor antenatal attendance less than 3 P=0.03 (OR) 2.5 O.1-5.6 (95%CI) were significantly associated with preterm premature rapture membranes.
Secondary outcomes of PPROM are associated with poor pregnancy outcomes like prematurity; gram negative organisms were isolated from the high virginal swab cultures.

Conclusion: Risk factors associated with PPROM included, alcohol intake during pregnancy, presence of urinary tract infection and having a short inter pregnancy period and a poor antenatal care clinic attendance during the pregnancy and high parity.

CHAPTER ONE: INTRODUCTION

1.1 Background

Premature rupture of membranes (PROM) is the rupture of the fetal membranes before the onset of labor. In most cases, this occurs near term, but when membrane rupture occurs before 37 completed weeks' gestation, it is known as preterm premature rupture of membranes (PPROM). PROM complicates 10 percent of pregnancies, with 3 percent of pregnant women having PROM before 37 weeks of gestation. Approximately one third of preterm births occur as a result of PPROM, which is more likely to occur in populations of lower socioeconomic status. As such, PROM and PPROM complicate more than 400,000 and 120,000 pregnancies annually in the United States respectively. The prevalence of PPROM both in Africa and Uganda is unknown, but a study by Kaye shows the prevalence of PPROM at 5% in Mulago hospital (2001, Mulago). From unpublished medical records of Maternity Ward; Mbarara Regional Referral Hospital between the months of January and March 2011, there were 88 admissions with Preterm PROM out of about 2,500 admissions

Preterm PROM increases the risk of prematurity and leads to a number of other perinatal morbidities, including respiratory distress syndrome, neonatal sepsis, cord prolapse, placental abruption, and fetal death that is up to 2% risk of fetal death.D Ashley Hill, 2006).

PPROM accounts for a third of all preterm births. Factors associated with PPROM include: smoking, multiple gestations, polyhydramnios, history of ante partum haemorrhage and previous history of PROM (ACOG 1998; Ezechi et al, 2003). However, the causes of PROM remain largely unknown. At term, programmed cell death and activation of catabolic enzymes such as collagenase and mechanical forces result in ruptured membranes. It is

speculated that PROM probably occurs due to premature activation of the same mechanisms due to underlying pathological processes such as inflammation or infection of the membranes. (Flynn HA et al, 2006)

In addition, the following clinical factors have been associated with PPROM: low socio-economic status, low body mass index, tobacco use as well as history of urinary tract infections, Preterm labour, vaginal bleeding (APH), cervical cerclage [Morgan, .O.F et al 2010]. Worldwide, 85% of neonatal morbidity and mortality is a result of prematurity. PPROM is associated with 30-40% of preterm deliveries and is the leading identifiable cause of preterm delivery, approximately 33% (ACOG, 1998). PPROM complicates 3% of all pregnancies and occurs in approximately 150,000 pregnancies yearly in the United States (AllahyarJazayeri, 2011). PPROM increases the risk of prematurity and leads to a number of other perinatal and neonatal complications, including a 1 to 2% risk of foetal death (Tanya. M. Medina. and D Ashley Hill, 2006). In MRRH, the prevalence of Preterm PROM is unknown: however, PPROM is associated with both maternal and prenatal morbidities/mortalities such as preterm birth, chorioamnionitis, and neonatal infections.

1.2 Problem Statement

Globally the prevalence of Preterm Premature Rapture of Membranes(PPROM)is unknown, PPROM complicate more than 400,000 and 120,000 pregnancies annually in the United States. The prevalence of PPROM both in Africa and Uganda is unknown, but a study by Kaye shows the prevalence of PPROM at 5% in Mulago hospital (2001, Mulago). Physicians caring for pregnant patients should be versed in the management of preterm PROM because rapid diagnosis and appropriate management improves outcomes for both mothers and their

infants.This study increases our understanding of the risk factors associated with PPROM as well as foetal outcomes of pregnancies complicated by PPROM in the MRRH setting with the overall aim of improving the clinical management and the outcomes.

1.3 Justification

The risk factors and foetal outcomes of deliveries complicated by PPROM have not been explored at MRRH. This study therefore seeks to increase our understanding of the factors associated with PPROM and the foetal outcomes as a way of reducing the problem of PPROM in South-western Uganda.

1.4 Research Question

What are the risk factors associated with PPROM in mothers admitted at MRRH?

1.5 Study Objectives

1.5.1 General Objective

To determine the causes and risk factors associated with PPROM at MRRH.

1.5.2 Specific Objectives

1. To determine the social demographic factors associated with PPROM in Mbarara Regional Referral Hospital
2. To determine the obstetric factors associated with PPROM in Mbarara Regional Referral Hospital
3. To determine the medical factors associated with PPROM in Mbarara Regional Referral Hospital

CHAPTER TWO: LITERATURE REVIEW

2.0: Introduction

Preterm Premature Rupture of Membranes is a growing public health problem that has significant consequences on families, and costs society a significant sum of money per year. One of the most common complications of preterm PROM is early delivery. The latent period, which is the time from membrane rupture until delivery, generally is inversely proportional to the gestational age at which PROM occurs. For example, one large study of patients at term revealed that 95% of patients delivered within approximately one day of PROM, whereas an analysis of studies evaluating patients with preterm PROM between 16 and 26 weeks' gestation determined that 57% of patients delivered within one week, and 22% had a latent period of four weeks (Tanya M. Medina, et al., 2006).

When PROM occurs too early, surviving neonates may develop sequelae such as mal-presentation, cord compression, oligohydramnios, necrotizing enterocolitis, neurologic impairment, intraventricular hemorrhage, and respiratory distress syndrome. About 30% of preterm births are iatrogenic, because of maternal illness or developmental foetal compromise. Many iatrogenic preterm births appear to be associated with renal or hypertensive pathology, diabetes or foetal indications such as severe intrauterine growth restriction (Philip 2005). Medically induced preterm births appear to be indicated with intensity of medical care, being higher in the university medical centres and lower for the poorest woman.

2.1: Social Demographic History and PPROM

In a Cross-sectional case control study done by D. Kaye (2001) to evaluate the epidemiological risk factors in patients admitted to Mulago Hospital with PPROM from their socio-demographic characteristics and reproductive history. It was found that maternal socio-demographic characteristics were similar for cases and controls. A history of hypertension, abortion, prior PROM, Caesarean section, cervical Cerclage, cervical incompetence or abnormal vaginal discharge; are significant risk factors for PPROM (p =0.05). Therefore, there are factors by which mothers at risk of PPROM can be identified before onset of rupture.

2.1.1: Maternal age

A retrospective, cohort study to investigate the impact of older maternal age on the risk of mortality associated with PPROM, (Aliyu MH, et al 2004) among triplets, found that the risk of stillbirth as well as neonatal and perinatal mortality was highest among teenagers and older mothers (above 40years). And, although older mothers (above 40years) demonstrated higher risk levels for all mortality indices in comparison to the younger and mature mothers, these findings were not statistically significant (Aliyu MH, et al., 2004).

2.1.2: Socioeconomic factors

There are several factors associated with preterm PROM. Black patients are at increased risk of preterm PROM compared with white patients. Other risk factors include: low socioeconomic status, smoking, a history of sexually transmitted infections, previous preterm delivery, vaginal bleeding and uterine distension (e.g., polyhydramnios, multiple pregnancy).

In a case-control study done by Sarah E. Fergusson, et al (2002), to investigate dietary or socioeconomic factors associated with PPROM, low maternal hemoglobin and low socioeconomic status were identified as predictive factors. The lower hemoglobin level may be a marker for subclinical infection**.**

2.1.3: Nutritional status

An adequate availability of nutrients during gestation is an important environmental factor influencing pregnancy outcome (Janet, 2003). Women with early and closely spaced pregnancies are at increased risk of entering a period of gestation with reduced reserves, (especially a short interpregnancy interval less than 18 months). Adequate nutrition is required to maintain the delicate balance between the needs of the mother and the foetus, and an inadequate supply of food will cause a state of biological competition between the mother and the conceptus putting the well-being of both mother and foetus at serious risk (Ingrid, et al., 2002; Rayco-Salon, et al., 2005). Such findings have been documented in studies conducted among young girls, showing that young girls who conceive within 2 years of menarche are at increased risk of entering pregnancy with low nutrient reserves as their own reserves have been depleted by their rapid growth (Shingairai, et al., 2004; Roy, et al., 2006; Samim, et al., 2006). Lower BMI (Ezechi, et al., 2003) was adversely associated with preterm births and under nutrition in women at the time of conception results in a precocious foetal cortisol surge and preterm birth.

2.1.4: Smoking and alcohol

In order to determine if tobacco, alcohol, or illicit drug usage were associated with alterations in pregnancy or neonatal outcome. Comparisons in outcome were made with respect to

tobacco, alcohol, and/or illicit drug usage. There were no associations among use of tobacco, alcohol, drugs of abuse, or cocaine and respiratory distress syndrome, intraventricular hemorrhage, or necrotizing enterocolitis. The use of tobacco and cocaine during pregnancy appear to shorten the latency period in pregnancies complicated by PPROM. These shortened latency periods could potentially contribute to increased neonatal morbidity (Myles T.D, et al., 1998).

2.2: Obstetric Factors and PPROM

To identify obstetric risk factors and to elucidate the effect of prolonged rupture of the membranes on the development of cystic periventricular leukomalacia (PVL) in preterm infants, a retrospective case–control study of 95 preterm infants with the diagnosis of PVL and 245 healthy controls matched for gestational age was carried out and the results showed that PPROM and prolonged rupture of the membranes may provoke adverse effects on the neurodevelopmental outcome of the preterm fetus. These findings may have implications on the obstetric management of PPROM beyond 30 weeks of gestation. Cesarean section without labor was less likely associated with the diagnosis of PVL (**Margit Bauer, et al., 2009)**.

2.2.1: Previous history of PPROM

Because the clinical course of PPROM is often unalterable once membrane rupture has occurred, it would be beneficial to identify women at risk and prevent membrane rupture from occurring. Women with a previous early preterm birth (23 to 27 weeks) have a 25% risk for preterm birth in a subsequent gestation, while those with a previous history of PPROM

have a 3.3-fold increased risk of preterm birth caused by PPROM and a 14-fold higher risk of PPROM before 28 weeks in a subsequent pregnancy (Brian M. Mercer, 2008).

A history of previous PROM is a significant risk factor for recurrence. As an example, the Preterm Prediction Study, a large prospective study conducted by the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, observed that women with a history of PROM had a 13.5% rate of PROM in a subsequent pregnancy compared to 4.1% in women with no such history.
http://www.womenshealthsection.com/content/obs/obs021.php3, 16th June 2011).

2.2.2: History of Ante partum haemorrhage

To determine whether the incidence of abruptio placentae is increased in pregnancies with preterm premature rupture of membranes and to assess whether certain clinical risk factors in this group predispose them to have abruptio placentae, a retrospective cohort study over a 2.5-year period was performed. Results showed that pregnancies complicated by PPROM that are managed expectantly are at significant risk for abruptio placentae. Preterm premature rupture of membranes in such cases is more often preceded by bleeding. Therefore, these abruptions may predispose the patient to intrapartum fetal distress (**Carol A. Major, et al., 1995).**

2.2.3: History of Cervical Cerclage

PPROM complicates approximately 1 in 4 pregnancies with a Cerclage in place; it complicates 1 in 2 pregnancies after emergency cerclage. Retrospective studies have suggested that when cerclage is removed after PPROM, the risk of adverse perinatal outcomes is similar to that seen after PPROM without cerclage.

Given the potential risk without evident neonatal benefit when the stitch is left in place after PPROM, the general approach should include early cerclage removal after membrane rupture occurs. The role for short-term Cerclage retention while attempting to enhance fetal maturation with antenatal corticosteroids in the periviable gestation has not been determined. (Mercer, B, et al., 2008).

2.2.4: History of preterm birth

The highest risk of PPROM exists in women with a history of one or more preterm deliveries. A history of a previous or more preterm birth is an important predictor of the likelihood of future preterm delivery in a woman, (Mercer, et al., 1999; Roy, et al., 2006; Samim, et al., 2006) although most women who have had a PTB will have subsequent pregnancies of a normal duration.

2.2.5: History of multi foetal gestation

Twin gestation is associated with a high incidence of spontaneous preterm birth with resultant infant morbidity and mortality. Despite extensive literature describing the clinical course of singleton pregnancy complicated by PPROM, there are few comparable data available concerning PPROM in twin gestation. One published study has reviewed the

clinical outcome of 99 twin pregnancies complicated by PPROM. Another study, reported in abstract form, revealed similar results.

Latency in conservatively managed twin PPROM is similar to that in singleton gestations, with 64% of pregnancies delivering within 48 hours of membrane rupture and 89% delivering within 1 week. Twin PROM occurring before 30 weeks' gestation have longer latency period than that occurring after 30 weeks (median 1.6 vs. 0.9 days; $p< 0.03$). Other than an increased incidence of cesarean delivery in twin pregnancies (42 vs. 27%; $p< 0.02$), maternal morbidity is remarkably similar between singleton and twin gestations. Complications of twin gestations were chorioamnionitis (19%), postpartum fever (15%), and placental abruption (6%) (Mercer, B, *Glob. library. women's med*., 2008).

2.2.6: Association between Coitus and PPROM

In a large case-control study done by Richard L. Sweet, et al., 2006, three factors were associated with preterm PROM in a multifactorial analysis. These were; previous preterm delivery, cigarette smoking (stopped during pregnancy) and bleeding during the third trimester using controls at the same gestational age as cases (thus correcting for decreasing frequency of coitus closer to term, and coitus was found not to be a cause of PPROM.

2.2.7: Recurrence of PPROM in relation to interval between pregnancies

In a study that was carried out by Getahun D. et al., to examine whether the recurrence risk of preterm premature rupture of membranes (PPROM) is modified by the interpregnancy interval (IPI), it was found that risks of PPROM in the second pregnancy among women with and without previous PPROM were 5.7% and 2.3%, respectively. Short IPI was associated

with increased risk for PPROM recurrence. Women with previous PPROM are at increased risk for recurrence, and a short IPI is associated with increased risk.

2.3: Maternal Medical Conditions and PPROM

2.3.1: Anemia

Anemia is a major health problem among women of reproductive age group, particularly in developing countries like India. A study was undertaken to determine the maternal and perinatal outcome in patients with severe anemia in pregnancy, with a hemoglobin concentration of < 7 g/dl. The in-hospital data were analyzed for 12 months between January 2007 and December 2007 and 2.15% (n = 96) of women were found to have severe anemia. Out of these, 18.75% had pre-term premature rupture of membranes and 5.12% of all deliveries were pre-term (Rohilla M, et al.).

In another study done by Zhang Q, et al., 2009, Anemia in early pregnancy was found to be associated with increased risk for preterm PROM, whereas exposure in late pregnancy was associated with reduced risk for spontaneous preterm labour (Zhang Q, et al., 2009; Merck & Co, Inc, Whitehouse Station, NJ, USA, 2009).

2.3.2: Intrauterine infection

Intrauterine infection has been implicated in the etiology of preterm premature rupture of ovular membranes (PPROM), which accounts for 30–40% of all preterm deliveries (Parry

and Strauss, 1998). Common pathways between PTB, PPROM and altered molecular routes of inflammation have been proposed. This common pathway could occur without even the presence of chorioamnionitis or clinical infection (Romero *et al*., 2006).

To examine whether preterm premature rupture of membranes (PROM), intrauterine infection, and oligohydramnios are risk factors for placental abruption, data for this retrospective cohort study were derived from the 1988 National Maternal and Infant Health Survey (N = 11,777). Association between abruption and these clinical risk factors was expressed as relative risk (RR) and 95% confidence interval (CI), with multivariate adjustment for potential confounders. Thus women presenting with preterm PROM are at increased risk of developing abruption, with the risk being higher either in the presence of intrauterine infections or oligohydramnios (Ananth C.V, et al., 2004).

2.3.3: Urinary tract infections and PPROM

A prospective study to identify the relationship of pregnancy outcome to bacterial vaginosis, (Michael G. Gravett, et al., 1986), and cervical infection with *Chlamydia trachomatis* was found in 9% of the women. Although women with and without bacterial vaginosis had similar demographic and obstetric factors, neonates born to women with bacterial vaginosis had lower mean birth weight than did neonates born to women without bacterial vaginosis. Bacterial vaginosis was significantly associated with preterm premature rupture of the membranes, preterm labor and amniotic fluid infection, but not with birth weight below 2500g. And then cervical infection with *C trachomatis* was independently associated with preterm premature rupture of the membranes, preterm labor, and low birth weight.

Although it is widely agreed that P PROM is multi factorial, findings from a study done by Karat C, in India in 2006 showed that exogenous risk factors such as UTI, BV, E. coli and S. aureus are significantly associated with the PPROM. It remains to be seen whether these are a direct cause of P PROM or are simply surrogate markers for another not yet identified pathogenic process.

2.3.4: HIV

AIDS is the acronym for Acquired Immunodeficiency Syndrome and the virus that causes this condition is the Human Immunodeficiency Virus (HIV). Because the virus mainly targets the immune system, especially the T-helper cells and the CD4 lymphocytes, the body's defence mechanisms are suppressed and other infections occur more frequently and more severely. Infection with HIV is associated with an increased risk of opportunistic diseases that will eventually lead to death. For instance in pregnancy it may lead to; spontaneous abortion, ectopic pregnancy, other sexually transmitted diseases, urinary tract infections, pneumonia, anaemia, intrauterine growth restriction, amniotic fluid infection syndrome, spontaneous preterm labour and preterm premature rupture of membranes (PPROM).

Due to the effects of HIV on the pregnancy and birth, HIV positive women have double the risk of spontaneous preterm premature rupture of membranes compared to HIV negative women, many babies die as a result of the complications of prematurity (Joanita de Kock, and Christa van der Walt; 2004).

According to Adam Brochert, et al., 2002, Human immunodeficiency virus (HIV) and Chlamydia are both sexually transmitted diseases that can complicate pregnancy. They both

are commonly seen in single, black women under age 25 from urban areas, and they can be transmitted to the foetus and therefore require treatment to reduce this risk. Maternal Chlamydia infection increases the risk of Prematurity, preterm premature rupture of membranes (PPROM), and postpartum endometritis, as well as neonatal conjunctivitis, otitis media and pneumonia. HIV in children markedly reduces life span and the quality of life.

2.4: Infectious Causes of PPROM

Substantial evidence is available to show that subclinical infection may be a cause of PROM, not merely its result. Support for a role of infection is provided by studies showing an association between clinically diagnosed bacterial vaginosis and preterm birth/PPROM. Some genital bacteria elaborate enzymes such as proteases, phospholipases, and collagenases that may act to weaken the membranes. When amniotic fluid is obtained by amniocentesis in cases of PPROM, positive cultures are found in approximately 30% if the specimen is properly handled for aerobes, anaerobes and genital mycoplasmas (Richard. L. Sweet, et al., 2006).

At term, programmed cell death and activation of catabolic enzymes, such as collagenase and mechanical forces, result in ruptured membranes. Preterm PROM occurs probably due to the same mechanisms and premature activation of these pathways. However, early PROM also appears to be linked to underlying pathologic processes, most likely due to inflammation and/or infection of the membranes. Clinical factors associated with preterm PROM include low socioeconomic status, low body mass index, tobacco use, preterm labor history, urinary tract infection, vaginal bleeding at any time in pregnancy, cerclage, and amniocentesis. (AllahyarJazayeri, et al., 2011).

2.5: Foetal Outcome of PPROM

In a retrospective study done by Lee C. Yang, et al., 2004, to evaluate maternal and fetal outcomesof 73 consecutive singleton pregnancies complicated by pretermpremature rupture of membranes, the meangestational age at the onset of membrane rupture and deliverywas 22.1 weeks and 23.8 weeks, respectively. The latency period frommembrane rupture to delivery ranged from 0 to 83 days with amean of 8.6 days. Among the 73 pregnant patients, there were22 (30.1%) stillbirths and 13 (17.8%) neonatal deaths, resultingin a prenatal death rate of 47.9%. The prenatal survival ratebased on gestational age at the onset of fetal membrane rupturewas 12.1% at less than 23 weeks of gestation, 60% at 23 weeks,and 100% at 24 to 26 weeks,membranes ruptured before 23 weeks of gestation.

CHAPTER THREE: METHODS AND MATERIALS

3.1 Study design

This was a prospective un- matched case control study where mothers admitted at Mbarara Regional referral Hospital with preterm premature rupture of membranes (PPROM) were recruited and followed to record foetal outcomes 24 hours after delivery. A case was defined as a pregnant woman after 28 weeks of pregnancy but before 37 weeks with preterm premature rupture of membranes. The next 3 consecutive women with normal delivery were recruited as controls.

3.2 Study site

The study was conducted at Mbarara Regional Referral Hospital, a public 300 bed capacity hospital located in Mbarara Municipality 266 km south west of Kampala, the capital city of Uganda. It serves as a referral hospital for the districts of south western Uganda with a population of approximately 8.5 million people (UBOS, 2012). It also receives patients from neighbouring countries like Rwanda, Northern Tanzania, and Eastern Democratic Republic of Congo. Mbarara Regional Referral Hospital is the main teaching site for the Medical School at Mbarara University of Science and Technology. It has an Obstetrics and Gynaecology department with a maternity wing that conducts approximately 7460 deliveries a year (Hospital annual report, 2010. The department has an in-patient section that offers emergency obstetric care inspite the inadequate staffing

3.3 Study Population

The study was conducted on pregnant women after 28 weeks of pregnancy but before 37 weeks with preterm premature rupture of membranes. Data was also collected from controls that had had a normal delivery.

3.4 Inclusion Criteria `

All pregnant mothers (defined as cases) admitted with ruptured membranes before 37 completed weeks of gestation were enrolled. For every case, 3 controls (defined as the next three women who had a full term normal delivery) were included in the study.

3.5 Exclusion criteria

Mothers who met the inclusion criteria but decline the consent.

3.6 Sampling procedure

The participants with PPROM who consented were consecutively enrolled in the study on admission until the targeted study number was attained. Patients were clerked and examined by the clinician as part of the routine procedure. For every case, 3 consecutive women who had had a normal delivery were included in the study. To avoid double entry, a unique study code number on a sticker was placed a specified location in the patient's case notes.

3.7 Sample Size Determination

This is sample size calculation formulae for a case control study with continuous exposure in the population. Meaning that the cases and the controls are all exposed to the same conditions

$$n = (\frac{r+1}{r}) \frac{\sigma^2 (Z_\beta + Z_{\alpha/2})^2}{(d\text{ifference})^2}$$

n Number of cases

r **ratio** of controls to cases. For this formulae where An equal number of cases and controls (r=1)

δ Standard deviation of the out come variable(10.0)

Z_β Represents the **desired power** (typically .84 for 80% power).

$Z\alpha 2$ Represents the desired **level of statistical significance** (typically 1.96).

Difference **Effect Size** (the difference in means) which we took as 5

For 80% power, Z_β=.84

- For 0.05 significance level, Z_α=1.96
- r=1 (equal number of cases and controls)
- σ=10.0
- Difference = 5.0

$$n = (2) \frac{10^2 (7.84)}{(5)^2} = (2) 2^2 (7.84) = 63$$

n=63

To reduce study bias, three controls we recruited for every case. This gave us a minimum study population of 252 (cases and controls).

3.8 Study Variables

3.8.1: Independent variables

Social demographic data included age, level of education, employment, household income and history of smoking and alcohol intake. Medical variables included history of diabetes and HIV serostatus. Obstetric factors included parity and history of Ante partum hemorrhage.

3.8.2: Primary Outcome variable

The outcome of interest was PPROM

3.8.3. Secondary outcome variables

- Foetal outcomes: status at birth (alive or still born), prematurity, neonatal sepsis, respiratory distress, birth asphyxia and admission to neonatal intensive care unit.
- Organisms cultured from High vaginal swab among women with PPROM

3.9 Data Collection Procedure

3.9.1 Data Collection Methods

A standardized questionnaire was used to record social demographic, medical and obstetric data for the cases and controls. A high vaginal swab was collected using sterile speculum and sent to the laboratory for culture to determine colonization of the amniotic fluid with pathogenic bacteria. Cases were followed throughout labour and delivery. The foetal outcomes were documented and live babies followed up for 24 hours after birth to record the outcome of labor for the cases.

3.9.2 Data Collection Tools

We used a standardized questionnaire to record and document study variables. A standard HIMS laboratory request/report form was used for all laboratory investigation.

3.10 Data Management and Analysis

Questionnaires for all 274 participants were checked for completeness before the patients were discharged from hospital. Data were entered in Microsoft Excel computer program and analyzed using Stata version 11. Univariate and multivariate analysis to determine the associations between PPROM and categorical variables was done. Associations, measured as odds ratio (OR) and adjusted for relevant confounding factors, were estimated using multivariate conditional logistic regression analysis. A degree of precision was set at a confidence interval of 95%. A p-value of 0.05 was taken to be statistically significant for variables of interest.

3.11 Quality Control

Data collection tools were pretested on 5 cases and 15 controls to ensure validity and reliability. These were not included in the final analysis. Data was double entered into a password protected computer. Standard operating procedures prescribed for sample collection and processing laboratory investigations were strictly observed. Investigations were conducted in the microbiology laboratory by a qualified technologist with every 10^{th} sample taken to an accredited independent lab for quality control.

3.12: Ethical Consideration

The research proposal was reviewed and forwarded to Faculty Research and Ethics Committee (FREC) of the faculty of medicine by the department of obstetrics and gynecology. The research protocol was forwarded to the MUST institutional review Board for approval before any data was collected. A written informed consent was obtained from all respondents and they were assured that they were free to withdrawal from the study at any point if they so wished. Confidentiality was ensured by use of numbers and codes instead of respondent's name. Filled questionnaires were kept secure in lockable cabinet.

3.13: Dissemination of Results

The finding off this study will be disseminated to the following areas to all stakeholders in the department of obstetrics and gynecology of Mbarara University of science and technology.

A copy of the dissertation will be kept in the University library for reference.

A manuscript will be prepared for publication in an appropriate peer reviewed journal.

3.12 Limitations of the Study

Data on the duration of ruptured membranes was not collected despite its known affect the outcome of the outcome of pregnancy complicated by PPROM.

CHAPTER FOUR: PRESENTATION OF RESULTS

A study to determine the risk factors for preterm premature rupture of membranes was conducted on 272 mothers admitted for delivery at Mbarara Regional referral Hospital labour ward. We recruited 76 cases and 198 controls in a prospective un- matched case control study between January and March 2012. Data was analyzed using Univariate and multivariate models to predict factors associated with PPROM. Results are presented in frequency tables, figures and charts below.

4.1 Social demographic, obstetric and other general health characteristics of cases and controls

A questionnaire was used to collect social demographic characteristics, obstetric and other general health factors from 76 cases and 198 controls enrolled in this study. The results are shown in the frequency table below.

Table 4.1: Participants' general health characteristics and obstetric Indicators

Total study population(n=274)		
Characteristic	**PPROM (n=76)**	**Controls (n=198)**
Socio-demographics		
Age (%) <21years 21-35 years >35 years	 13(17.1%) 58(76.3%) 5 (6.6%)	 26(13.1%) 163(82.3%) 9(4.5%)
Less than Secondary School Education (%)	43(56.6%)	54(27.3%)
Unemployed (excluding Farming) (%)	42(55.2%)	23(11.6%)
Household monthly income less than 100,000/=	53(69.7%)	78(39.4%)
Living Children (%) <2 2-4 >4	 46 (60.5%) 36(47.3%) 18(23.8%)	 45(27.7%) 39(19.7%) 16(8.1%)
General Health Indicators		
Alcohol Use During Pregnancy	22(28.9%)	7(3.5%)
Smoking During Pregnancy (%)	0(0%)	4(2.0%)
HIV Seropositive (%)	32(42.1%)	19(9.6%)
Urinary Tract Infection (%)	40(52.6%)	17(8.6%)
Hypertension (%)	0(0%)	4(2.0%)
Diabetes Mellitus (%)	1(1.3%)	1(0.5%)
Obstetric Indicators		
Last pregnancy normal (%)	66(88.1)	94(47.5)
<2 Antenatal Visits (%)	67(88.2%)	30(15.1%)
Parity (%) 1 2-4 >4	 18(32.7%) 57(75%) 25(32.9%)	 37(18.7%) 50(25.2%) 14(7.0%)
History of Ante-partum Hemorrhage (%)	9(11.8%)	1(0.5%)

From the table above its evident that conditions like symptomatic urinary tract infections and proportion of HIV infected mothers and alcohol consumption high parity and poor antenatal attendance were more common in cases as compared to the controls..

4.2: Characteristics of the study population (un-adjusted)

A bivariate analysis of the characteristics of 274 women included in the study was done to reveal associations with PPROM. A P-value of 0.05 was considered significant. Un-adjusted results are presented in the table 4.2.1 below

Table 4.2: Factors associated with PPROM from the Bivariate Analysis (N=274)

Characteristic	Bivariate Model		
	OR	95%CI	p-value
Age			
<21years	REF		
21-35 years	2.4	1.2 – 4.5	0.01
>35 years	0.6	0.2 – 1.7	0.30
Less than secondary school education	1.5	0.9 – 2.6	0.14
Unemployed (excluding Farming)	2.5	1.4 – 4.3	0.01
Household monthly income <100,000/=	0.3	0.2 – 0.6	0.01
Living Children			
<2	REF		
2-4	0.9	0.5 – 1.5	0.61
>4	1.2	0.6 – 2.3	0.65
Alcohol consumption during pregnancy	3.8	1.8 – 8.1	0.01
HIV sero positive	2.0	1.1 – 3.7	0.02
Urinary tract infection	3.1	1.7 – 5.6	0.01
Diabetes mellitus	2.6	0.2 – 42.5	0.50
Antenatal care visits less than 2	4.7	2.7 – 8.3	0.01
Parity			
1	REF		
2-4	1.3	0.8 – 2.3	0.30
>4	2.1	1.1 – 4.1	0.03
History of ante-partum hemorrhage	20.0	2.4 – 165.4	0.01

Factors significantly associated with PROM in this population before adjusting for confounding include age of 21-35 (p= 0.01), parity greater than 4 (p= 0.03), unemployed, (p=0.01), low family income less 100,000/= (p=0.01), alcohol consumption during pregnancy (p= 0.01), HIV infection (P=0.02), Urinary tract infection (p=0.01). Antenatal care visits less that 2 (p=0.01), parity greater than four (p=0.03) and Ante partum hemorrhage (p=0.01) were also associated with PPROM. Further analysis using multivariate model to adjust for confounding and establish independent predictors of preterm premature rupture of membranes was done.

4.3: Factors associated with PROM

To study the factors associated with PPROM in this population, we did multivariate analysis using a backward stepwise model starting with all potential co variables. Only those with p-values less than 0.05 were considered as the most likely factors associated with PPROM.

Table 4.3: Factors associated with PPROM after multivariate analysis

Associated Factors	Adjusted Odds Ratio	95% CI	P-values
Alcohol consumption during the current pregnancy	3.8	1.3-11.2	0.01
HIV Sero-positivity	2.5	1.1-5.6	0.02
Symptomatic urinary tract infection	2.6	1.2-5.6	0.01
Antenatal care visits less than 2	2.5	4.0-54.9	0.01
Parity greater than four	14.9	1.1-56	0.03

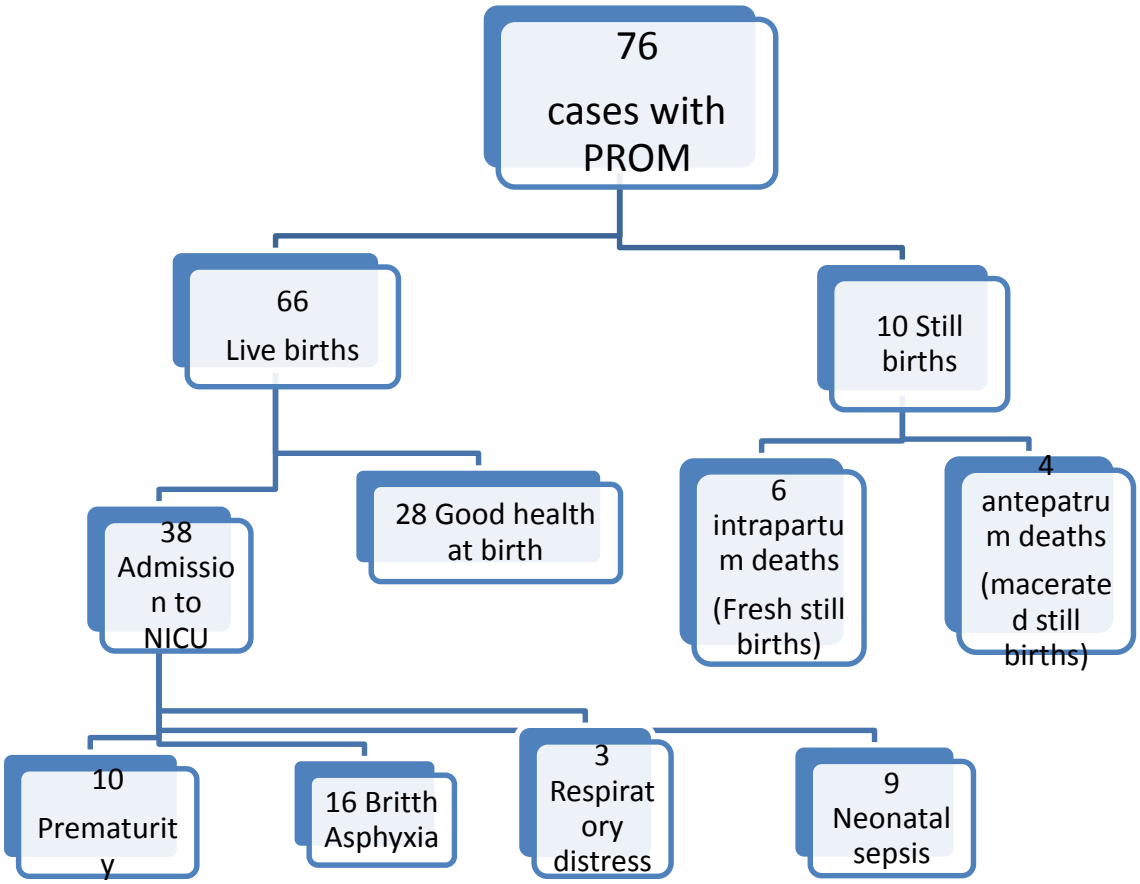
The factor associated with PPROM included

1. Pregnancies of mothers who consumed alcohol were about four times more likely to be complicated by PPROM compared to their alcohol naïve counterparts (OR 3.8 CI 1.3-11.2, P-value 0.01)
2. Parity greater than four was significantly associated with PPROM (OR 14.9 CI 1.1-56, and –value 0.03)
3. Infection with HIV (P-value 0.02), urinary tract infection (P-value 0.01) and one or no antenatal care visits (P-value 0.01) were also strongly associated with PPROM in this population

4.4 Outcomes of pregnancies complicated by preterm premature rupture of membranes

76 pregnant women with PPROM were followed from admission till 24 hours after delivery and fetal outcomes documented. The outcomes are presented in the flow chat below.

Figure 4.1: Flow chart showing the outcomes of pregnancies complicated by PPROM

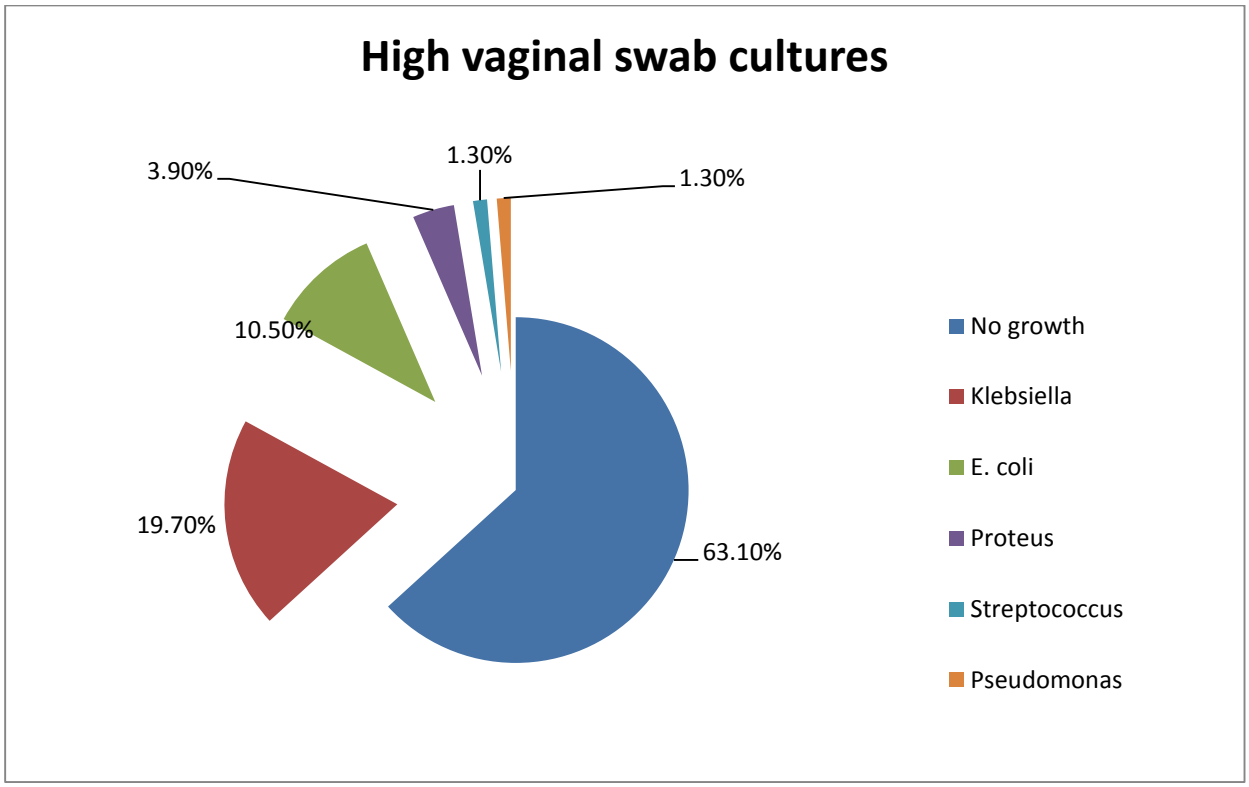


This follow chart shows that preterm premature rupture of membranes is associated with poor pregnancy outcomes in MRRH, like the still birth percentage was 13% and even out of the live birth 60% required admission to the neonatal ward for various reasons that included prematurity(16%),birth asphyxia(25%),sepsis(14%),respiratory distress(5%).

4.5: Organisms cultured from High vaginal swab among women with PROM

A sterile swab was used to collect a high vaginal swab for culturing amniotic fluid in suitable culture media. Results are presented in the pie chart below.

Figure 4.2: Figure showing the frequency of organism isolated from the high vaginal swab cultures



The majority of the women with ruptured membranes (63.1%) had no infection in the amniotic fluid as seen in the cultures with no growths. Those that had any kind of growth isolated gram negative organisms including Klebsiella (19.7%), E. coli (10.5%) and Proteus (3.9%), Pseudomonas (1.3%)

CHAPTER FIVE: DISCUSSIONS

low income of less than 100,000/= per month, alcohol use during pregnancy, HIV infection, urinary tract infection, short interpregnancy interval, poor antenatal attendance and parity >4 was significantly associated with preterm premature rapture of membranes.

The study found out that the socio-demographic characteristics of the cases and the controls were similar apart from the level of education and income per month which was similar to what Kaye (2001) found out in the similar study done in Mulago. Which statement should come first?

5.1: Risk Factors Associated With PPROM

5.1.1: Alcohol use during pregnancy

Alcohol use during pregnancy was also found to be significantly associated with PPROM with an odds ratio (OR) of 3.8 and p value of 0.01 with 1.3-11.2 (95% CI) contrary to what Myles T.D, et al. found in 1998 that there was no association between smoking and alcohol use during pregnancy with PPROM.

Tumor necrosis factor- like weak inducer of apoptosis (TWEAK) has been implicated as a pro inflammatory cytokine and alcohol intake increases serum levels of TWEAK. So this might explain why alcohol intake is associated with PPROM(Flynn HA et al,2006).

At term, programmed cell death (apoptosis), activation of catabolic enzymes, such as collagenase and mechanical forces, result in ruptured membranes. Preterm PROM occurs probably due to the same mechanisms and premature activation of these pathways. PPROM

also appears to be linked to underlying pathologic processes, most likely due to inflammation and/or infection of the membranes.

5.1.2: Short inter pregnancy Interval

In a study that was carried out by Getahun D. et al., 2003 to examine whether the recurrence risk of preterm premature rupture of membranes (PPROM) is modified by the interpregnancy interval (IPI), it was found that risks of PPROM in the second pregnancy among women with and without previous PPROM were 5.7% and 2.3%, respectively. Short IPI was associated with increased risk for PPROM recurrence. Women with previous PPROM are at increased risk for recurrence, and a short IPI is associated with increased risk. This is in line with the findings which revealed that short interpregnancy interval was associated with PPROM with p value of <0.01, odds ratio (OR) 0.2 and 0.1 -0.5(95% CI).

Women with early or closely spaced pregnancies are at risks of entering a period of gestation with reduced reserves. Medically, a short interpregnancy interval means she starts pregnancy with reduced nutrients which may result into membrane formation which are weak are prone to rupturing.

5.1.3: Other findings

Further data from our research tools revealed that high parity greater than 4(GMP) and few antenatal visits (less than 3) were significantly associated with PPROM with p value <0.01, Odds Ratio(OR) 14.9 and 4.0-54.9 (95% CI) as well as p value 0.03,Odds Ratio(OR) 2.5 and 0.1-5.6(95% CI) respectively. This could be that grand multiparous mother don't attend antenatal more regularly so conditions like urinary tract infections are missed thus putting them at risk of preterm premature rupture of membranes.

5.1.4: HIV infection

HIV infection during pregnancy was found to be significantly associated with PPROM with p value of 0.03, Odds Ratio(OR) of 2.5 and 1.1-5.6 (95% CI) after multivariate analysis which was similar to Adam Brochert, et al., 2002, who asserted that Human immunodeficiency virus (HIV) and Chlamydia which are both sexually transmitted Diseases that can complicate pregnancy and increases the risk of Prematurity, preterm premature rupture of membranes (PPROM), and postpartum endometritis, as well as neonatal conjunctivitis. Human immune deficiency virus (HIV) targets the immune system especially the t-helper cells and CD4 lymphocytes, the body's defence mechanism are suppressed and other infection will occur more frequently and more severely.

This is in line with Joanita de Kock, and Christa van der Walt; 2004 who said that due to the effects of HIV on the pregnancy and birth, HIV positive women have double the risk of spontaneous preterm premature rupture of membranes compared to HIV negative women, many babies die as a result of the complications of prematurity.

5.1.5: Urinary tract infection

A prospective study to identify the relationship of pregnancy outcome to bacterial vaginosis, (Michael G. Gravett**, et al**., 1986) Bacterial vaginosis was significantly associated with preterm premature rupture of the membranes, preterm labor and amniotic fluid infection. Similarly, in the study findings, it was found out that a urinary tract infection was associated with PPROM with p value of 0.02, Odds Ratio (OR) 2.6 and 1.2-5.9(95% CI). Although it is widely agreed that PPROM is multi factorial, findings from a study done by Karat C, in India

in 2006 showed that exogenous risk factors such as UTI, BV, E. coli and S. aurous which may release catabolic enzymes like collagenase and protease that may degrade collagen and weaken the foetal membranes leading to PPROM are significantly associated with the PPROM. It remains to be seen whether these are a direct cause of P PROM or are simply surrogate markers for another not yet identified pathogenic process.

5.2: Pregnancy outcomes

To evaluate maternal and foetal outcomesof singleton pregnancies which were complicated by pretermpremature rupture of membranes. Lee C. Yang, et al., 2004 found that among the 73 pregnant patients, there were22 (30.1%) stillbirths and 13 (17.8%) neonatal deaths, resultingin a perinatal death rate of 47.9%.

In comparison, It was found in this study that out of the 76 mothers who presented with PPROM, 66(87%) had live births, still births 10 (13%) with 6(8%) intrapartum stillbirths and ante partum stillbirths were 4(5%).Out of the live births, 38(60%) required admission to the neonatal unit and the reasons for admission included birth asphyxia (16), prematurity (10), neonatal sepsis (9) and 3 with respiratory distress. Showing that PPROM is associated with poor pregnancy out comes.

5.3: Organisms cultured

From the results obtained from the amniotic fluid cultured, it was found that 36.9% showed a positive culture of organisms which were mainly gram negatives with Klebsiella accounting for 15(19.7%), E-coli 8(10.5%), Proteus 3(3.9%),Streptococcus and Pseudomonas ssp accounted for (1.3%) respectively.

Substantial evidence is available to show that subclinical infection may be a cause of PPROM, not merely its result. Support for a role of infection is provided by studies showing an association between clinically diagnosed bacterial vaginosis and preterm birth/PPROM Some genital bacteria elaborate enzymes such as proteases, phospholipases, and collagenases that may act to weaken the membranes. When amniotic fluid is obtained by amniocentesis in cases of PPROM, positive cultures are found in approximately 30% if the specimen is properly handled for aerobes, anaerobes and genital mycoplasmas (Richard. L. Sweet, et al., 2006).

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1: CONCLUSIONS

The study concludes that Maternal risk factors associated with Preterm premature rapture of membranes at Mbarara Regional Referral Hospital included HIV infection alcohol intake during pregnancy, presence of urinary tract infection and having a short inter pregnancy period (less than 18 months) and a poor antenatal care clinic attendance of less than 3 visits during the pregnancy and grand multiparity.

SECONDARY OUTCOMES

Among women who presented with Preterm Premature Rapture of Membranes, the most frequent organisms cultured included klebsiella (19.7%), proteus (3.9%) , E-coli (10.5%) and pseudomonas (1.3%) ,Streptococcus (1.3%). The majority of cultures showed no growth (63.1%).

Preterm Premature Rapture of Membranes often results in poor foetal outcome like prematurity, birth asphyxia and neonatal sepsis.

6.2: RECOMMENDATIONS

- All pregnant mothers with symptomatic urinary tract infections, HIV and grand multiparous should get a high vaginal swab to rule out genital infection.
- Further studies to find out the association between Preterm Premature rapture of Membranes and antenatal attendance and parity should be done to find out if there is any relation.
- Antibiotic targeting gram negative organisms should be given to mothers who present with preterm premature rapture of membranes.

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APPENDICES

APPENDIX I: Consent Form

KAMPALA INTERNATIONAL UNIVERSITY WESTERN CAMPUS

INSTITUTIONAL REVIEW COMMITTEE [KIU-IRC]

INFORMED CONSENT FORMAT

Study Title: **CAUSES AND RISKFACTORS ASSOCIATED WITH PRETERM PREMATURE RUPTURE OF MEMBRANES AND FOETAL OUTCOMES AT MBARARA REGIONAL REFERRAL HOSPITAL**

Principal Investigator[s]: Tezita Alex

INTRODUCTION

What you should know about this research study:

- You are being asked to join this study:
- This consent form explains the research study and your role in the study
- Please read it carefully and take your time to decide
- You are a volunteer. You can choose to take part and if you join, you may quit at any time. There will be no penalty if you decide to quite the study

Purpose of this research

- To determine the causes and risk factors associated with preterm premature rupture of membranes at MRRH and foetal outcomes of pregnancies complicated by PPROM .

Why you are being asked to participate

- To help determine the causes and risk factor of PPROM at MRRH

Procedures

- After you consent you shall be asked to give samples that include blood sample, urine and Amniotic fluid through Non-invensive processes

Risks/discomforts

- Needle prick for blood samples
- Speculum discomfort while taking the amniotic fluid

Leave blank for IRC Office only KIU-IRC Stamp	IRC OFFICIAL USE ONLY Approval date: Approved consent IRB version number PI NAME: IRB NO.

Benefits:

This research will help answer questions of the causes of preterm Premature Rapture of Membrane at MRRH and risk factors.

Incentives/rewards for participating

None

Protecting data confidentiality

- Data will be entered in a personal computer by the P.I that has a protected secret pass word.
- Hard copies will be stored in a lockable cabinet

Protecting subject privacy during data collection

- No names of patients shall be attached to the questionnaire by secret cards
- Questionnaire will be administered in a secluded room on ward.

Right to decline/withdraw

It's your right to choose to participate in this research and withdraw at your will.

What happens if you leave the study?

- Nothing but you will still receive the standard treatment given to patients with this condition.

Who do I contact if I have questions or a problem?

- Contact for principal investigator [Tezita Alex [0774 020 734, 0701 082 263]
- Contact for IRC Office

What does your signature [or thumbprint/mark] on this consent form mean?

Your signature on this form means

- You have been informed about this study's purpose, procedures, possible benefits and risks
- You have been given the chance to ask questions and response given before you sign
- You have not waivered any of your human rights
- You have voluntarily made an informed decision to participate in this study

Leave blank for IRC Office only KIU-IRC Stamp	IRC OFFICIAL USE ONLY Approval date: Approved consent IRB version number PI NAME: IRB NO.

…… ……

Print Name of Adult participant **Signature of adult participant**

Date

---------- ----------

Print Name of person obtaining consent **Signature**

Date

…… …….

Thumbprint/mark

Signature of witness **Date**

……..

APPENDIX II: Consent Form Lunyankole version

KAMPALA INTERNATIONAL UNIVERSITY WESTERN CAMPUS

AKAKIIKO AKARIKUSHWIJUMA EBY'EITENDEKYERO

[INSTUTITIONAL REVIEW COMMITTEE [KIU-IRC]

OBUHAME OBUHAIRWE OKU BUTEBEEKANISIIBWE

- **Omutwe gw'omushomo :** Kusharamu ebirikutuma kandi n'enshonga nyingi ezirikureeta ebizibu ebikwatiraine n'okwatika kw'enshoha eshaaha etakahikire ahari Mbarara University Regional Referral Hospital

Omucondooza Mukuru: Tezita Alex

OKWANJURA

Ebi oshemereire kumanya aha mushomo gw'okucondooza ogu

- Nooshabwa kwegeita aha mushomo gw'okucondooza ogu
- Foomu y'obuhame egi, neeshoboorora aha mushomo gw'okucondooza n'omugasho gwawe omu mushomo ogu
- Nooshabwa kugishoma n'obwegyendesereza kandi otware obwire kweshariramu
- Nookora oyekundiire. Noobaasa kusharamu obutabizamu kandi waazamu, noobaasa kurugamu ahu orikwendera. Tihariho kufubirwa waasharamu kuruga omu mushomo ogu.

Ekigyendererwa ky'okucondooza

- Kusharamu ebirikutuma kandi n'enshonga nyingi ezirikureeta ebizibu ebikwatiraine n'okwatika kw'enshoha eshaaha etakahikire ahari Mbarara University Regional Referral Hospital

Ahabw' enki nooshabwa kubyejumbamu

- Kuyamba kusharamu ebirikutuma kandi bikareeta ebizibu by'okwatika kw'enshoha eshaaha etakahikire ahari Mbarara University Regional Referral Hospital

Oku biraakorwe

- Waaheza kuhayo obuhame, noija kushabwa kuheereza eby'okukyebera ebirimu eshagama, enkari hamwe n'amaizi g'omu mubiri orikurabira omu muhanda gutari gw'obukugu [*non-invensive process*]

Oburemeezi n'obutaba gye

- Okwihwaho eshagama orikukozesa okucumita empitirizo
- Okushaasha omugongo baaba nibaihaho amaizi g'okukyebera

Rekaho omwanya ahabwa Ofiisi ya IRC	Nihakozesibwa aba IRC Eizooba obu kyahamibwa Obuhame bw'aba IRC n'enamba Eiziina rya PI Enamba ya IRB

Amagoba

Okucondooza oku nikuza kuyamba kugarukamu ebibuuzo ekirikutuma haabaho okwatika kw'enshoha eshaaha etakahikire ahari Mbarara University Regional Referral Hospital kandi n'ekirikureeta oburemeezi

Ebirikwetereza/Ebihembo by'okwetaba omu kucondooza

Tibiriho

Okubiika ebihandiiko bwesherekye

- Ebihandiiko nibiija kutaahibwa omu kompyuta y'omuntu omwe aha ba P.1 ahabw'okuba nibo baine enyuguta erikugiigura
- Kope z'ebihandiiko ezindi, nizibiikwa omu kabada y'ekyoma

Okurinda ebihandiiko nk'ebihama mwaba nimubirundaana

- Tihariho eiziina ry'omurwaire eriraije kuteebwa aha kipande
- Ebibuuzo nibiija kushwijumwa abeebembezi omu kishengye kyehereire omu woodi

Oine obugabe kwanga nari kuruga omu kucondooza

- N'obugabe bwawe kusharamu kwejumba omu kucondooza nari okakurugamu oyekundiire.

Ni habaho ki, waareka omushomo?

Tikiriho kandi noija kutunga okujanjabwa okuhikire nk'okurikuheebwa abarwaire abandi

N'oha ou naakubaasa kureeba naaba nyine ekibuuzo nari oburemeezi?

- Reeba omucondooza mukuru
- Hika omu ofiisi ya IRC

Omukono nari ekinkumu aha foomu y'obuhame egi, nibimanyisa ki?

Omukono gwawe aha foomu egi nigumanyisa:

- Waamanyisibwa aha bigyendererwa, amagoba agarikubaasika n'oburemeezi
- Waatunga omugisha gw'okubuuza ebibuuzo n'okugarukwamu
- Torikwihwaho bugabe bwawe
- Oyekundiire, oyeshariremu kwetaba omu mushomo ogu.

…… ……. ……..

Handiika amaziina g'omuntu Omukono gw'omuntu okuzire Ebiro by'okwezi Okuzire

…… …… ……

Handiika eiziina ry'omuntu Omukono gwe Ebiro by'okwezi

Oihirweho obuhame Ekinkumu

Omukono gw'omujurizi Ebiro by'okwezi

Rekaho omwanya ahabwa Ofiisi ya IRC	Nihakozesibwa aba IRC Eizooba obu kyahamibwa Obuhame bw'aba IRC n'enamba Eiziina rya PI Enamba ya IRB

APPENDIX III: Questionnaire

Patient serial number…….. Date……

Section A: Biographic Data

1. Marital status
   i) Single parent ii) Monogamous marriage iv) Polygamous marriage
2. Number of children
   i) Below 2 ii) 2 -4 iii) above 4
3. Level of education
   i) No formal education ii) Primary education iii) Secondary education
   iv) Tertiary education
4. Occupation
   i) Public service ii) Private business iii) Farming
   iv) None. v) Others (specify)…….

Section B: Maternal Risk Factors

1. Maternal Age in years
   i) Below 16 ii) 16 –<18 20 iii) 21 – 25
   iv) 26 – 30 v) 31 – 35 vi) 36 – 40>40!
   vii) Above 40
2. Average income per month?
   i) Below 100000/= ii) 100000/= -200000/= iii) 200000/= - 300000/=
   iv) 300000/- - 400000/= v) 400000/- - 500000/= vi) Above 500000
3. Do you smoke?
   i) Yes ii) No iii) Stopped during pregnancy
4. Do you drink alcohol?
   i) Yes ii) No iii) Stopped during pregnancy
6. Inter-pregnancy period
   i) below one year ii) 1 – 2 years iii) above 2 years
7. Outcome of the previous pregnancy
   i) Live baby (full term) ii) Preterm birth iii) Stillbirth
   iv) Abortion v) Early Neonatal death
8. Obstetric History
   i) Parity: 1 ii) 2 – 4 iii) 5 and more
   LNMP……. EDD…….. WOA……
9. ANC visits i) None☐ ii) Once☐ iii) 2 – 3☐ iv) > 3☐
10. Mode of delivery:
    i) SVD ☐ ii) Vacuum extraction☐ iii) C-section ☐
    iv) Assisted breech extraction☐
11. Indications for C-section:
    i) Fetal distress☐ ii) PPROM with severe reduction in liquor☐
    iii) Cord prolapse☐ IV) APH☐ v) Non-reassuring fetal heart☐
    vi) Others (specify)…….

Section C: Infectious causes of PPROM

1. HIV serostatus
   i) Positive ii) Negative iii) Not Sure

   i) No

2. Urinary tract infections?
   i) Yes ii) No
3. Other maternal medical conditions?
   a) Hypertension
      i) Yes ii) No
   b) Diabetes
      i) Yes ii) No
   c) Anemia
      i) Yes ii) No
   d) History of APH
      i) Yes ii) No

Investigations

Blood pressure
Urinalysis
Sterile Vaginal swab – organisms cultured:..……..
Sensitivity pattern……..

Section D: The outcomes of pregnancies complicated by PPROM

1. Outcome of pregnancy?
   i) Live birth ii) Fresh stillbirth iii) Macerated stillbirth
   iv) Prenatal death
2. Weight of the child?
   i) 0.5 Kg ii) 0.5 -1kg iii) 1-1.5 kg iv) 1.5 -2 kg
   v) Above 2kg
3. Sex of the baby
   i) Male ii) Female iii) Female/Female
   iv) Male/Male v) Male/Female
4. APGAR score
   i) 0 ii) 1 – 3 iii) 4 – 6
   iv) 7 – 10
5. Baby admitted to Pediatrics Ward
   i) Yes ii) No
6. Adverse Pregnancy Outcome
   i) Previous first trimester abortion ii) Previous second trimester abortion
   ii) Previous spontaneous abortion iv) Previous preterm birth

APPENDIX IV: LETTER OF INTRODUCTION

KAMPALA INTERNATIONAL UNIVERSITY
EXPLORING THE HEIGHTS

Ishaka Bushenyi * PO BOX 71 Ishaka, Uganda
Tel: +256 (0) 774365765* Fax: +256 (0) 41 - 501 974
E-mail: admin@kiu.ac.ug * Website: http://www.kiu.ac.ug

OFFICE OF THE DEAN,

FACULTY CLINICAL MEDICINE &DENTISTRY

06/02/2014

TO WHOM IT MAY CONCERN

RE: TEZITA ALEX (BMS/0099/91/DU)

The named is a student of fifth year at Kampala International University pursuing a Bachelor of Medicine, Bachelor of Surgery (MBChB) programme.

He wishes to conduct his research project in your hospital.

Any assistance given will be appreciated.

Thank you

Dr. Akib Surat
Asso. Dean, FCM &D

APPENDIX V: TIME FRAME/WORK PLAN

Objectives	Activities	Oct 2013	Nov 2013	Dec 2013	Jan 2014	Feb 2014	Mar 2014	Apr 2014	May 2014	Jun 2014
Proposal Submission	Research proposal review and approval by the KIU research committee									
Proposal Review	Institutional Research Committee									
Proposal	Proposal corrections									
First progress report										
Data	Data and HVS samples' collection									
Antibacterial test	Microbial Culture and Sensitivity studies of the HVS sample specimens.									
Compiling	Data analysis, Compiling the results, and report writing Final report & Submission									

APPENDIX VI: RESEARCH BUDGET BREAKDOWN

PARTICULARS	JUSTIFICATION	QUANTITY	UNIT COST (UGSH)	AMOUNT (UGSH)
Stationary	Photocopying papers	02 Rimes	20,000	40,000
	Ruled papers	02 Rimes	15,000	30,000
	Pens	25 Pens	500	12,500
	File folders	05 Pieces	3,000	15,000
	Printing Services			100,000
	Sub Total			**197,500**
Laboratory Supplies / Tests	Sterile swabs for HVS + Culture & Sensitivity Tests	100 Tests	10,000	1,000,000
	Surgical Gloves	02 Boxes	50,000	100,000
	Examination Gloves	01 Boxes	15,000	15,000
	Sub Total			**1,115,000**
Transport	Ishaka to & fro Mbarara			100,000
	Sub Total			**100,000**
Personnel's Allowances	Lab. Technicians / Technologists	02 People	200,000	400,000
	Research Assistants	03 People	100,000	300,000
	Sub Total			**700,000**
Miscellaneous	Air time	10 Pieces	10,000	100,000
	Feeding			100,000
	Sub Total			**200,000**
GRAND TOTAL				**2,312,500**