# CURRENT MICROBIAL PATTERN OF PATIENTS PRESENTING WITH PRELABOUR RUPTURE OF MEMBRANES (PROM) AT LABOUR WARD IN KENYATTA NATIONAL HOSPITAL.

A DISSERTATION SUBMITTED AS PART FULFILMENT FOR THE AWARD OF MASTER OF MEDICINE (MMed) DEGREE IN OBSTETRICS AND GYNECOLOGY OF THE UNIVERSITY OF NAIROBI.

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## DECLARATION

I hereby declare that this dissertation is my own original work and has not been submitted at any other university for the award of a degree.

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**DEDICATION**

To my loving wife Alice Awuor and our daughters Nereah and Noelle who have borne my long absence and great distance from home. You make life worth living.

To my late parents Mr. George Dixon Onyango and Mama Nereah Akeyo Onyango. Thank you for encouraging us and showing us the benefits of education.

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## ABBREVIATIONS

KNH.....Kenyatta National Hospital

ACOG .....American College of Obstetricians and Gynecologists.

RCOG..... ..Royal College of Obstetricians and Gynecologists.

PROM ..... .Prelabour rupture of membranes.

PPROM ..... Preterm Prelabour rupture of membranes.

RDS ..... .. Respiratory distress syndrome.

USA ..... .. United States of America.

IVH ..... .. Intraventricular haemorrhage

BV ..... .. Bacterial vaginosis.

MMP ..... .Membrane metalloproteinase

PG ..... .. Prostaglandins

TNFα ..... Tumour necrosis factor alpha

UTI ..... .. Urinary Tract Infection.

UoN ..... University of Nairobi

MMed ..... Master of medicine.

CBA ..... .. Chocolate blood agar

Sba ..... .. Sheep's blood agar

Mac ..... .. MacConkey's agar

Sab ..... .. Saboraud's medium

**)efinitions.**

**'relabour rupture of membranes (PROM):** refers to rupture of fetal membranes at any me before the onset of contractions.

**reterm prelabour rupture of membranes (PPROM):** refers to PROM prior to thirty-even weeks of gestation.

**ROM group:** participants in the study having confirmed prom. The participants in this roup were at gestation of thirty-two weeks and above. They were recruited at the labour ards.

**ON-PROM:** the control study participants not having drainage of liquor. . Their cruitment was at the antenatal clinics of KNH.

**atent period:** this is the time from the membrane rupture to the onset of contractions.

**erm:** 37 weeks of gestation and above.

**reterm:** less than 37 weeks of gestation.

**PGAR score:** American paediatric gross assessment record (APGAR) score: this scribes the cardio respiratory and neurological depression in the baby. Conventionally scribed at 1 and 5 minutes. A low apgar score signifies a problem that needs planation and management. It involves checking the following; heart rate, respiratory fort, muscle tone, reflex irritability and colour with scores of 0-2 and summation giving result.

**espiratory distress syndrome:** as a result of premature birth or immaturity of the spiratory system due to deficiency of surfactant the neonate has respiratory problems.

**Culture and sensitivity:** swab was inoculated into appropriate media and incubated. After establishing a colony, reinnoculation done with various antibiotic discs in the new media and assessing any inhibition of growth as an effect of the antibiotic disc.

**Gram stain:** after taking a swab it's processed in the lab and depending on uptake of stain described as gram positive or negative.

**Fetal outcome:** refers to the newborn features that were looked for. This included the birth weight, gestation at delivery, Apgar score at five minutes, admission to newborn unit and duration of stay in newborn unit.

**Demographic characteristics:** refers to age, parity and race of the study participants. Also included the employment and the nature of the same.

**Maternal outcome**: this refers to various parameters that was recorded in regard to the participants after delivery and included mode of delivery, any complications at delivery such as postpartum hemorrhage, placental retention, puerperal infections and fever and duration of hospital stay.

## ABSTRACT

**Background;** in spite of the advances that have been made in neonatal care over the past years. preterm birth and Prelabour rupture of membranes have not reduced. Neonatal mortality and morbidity remains. PROM has been attributed in 30-40 % of preterm birth. Infection has also been shown to be a leading cause of PROM. Wanjala in a study at KNH found an infection rate of 28.57% in PROM. Studies have shown improved outcome when antibiotics are used in PROM.

**Main objective:** To determine the microbial pattern of patients presenting with PROM at KNH labour ward.

**Main outcome measure:** *Escherichia coli* was the main pathogenic bacteria isolated accounting for 66.7% in the PROM group.Other bacteria were *enterococci. streptococcus viridans. staphylococcus sp* and *staphylococcus aureus.*

**Study design:** Case control study.

**Study population:** Women who presented with PROM at the labour ward of KNH with control group recruited from the antenatal clinics. There was no matching of the two groups. The sample size was 100 with equal proportion of 50 in each arm.

**Data analysis:** this was done using SPSS version 13. Data entry was done into SPSS and data cleaning done by use of the questionnaires.descriptive data was obtained and further analysis done.

**Results :** A total of 100 questionnaires and laboratory results were analysed. 50 from the PROM group and 50 in the control group. There was no statitistically significant difference in baseline sociodemographic and obstetric characteristics between the two groups.

As for the mode of delivery 70% in PROM had SVD compared to 48% of controls with 30% undergoing caearean section in PROM group and 52% of controls. There was no

complications recorded in the mothers both at and after delivery. *Escherichia coli* was the most common bacterial isolate accounting for 66.7% of bacterial isolate in the PROM group. Other isolates were *staphylococcus sp. staphylococcus aureus and streptococcus viridans.*

With regard to antibiotic sensitivity. there was 100% sensitivity to ceftriaxone. 83.3% sensitivity to both cefuroxime and gentamicin while augmentin had 67.7% sensitivity. Among the newborns. in the PROM group10% had apgar score <7. while none. 0%. of the controls had apgar score <7 with NBU admission rates of 20% and 6% respectively among the PROM and control groups respectively.

**Conclusion and recommendations:** We recommend that cefuroxime be the antibiotic of choice where its not possible to do endocervical swab. culture and sensitivity.

## oduction and literature review

:rm deliveries are those that occur at less than thirty-seven weeks' of gestational however the low gestational age cutoff or that used to distinguish preterm birth spontaneous abortion varies by location. At Kenyatta National Hospital(KNH) the r cutoff is less than twenty-eight weeks of gestation while in the United States its ty-four weeks.

abour rupture of membranes {PROM} refers to the rupture of fetal membranes re labour. When this occurs before thirty-seven weeks of gestation it's referred to as rm Prelabour rupture of membranes {PPROM}. PPROM is the spontaneous re of the membranes at less than 37 weeks gestation but at least one hour before t of contractions (**1, 2, 3, 4**)

## lemiology of PROM.

e United States of America preterm birth accounts for 12-13% of all deliveries. In pe and other developed countries rates are 5-9% with PPROM accounting for 30- of the preterm deliveries (**5, 6,** 7)

rm births account for 75% of perinatal mortality and more than half of the long morbidity. Although most of the preterm births survive in the developed countries are at increased risk of neurodevelopmental impairment, respiratory and ointestinal complications. PROM accounts for 25-30% of preterm births. **(8)**

s that follow spontaneous labour and PPROM are designated spontaneous rm births. Spontaneous preterm births are most commonly caused by preterm r in white women, but PPROM in black women. The explanation for this rence is unclear but it has been hypothesized to be due to high prevalence of rial vaginosis among the black population. There has been sub classification of rm births as follows: 5% occur at less than 28 weeks (extreme preterm), 15% at een 28 and 31weeks (severe prematurity), 20% at between 32 and 33 weeks erate premature) and 60-70% at 34-36weeks (near term (**5, 9**)

causes of rupture of membranes in most cases are unknown but asymptomatic rine infection is a frequent precursor. The most common microorganisms reported in niotic cavity include: genital *mycoplasma spp. ureaplasma urealyticum* and *ptococcus agalactiae*. Bacteria have been cultured from chorioamnion in 15% of labouring women with intact membranes undergoing caesarean delivery. (1)

k factors for PROM are generally similar to these for preterm spontaneous labour n intact membranes, though infection and tobacco exposure play important parts. st women with PROM begin labour spontaneously within several days but a small portion remain undelivered for several weeks and months. The duration from rupture nembranes to onset of labour is called latent phase and is inversely proportional to gestation at which PROM occurs. The commonest complication is development of uterine infection and preterm labour. The greatest complication of preterm labour is naturity that can result in neonatal death or long term disability (cerebral palsy, dness, deafness). The complications of infection include chorioamnionitis, maternal nd infection, and neonatal sepsis. Other complications of prolonged rupture of nbranes include oligohydramnios and its attendant pulmonary hypoplasia, umothorax and skeletal deformity.

erm 8-10% of women present with PROM They are at increased risk of intrauterine ction when the interval between rupture and delivery is prolonged. PROM occurs in roximately 10.7% of all pregnancies and associated with 30-40% of preterm veries thus being a leading cause of preterm deliveries with consequent sequele: iratory distress syndrome (RDS) neonatal infection and intraventricular norrhage (IVH). (**1, 2**)

litionally rupture of membranes was attributed to physical stress particularly in ur. Recent evidence suggests membrane rupture is also related to biochemical ursors including disruption of collagen within extra cellular matrix of the amnion chorion and programmed cell death (apoptosis) of fetal membranes.

**Structure of fetal membranes.**

The fetal membranes are composed of the amnion and chorion. Fetal amnion composed of five distinct layers. It contains no blood vessels or nerves, the nutrients it requires are supplied by the amniotic fluid. (**10**)

The innermost layer, nearest the fetus, is the amniotic epithelium. The amniotic epithelial cells secrete collagen type three and four and non collagenous glycoproteins (laminin, nidogen and fibronectin) that form the basement membrane, the next layer of amnion.

Compact layer of connective tissue adjacent to the basement membrane forms the main fibrous skeleton of the amnion. The collagen of the compact layer is secreted by mesenchymal cells in the fibroblast layer. (**11**)

Interstitial collagens types I and III predominate and form parallel bundles that maintain mechanical integrity of amnion. Collagens type V and VI form filamentous connection between the interstitial collagens and the epithelial basement membrane. There is no interposition of amorphous ground substance between collagen fibres in amniotic connective tissue at term, so amnion maintains its tensile strength throughout the later stages of normal pregnancy. (**12**)

Fibroblast layer is the thickest of the amniotic layers consisting of mesenchymal cells and macrophages within an extra cellular matrix. Collagens in this layer form a loose network with islands of non collagenous glycoprotein. (**12**)

Intermediate layer (spongy layer or zona spongiosa) lies between amnion and the chorion. Its abundant content of hydrated proteoglycans and glycoproteins give this layer its spongy appearance in histological preparations and it contains nonfibrillar meshwork of mostly type III collagen. Although chorion is thicker than amnion the later has greater tensile strength.

**Mechanisms of fetal membrane rupture preceding and during labour**

ıtrapartum rupture of membranes has been attributed to generalized weakening due to terine contractions and repeated stretching. Tensile strength is reduced in specimen btained after labour as compared to those obtained during caesarean section without ıbour. Generalized weakness of membranes has been more difficult to establish when remature rupture of membranes compared with artificially ruptured membranes during ıbour.

Membranes in PROM appear to be focally defective rather than generally weakened. he area near the rupture site have been described as restricted zone of extreme altered ıorphology characterized by marked swelling and disruption of fibrillar collagen etwork within the compact fibroblast and spongy layers. Due to the fact that not the ıtire rupture site is included, it may appear before membrane rupture and represent ıitial breaking point. Thus PROM represents an acceleration or exaggeration of the ·ocess precipitating spontaneous rupture of the membranes during labour.

he maintenance of the tensile strength of the fetal membranes appears to involve ıuilibrium between the synthesis and degradation of components of extra cellular atrix. It is proposed that changes in the membranes including decreased collagen ɔntent, altered collagen structure and increased collagenase lytic activity associated ith PROM. Connective tissue disorders and nutritional deficiencies are risk factors.

onnective tissue disorders are associated with increased incidence of PROM Ehlers anlos syndrome, a group of connective tissue disorders characterized by hyper asticity of joints and skin is caused by various defects in synthesis of collagen ructure.

lso it has been noted that certain nutritional deficiencies are a risk factor for PROM; ysyl oxidase a copper dependent enzyme is one. Women with PROM have lower vels of copper in maternal and umbilical cord serum than women with intact embrane and those who have artificial rupture of membranes done.

Tobacco smoking independently increases the risk of PROM. Smoking is associated with decreased serum concentration of ascorbic acid. Cadmium in tobacco also found to increase the maternal binding of metallothionein in trophphoblasts which may result in sequestration of copper. (13)

Increase in degradation of collagen mediated primarily by matrix metalloproteinase is inhibited by specific tissue inhibitors and other proteinase inhibitors.

**Clinical factors associated with PROM**

There has been a long-term debate on whether intrauterine infection is a consequence or cause of premature rupture of membranes. There is indirect evidence that genital tract infection precipitates rupture of membranes in humans and animals.

In a reported study of pregnant rabbits cervical inoculation with *Escherichia coli* resulted in positive culture for *E. coli* in the amniotic fluid and deciduas of 97% of the treated animals and preterm delivery in half the treated animals. In contrast, cervical inoculation with saline resulted in no infection or preterm birth. (14)

The identification of pathologic microorganism in human vaginal flora soon after membrane rupture lends credence to the concept that bacterial infection may have a role in the pathogenesis of PROM (15)

Released epidemiologic data demonstrate an association between colonization of the genital tract by groupB streptococci, *Chlamydia trachomatis*, *Neisseria gonorrhea*, and other organisms causing bacterial vaginosis (*Gardnerella vaginalis*, *Mobiluncus spp.*, genital *Mycoplasma)* and increased risk of PROM. Furthermore in some studies treatment of infected women with antibiotics decreased the rate of PROM. Bacterial vaginosis has been associated with a 1.5 to 3 fold increase in the rate of preterm birth. Black women in the USA and UK are three times more likely to have bacterial vaginosis than are white women and this difference might explain the 50% excess preterm births in black women. (16, 17)

Mwangi (2002) in a study of women attending antenatal clinic at Kiambu District Hospital found a bacterial vaginosis incidence of 25.6 % with 9.1% having mixed flora. He found increased risk of bacterial vaginosis associated with current presence of vaginal discharge, lower parity and low gestational age. In pregnancy bacterial vaginosis has been linked with PROM, preterm labour, endometritis, chorioamnionitis, post surgical wound infection and neonatal sepsis. At Kiambu treatment of BV was achieved by use of metronidazole, clindamycin or povidone iodine solution. In sub-Saharan Africa some areas have reported rates of BV of upto53 %.( **18**)

Intrauterine infection may predispose women to PROM through various mechanisms with each inducing degradation of extra cellular matrix. Several organisms that are commonly present in the vaginal flora including group B *streptococci, staphylococcus aureus Trichomonas vaginalis* and microorganisms causing bacterial vaginosis secrete proteases that can degrade collagen and weaken fetal membranes which release prostaglandins precursors within the amnion.

The host inflammatory response is another mechanism that may account for association between bacterial infection of genital tract and PROM Inflammation mediated by polymorphonuclear neutrophils and macrophages recruited to the site of infection and produce cytokines, matrix metalloprproteinases and prostaglandins. Inflammatory cytokines including interleukin 1(IL-1), tumour necrosis factor α (TNFα) produced by stimulated monocytes and these increase MMP-1 and MMP-3 expression at the transcriptional and post translational levels in human choruionic cells.

Bacterial infection and host inflammatory response also induce prostaglandin production by the fetal membrane which increases the risk of prom by causing uterine irritability and collagen degradation within the membranes. Certain strains of vaginal bacteria produce phiospholipase $A_2$ which release prostaglandin precursors within the amnion. Bacterial infection and cytokine production by activated monocytes that increase prostaglandin $E_2$ production by chorionic cells. This involves induction of cyclooxygenase 2, converting arachidonic acid into prostaglandins. PG $E_2$ and PG $F_2\alpha$

are mediators of labour in all mammals. PG $E_2$ diminishes collagen synthesis in fetal membranes and increase MMP-1 and MMP-3 expression in human fibroblast.

The normal host response to infection is production of glucocorticoids. In most tissues the anti-inflammatory action of glucocorticoids is mediated by suppression of PG production. However in some tissues including amnion the glucocorticoids paradoxically stimulate prostaglandin production. Furthermore dexamethasone reduces the synthesis of fibronectin and type III collagen in primary cultures of amniotic epithelial cells. suggesting that glucocorticoids produced in response to stress of microbial infection facilitate rupture of membranes. The role of hormones Oestrogen. progesterone and relaxin fetal membrane rupture remains uncertain.

As can be deciphered from above preterm birth is closely interlinked with PROM and therefore risk factors of one will be significant in the other. Several maternal and fetal factors have been linked with preterm birth/PROM (**19**)

- Maternal demographic characteristics: reported significance is black race. In use preterm birth of 16-18% among blacks and 5-9% among whites it has been alluded to be due to the higher rates of bacterial vaginosis in the former. Other maternal factors include low socioeconomic status. low and high maternal ages. single marital status.
- Nutritional status
- Pregnancy history;
- Present pregnancy characteristics; multiple gestation account for 2-3% of all pregnancies. Infants carry a substantial risk of preterm delivery. and result in 15-20%of all preterm births. Nearly 60% of twins born preterm. About 40% of twins have PROM before 37weeks. Uterine over distention result in contractions and PROM believed to be the causative mechanism for increased rate of preterm labour in higher multiple gestation.
- Psychological characteristics
- Adverse behaviors
- Infection

- Cervical length
- Biologic/genetic markers.

**Diagnosis of PROM**

The diagnosis of Prelabour rupture of membranes (PROM) is made with the following criteria:

- Visualization of amniotic fluid pooling in the posterior fornix as clear fluid passing from the cervical canal.
- The pH of the fluid. Normal pH of vaginal fluid 4.5-5.5 with amniotic fluid pH 7.0.-7.5 thus nitrazine test employs the principle of colour change with difference in pH. Nitrazine paper will turn blue in presence of amniotic fluid. pH above 6.5 consistent with PROM. False positive results obtain in presence of blood. semen.
- Observation of ferning pattern/arborization of vaginal fluid. Due to concentration of sodium chloride. proteins and carbohydrates in amniotic fluid.
- Injection of various dyes. including Evans blue. Methylene blue. indigo carmine or fluorescein in amniotic sac via abdominal amniocentesis.
- Serial ultrasound evaluation of amniotic fluid volume. This is of limited value as oligohydramnios is only demonstrable with large fluid losses that are usually clinically obvious.
- Fetal fibronectin (FFN) cervicovaginal test .fibronectin is a glycoprotein that when present in cervicovaginal fluid is a marker of choriodecidual interruption. Typically FFN is absent from cervicovaginal secretions from 24weeks until near term; however 3-4% of women undergoing routine scanning at 24-26weeks are positive and are at increased risk of preterm delivery. Fibronectin is of variable positive predictive value for preterm delivery (13-83%). Negative FFN result implies preterm birth/PROM highly unlikely (81-99%0 negative predictive value. (**2, 3, 20, 21**).

**Management of PROM**

From the foregoing it has been clearly demonstrated that etiology of PROM is multifactorial. There is a recognized association between vaginal infection and bacteriuria with sub clinical chorioamnionitis. (**21**)

In case of prom before thirty weeks of gestation the risks of fetal prematurity far outweigh those that may arise like materno-fetal sepsis. The aim of management in such scenario is to prolong pregnancy through conservative management to achieve maximum fetal maturity prior to delivery and onset of chorioamnionitis or neonatal sepsis.

The main indication for delivery is sepsis with incidence of chorioamnionitis (30-50%) endometritis (15-20%) and neonatal sepsis (11-13%) following midtrimester prom. one of the most serious consequences of prom is oligohydramnios with the attendant sequele of pulmonary hypoplasia. Pulmonary hypoplasia after PROM depends on; gestation at onset, severity of oligohydramnios and latency period. Severe oligohydramnios also produces the fetal 'deformatioion 'syndrome (facial anomalies, limb positional defects and impaired fetal growth.

In general the earlier the gestation at which PROM occur the longer the latency period. Studies have shown that in women with prom at 28-36 weeks, 80% cases delivered within one week of membrane rupture. In conservative management of prom before 32 weeks, the mean latency period around 10days, with about 75% cases delivering within 2weeks of prom. The incidence

overall Perinatal survival of 40-80% depending on birth weight, gestation and latency period have been reported. Amongst these, Survival without major neurological and developmental defects occurs in around 60-75% of survivors.

As already stated above in management of prom one must always look out for the occurrence of infection. Bacterial infection within the uterus can occur between

maternal tissues and the fetal membranes (i.e. within the choriodecidual space.) the fetal membranes (amnion and chorion) the placenta, amniotic fluid or umbilical cord or the fetus. Infection of fetal membranes called chorioamnionitis, infection of umbilical cord funisitis and infection of amniotic fluid amnionitis. The first substantial microbiologic evidence relating intrauterine infection before membrane rupture to preterm delivery was presented only in the late 1970 when bacteria were cultured in preterm labour women who had intact membranes. Bacteria may invade the uterus by migration from the abdominal cavity through the fallopian tubes, inadvertent needle contamination at the time of amniocentesis or chorionic villus sampling, haematogenous spread through the placenta, or passage through the cervix from the vagina. Overall the prevalence of positive amniotic cultures in women with PROM is 32-35 %.( **22**)

An important factor in the occurrence of PROM is recurrent urinary tract infection (UTI). As one of the leading causes of preterm birth, UTI has been implicated in development of PROM. Essajee (2002) found the prevalence of UTI at the antenatal clinic of KNH of 23%. Escherichia coli was the major pathogen isolated accounting for 34.4% of cases. Other isolates were *Candida albicans* and *staphylococcus aureus* at 25 and 15.6% respectively. Group B streptococcus (GBS) and *streptococcus faecalis* were isolated in 6.25%. The antibiotic of choice was Augmentin with 100% efficacy. Nitrofurantoin was also effective though only 81.8% in *E. coli* and 50% in GBS. The cephalosporins were the most effective against GBS at 100 %.( **23**)

Wanjala (1980) conducted a study on PROM at Kenyatta national hospital. He found an incidence of 8.2%. In the study conducted between November 1978 and March 1979 amongst 2004 deliveries 165 patients' presented with prom. At the time of rupture 25% of patients were at gestation<32weeks, 53.57% at > 36weeks. Pieces of membranes were taken for culture immediately after delivery and also use of nasogastric tube to obtain fluid from fetal throat for culture. The organisms that were grown included *Escherichia coli staphylococcus* and *proteus spp*. E coli were the commonest organism cultured. Pathogenic organisms cultured gave an infection rate of 28.57%. He found that most infections occurred in patients who ruptured less than 36weeks. Among

patients who were on antibiotics at the time of delivery an infection rate of 12.5% found compared to 35% for those not on antibiotics. (**24**)

In another study at KNH Kirumbi (1988) had comparison of cervical micro flora on patients with Mac Donald stitch in situ. The results were that patients with Mac Donald stitch had higher colonization rates by anaerobes and yeast. Most of the patients had more than one type of micro flora in the endocervical canal, while controls were found to have higher colonization by aerobic microorganisms. Species of microorganisms isolated in positive culture included the following *peptostreptococcus, peptococcus, fusobacterium, veillonella and bacteroides.* (**25**)

In women in spontaneous preterm labour with intact membranes the most commonly identified bacteria are: *ureaplasma urealyticum, mycoplasma hominis, gardnerella vaginalis*, peptostreptococci, bacteroides spp. All of which are vaginal organisms of low virulence. The organisms more often associated with genital tract infection in non pregnant women *neisseria gonorrhoeae* and *Chlamydia trachomatis* are rarely found before membrane rupture. (**22**)

On the other hand organisms most commonly associated with chorioamnionitis and fetal infection after membrane rupture includes Group B streptococci and *Escherichia coli*. Rarely non genital tract organisms such as mouth organism of the genus Capnocytophagia found in the uterus in association with preterm labour and chorioamnionitis.

Chorioamnionitis is characterized by the following features maternal pyrexia, tachycardia, uterine pain, uterine tenderness and purulent vaginal discharge. Laboratory work-up will reveal elevation of blood C-reactive protein and leucocytosis.

Expectant conservative management with feto maternal monitoring is often initiated with prom before 24weeks in the western world. After 24weeks active conservative

management should be considered where the usage of pharmacological agents has been suggested to improve pregnancy outcome.

Evidence of role of sub clinical chorioamnionitis in PROM comes from case control and cohort studies that show that women with PROM have higher colonization of lower genital tract than women with normal births from microbiological studies of amniotic fluid taken by amniocentesis from women with prom.

The importance and potential effects of PROM on brain development in children is illustrated by results of two clinical studies. Murphy and colleagues did a case control study of 59 children with cerebral palsy who were singleton and less than 32 weeks of gestation at birth. In their finding the most important antenatal risk factor are prolonged (>24hours) rupture of membranes, chorioamnionitis and maternal infection. the results of second report showed a five fold increase in the likelihood of severe neurological handicap in infants born after PROM at between 24-34 weeks gestation compared with infants who had been born after spontaneous preterm labour and that the risk of handicap was related to the duration of membrane rupture.(**26**)

Between 30-33 weeks the risks of fetal prematurity (morbidity/mortality) marginally outweigh those that may come due to feto-maternal sepsis and active conservative management is recommended on balance.

If a pregnancy progress to 34weeks without complication then delivery is commonly recommended. Surfactant deficiency is not a problem and further prolongation of pregnancy will increase the risk of sepsis with little gain, although good evidence to support this might be lacking.

The role of monitoring in conservative management cannot be overstated and it entails the following: in the mother daily pulse rate, temperature,vaginal discharge, abdominal pain, tenderness and contractions with twice weekly white blood cell differential count, serum C reactive protein and vaginal swab with urine culture. In the fetus monitoring

entails daily non-stress cardiotocograph. twice weekly ultrasound for biophysical profile and umbilical artery Doppler recording. It is recommended to fortnightly have ultrasound for growth and estimated fetal weight. (21)

Administration of maternal antenatal corticosteroids to women with prom is controversial. The royal college of obstetricians and gynecologists (RCOG) recommend prophylactic antenatal corticosteroids for pregnancy at risk of preterm delivery between 24-36 weeks irrespective of rupture of membranes whereas 24-32 weeks (with ruptured membranes) and 24-34weeks (with intact membranes) are the gestational limits of ACOG.

Corticosteroids reduce the incidence of respiratory distress syndrome (RDS). neonatal death and intraventricular haemorrhage (IVH) in preterm infants. Cochrane metaanalysis shows that whilst single dose antenatal corticosteroid use in presence of rupture membranes did not increase the risk of fetal/neonatal infection or overall maternal infection rate. In women whose membranes were ruptured for more than 24hours before delivery the rate of maternal infection was increased.

Other randomized trials evaluating single corticosteroid administration in PROM have reported small increase in both neonatal and maternal infectious morbidity. A recent randomized study did not find this increase in maternal or neonatal infectious morbidity. In women with PROM who were concurrently receiving prophylactic antibiotics.

It has become accepted practice in some centers to repeat the corticosteroid course one week after the initial course in these women who remain undelivered and at continued risk of preterm delivery. No evidence is currently available to either condemn or support the use of multiple steroid doses.

Just like corticosteroids the use of tocolytics in PROM/threatened preterm delivery is controversial.metaanalysis have shown that use of beta sympathomimmetic tocolytics may delay the onset of preterm labour and reduce the proportion of women who deliver within 48hours. Based on this RCOG recommend that beta agonist tocolytics should only be used if the expected delay inn delivery of 24-48 hours will be used to implement measures to improve pregnancy outcome by administering of antenatal corticosteroids or by inutero transfer to a tertiary institution. Meta analysis of tocolytics use shows no reduction in neonatal mortality o serious neonatal morbidity. (**21**)

There is concern that tocolytics may mask the onset and progress of chorioamnionitis especially in cases of PROM.

Another important aspect in management of PROM is the use of prophylactic antibiotics. As can be seen from above discussion, infection may be a cause or complication of PROM. The routine use of antibiotic prophylaxis in PROM awaits further evaluation. The aims of antibiotic are for preventing maternal and infectious fetal morbidity also prolonging the latency period prior to delivery thereby reducing the consequence of prematurity. (**21**)

Cochrane review of treatment with antibiotics in PROM reported that antibiotics seem to be of benefit in reduction of rate of neonatal infection, and reduction of the number of babies requiring neonatal intensive care admission and ventilation for more than 28 days. No evidence reported on benefit for necrotizing enterocolitis, major cerebral abnormality, respiratory distress syndrome or death (stillbirth or neonatal death.) the antibiotics used included amoxicillin, co-amoxiclav (amoxicillin/clavulanic acid), clindamycin, erythromycin, metronidazole and tetracycline. However due to its effect on infant dentition the use of tetracycline not recommended.

One of the largest studies undertaken on PROM and antibiotic use is the ORACLE I randomized trial on broad spectrum antibiotics for preterm premature rupture of membranes. In the study 4826 women with PPROM were randomly assigned to 250mg

erythromycin. 325mg co-amoxiclav (250mg amoxicillin plus 125mg clavulanic acid), both or placebo, four times daily for 10days or until delivery. The outcome measures were neonatal deaths, chronic lung disease, and major cerebral abnormality on ultrasound before discharge from hospital. (27)

The findings were that erythromycin was associated with a range of health benefits for the neonate and thus probable reduction in childhood disability. Erythromycin associated with prolongation of pregnancy, reduction of neonatal treatment with surfactant, decrease in oxygen dependence at 28days of age and older, less major cerebral abnormality on ultrasound before discharge and fewer positive blood cultures. The health benefits of erythromycin in PROM are therefore not likely to be mainly due to merely prolongation of pregnancy but to a reduction of the effects of fetal and neonatal lung infection or inflammation. (27)

The other groups on co-amoxiclav only, co-amoxiclav with erythromycin associated with prolongation of pregnancy but also with significantly higher rates of necrotizing enterocolitis. (27)

In the previous discussion it has been demonstrated that both antibiotics and glucocorticoids individually improve neonatal outcomes in PROM. It would therefore be expected that in theory they would have an additive beneficial effect if they are both combined. However a recent metaanalysis suggest that the benefits of antibiotics treatment may be diminished when glucocorticoids are used concomitantly. Antibiotic therapy without concomitant glucocorticoids reduced odds of chorioamnionitis, postpartum endometritis, neonatal sepsis and IVH by 62, 50, 68 and 50% respectively whereas antibiotic treatment and glucocorticoids showed no significant improvement)

Amniocentesis could provide direct information regarding infection, fetal lung maturity and karyotype in pregnancy complicated by PROM. Amniocentesis may be complicated by miscarriage and fetal infection in a small number of women. There is limited evidence from non randomized studies suggesting that serial amnioinfusion in PPROM

less than 25weeks may reduce incidence of pulmonary hypoplasia and neonatal mortality. Further research needed to define the safety and efficacy, optimal interval between infusions and optimal gestation to amnioinfusion, optimal fluid required to maintain amniotic fluid volume.

**Study justification**

The use of antibiotics has not been shown to prevent preterm labour. However studies have indicated antibiotics improve neonatal outcomes in PROM. In the ORACLE study there was comparison of use of erythromycin, coamoxiclav, both in combination or placebo. Use of erythromycin was found to be superior.

Reports abound about the increasing incidence of antibiotic resistance. At the same time at KNH there is no current hospital protocol based on studies done in Kenya on antibiotic use in PROM. Thus our study will delineate the bacterial patterns found in PROM in our setup and also the ideal antibiotics to be used. Results can also be used in the rest of the country and where it's not possible to undertake culture and sensitivity studies.

**Objectives: broad objective**

- To determine the microbial pattern and antibiotic sensitivity in patients presenting with PROM at KNH labour ward.

**Specific objectives**

- To determine the demographic characteristics of women presenting with PROM.
- To determine the bacteriology, culture and antibiotic sensitivity in PROM.
- To determine maternal outcomes in PROM.
- To determine the fetal outcomes in PROM at KNH.

**Methodology**

**Study design**

This study was a case control study.

**Study site**

The study was conducted at Kenyatta national hospital. Study participants were recruited at the labour wards and the antenatal clinics. Kenyatta National Hospital is one of two national referral hospitals in Kenya. It is located about six kilometers from the town centre, Nairobi the capital city of Kenya.

The Department of Obstetrics and Gynaecology is run by consultants from both the national hospital and the University of Nairobi who use it as a teaching hospital. Thus for ease of operations the staff are divided into three firms who each have weekly running of the labour ward and antenatal clinic days on Tuesday, Wednesday and Thursday each morning of the said days for an individual firm.

While some patients who deliver at our labour ward are clinic attendants at KNH, hospital records suggest that majority do not attend the ANC clinics at KNH. Most of them attend the city council of Nairobi clinics. Being a referral institution some patients also come from allover the country.

**Study population**

The study participants were women with confirmed clinical diagnosis of PROM and a control group who were women at the antenatal clinic but not having drainage of liquor, that is PROM attending the antenatal clinics.

**Inclusion criteria.**

- Women presenting with PROM at 32 weeks of gestation and above.
- Women at the antenatal clinic above 32 weeks gestation who consented to participate and had no PROM to be controls.

**Exclusion criteria.**

- Women who presented with PROM but already were on some form of antibiotic medication were excluded from the study.
- Also patients who declined to participate in the study.
- Patients who had had a digital vaginal examination already.

- Participants in labour.

**Sample size estimation**

Sample size calculated using the formula below:

Let $p_i$ be the proportion of subjects in group $i$ having the outcome of interest, $\overline{p} = (p_1 - p_2)/2$ and $\overline{q} = 1 - \overline{p}$.

$$H_0: p_1 - p_2 = 0$$
$$H_1: p_1 - p_2 = d$$

The sample size per group is

$$n' = \frac{\{z_{\alpha}\sqrt{2\overline{p}\,\overline{q}} - z_{\beta}\sqrt{p_1q_1 - p_2q_2}\}^2}{d^2}$$

$$n = n'/4\left(1 + \sqrt{1 + 4/n'|d|}\right)^2 \text{ "continuity correction"}$$

**Reference**

Fleiss JL Statistical Methods for Rates and Proportions (2nd edition). Wiley:New York. 1981.

| **Factor under consideration** | | "bacterial growth" |
|---|---|---|
| 1ST GROUP<br>2ND GROUP | | "PROM"<br>"Non PROM" |
| **Parameter** | **Symbol** | **Value** |
| Prob of "bacterial growth" in "PROM" group | $p_1$ | 20.0% |
| Prob of "bacterial growth" in "Non PROM" group | $p_2$ | 1.0% |
| $p_1 - p_2$ | D | 0.19 |
| Odds Ratio | OR | 24.75 |
| Proportion of participants expected in "PROM" group | $m_1$ | 50.0% |
| Proportion of participants expected in "Non PROM" group | $m_2$ | 50.0% |
| Ratio of ("PROM":"Non PROM") sizes | R | 1.00 |
| Corrected | p-bar | 0.105 |
| Power | 1-β | 80% |

| | | |
|---|---|---|
| | $z\text{-}\beta$ | 0.84 |
| Confidence level | $1\text{-}\alpha$ | 95% |
| | $z\text{-}\alpha$ | 1.96 |
| Number of participants required for "PROM" group | $n_1'$ | 40 |
| Number of participants required for "Non PROM" group | $n_2'$ | 40 |
| Continuity correction for $n_1'$ | $n_1$ | 50 |
| Continuity correction for $n_2'$ | $n_2$ | 50 |
| **Sample size** | | **99** |

From Wanjala (1980) the rate of infection in PROM was 28.57%. this would give a sample of 63. However to be conservative an assumption of infection rate of 20% has been made hence the sample size in our study shall be 100 with 50 in each arm.

**Sampling technique**

**Recruitment of PROM participants.**

This took place in the labour ward of KNH. As per the current protocol of management in the labour ward, once a patient arrives is allocated to a primary nurse who takes her into one of the "first stage" rooms. The registrar on duty then reviews the patient and management prescribed accordingly.

For the purpose of our study the registrars were recruited as study assistants.two midwives at the labour ward were also recruited as study assistants and trained on recruitment of cases and specimen collection.

Once a mother presented with complaint of drainage of liquor, an explanation was given to her about the purpose of the study and consent obtained. the participant recruited would undergo a speculum examination where assessment for pooling of fluid in the posterior vaginal fornix was done. Also swabbing was done by asking the participant to cough and the spurting fluid bathed the swab. After which the questionnaire was

administered. This was done sequentially for mothers presenting with PROM at 32weeks and above and willing to participate in the study until the required sample size was attained.

The following is a flow chart of screening, recruitment and enrollment as it occured in labour ward and antenatal clinic:

Screening of patients/ identification of controls (registrar on duty labour ward)

|

Recruitment of participant (principal investigator/assistant)

|

Administration of consent (principal investigator/assistant)

|

Enrollment of participant

|

Speculum examination (principal investigator/assistants)

**Recruitment of non PROM (control)**

The controls were recruited at the antenatal clinics and they were not of corresponding gestation to the PROM group. No matching of the groups was done.

. Exit interview of mothers attending the antenatal clinic was done by the principal investigator and the assistants to identify mothers to be recruited. The mothers to be recruited were those willing to participate in the study and of 32 weeks gestation and above.After explanation of the purpose of the study, consent was administered. Thus the participant being so recruited, a questionnaire was administered and then a swab taken after insertion of sterile speculum. This took take place in a side room at the clinic. The participants had her details taken to facilitate follow-up on fetal outcomes at delivery and even maternal outcome. This was done sequentially until the desired sample size was attained.

For the purpose of this study the cut off gestation was thirty –two weeks and above.

**Diagnostic scale/criteria**

The diagnosis of PROM was by clinical criteria. Any mother presenting with complaint of draining of liquor underwent a sterile speculum examination that entailed having the mother in a semilithotomy position and with adequate light source a sterile speculum was inserted to look for drainage from the cervical os or pooling in the vaginal fornix.

Subsequently an endocervical swab was taken and this was subjected to gram staining, culture and sensitivity. Further management followed the usual hospital protocol as described above.

**Data collection**

Data collection was conducted by trained midwives and the principal investigator by use of a questionnaire.

**Speculum examination.**

- Having already explained to the patient the nature of the study and being in the examination room, the patient was put in a semi-lithotomy position. Vulval toilet was done by use of chlorhexidine.
- A sterile speculum was then inserted to visualize the cervix. The speculum was lubricated with normal saline.
- On visualizing the cervix, it was checked for any active drainage of liquor or pooling sign. When none was seen the Valsalva maneuver was attempted.
- Then carefully without touching any surface of the speculum or genital region a sterile swab was introduced into the cervical canal and the patient asked to cough. This caused a slight spurt of fluid that stained the swab. This was subsequently taken to the lab for processing.
- The same procedure was undertaken for the control groups at the antenatal clinic.

For the patients who were unwilling to participate in the study, the management followed the current practice in the hospital.

**Processing of specimen in the lab.**

**Inoculation method.**

This was done on one half of the plate per specimen. Streaking of the innoculum on the surface of the medium so as to obtain discreet colonies with heat sterilizing of the wire loop in between.

**Incubation temperature, atmosphere and duration of incubation.**

Inoculate Mac. SBA. CBA and Sab. Mac. SBA. and Sab are incubated in air at 35-37°C overnight.

If there was no growth on Sab after 18-24hours. reincubated for a further 24 hours. This was because yeasts sometimes require 48 hours to grow.

CBA incubated in CO2 candle jar at 35-37 oC overnight.

Made a smear; performed gram stain and findings reported.

**Gram staining technique.**

- Fixation of the slide using methanol.
- Covered the fixed smear with crystal violet stain or (gentian violet) for 30-60 seconds.
- Rapidly washed off the stain with clean water.
- Tipped off all the water. and covered the smear with lugols iodine for 30-60 seconds.
- Washed off the iodine with clean water.
- Decolorized rapidly (few seconds) with acetone alcohol. Washed immediately with clean water.
- Covered the smear with neutral red stain for 2minutes.
- Washed off the stain with clean water.
- Wiped the back of the slide clean. and placed it in a draining rack for the smear to air dry.
- Examination the smear microscopically, first with the 40x objective to check the staining and to see the distribution of material and then the oil immersion objective used to report the bacteria and cells.

**Sensitivity testing.**

Kenyatta National Hospital has developed its antibiotic discs from suppliers depending on the anticipated micro-organisms. They are labeled KNH-1 to KNH-6. As KNH-1 is used in urine culture it was not appropriate in our study.

The following discs were used:

- KNH-2: gram negative rods: Augmentin. Cefuroxime. Gentamicin. Ciprofloxacin. Ceftriaxone. Minocycline. Piperacillin. Ceftazidime.
- KNH-3: staphylococcus and streptococcus: Augmemtin. Amoxicillin. Oxacicillin. Erythromycin. Genatamicin. Ciprofloxacin. Minocycline. Cefuroxime.
- KNH-4: pseudomonas: Piperacillin. Tazobactam. Gentamicin. Amikacin. Ceftazidime. Ceftriaxone. Tircacillin. Clavulanic acid.
- KNH-5: enterococcos species: Vancomycin. Amoxicillin. Augmentin. Ciprofloxacin. High Genatamicin. Nitrofurantoin. Nalidixic acid.
- KNH-6: other streptococci: Amoxicillin. Cefuroxime. Augmentin. Erythromycin. Chloramphenicol. Ceftriaxone. Tetracycline. Ciprofloxacin.

Organisms are defined as susceptible if a normal dose of an antibiotic is likely to result in cure. Moderately resistant cure is likely with larger dose and resistant if antibiotic therapy is likely to fail.

Paper discs impregnated with antibiotic are placed on agar inoculated with the test organism. The antibiotic diffuses into the surrounding agar and inhibits bacterial growth. The extent of this inhibition reflects the susceptibility of the organism.

**Ethical consideration/clearance**

The study seeked permission and approval from the Kenyatta national hospital ethics committee which is the institutional review board at the university on health research matters. The proposal of the study was submitted to them before commencement of the study.

**Study limitations.**

- Loss of participants during follow-up. This is especially among the control group. Unpublished data indicate not all clinic attendants have their delivery in the hospital.
- Limited resources. As the study was funded from the principal investigators personal resources, it caused some financial pressure.
- Laboratory culture may have shortcomings e.g capture of organisms.

**To overcome above limitations the following measures were undertaken:**

- It was emphasized a lot to the control participants the significance of the study and the abounding benefits of hospital delivery. They were also encouraged to come for delivery at KNH.
- Help was requested for from family, friends and colleagues to ensure the study is successful in spite of limited resources.

RESULTS.

**Table 1: Socio-demographic characteristics (N=100)**

| Characteristic | PROM) (%) | Control (non PROM) (%) | p-value |
|---|---|---|---|
| **Age (years)** | | | |
| ≤20 | 6(12.0) | 1(2.0) | |
| 21-25 | 20(40.0) | 13(26.0) | |
| 26-30 | 20(40.0) | 33(33.0) | 0.907 |
| 31-35 | 6 (12.0) | 10(20.0) | |
| 35+ | 5(10.0) | 6 (12.0) | |
| **Education** | | | |
| Primary | 11(22.0) | 9(18.0) | |
| Secondary | 26(52.0) | 21(42.0) | 0.900 |
| College | 12(24.0) | 20(40.0) | |
| None | 1 (2.0) | 0 | |
| **Marital status** | | | |
| single | 9 (18.0) | 4(8.0) | 0.834 |
| married | 41(82.0) | 46(92.0) | |
| **Employment** | | | |
| employed | 14(28.0) | 27(54.0) | 0.886 |
| unemployed | 36(72.0) | 23(46.0) | |
| **Nature of employment** | | | |
| manual work | 38(76.0) | 39(78.0) | 0.867 |
| office work | 12(24.0) | 11(22.0) | |

Mean age of the study participants was 27.9 years, median 28.0 with a range of between 18 and 41 years.

There was no statistical significance in the sociodemographic characteristics between the prom and control groups.

**Table 2:Past obstetric history (n=100)**

| | Prom, n (%) | Control n (%) | p-value | Odds ratio | 9 5%(CI) |
|---|---|---|---|---|---|
| **History of PROM** | | | | | |
| yes | 11(22.0) | 5(10.0) | 0.84 | 1.00 | 0.44-2.27 |
| no | 39(78.0) | 45(90.0) | 7 | | |
| **If yes, gestation (n=16)** | | | | | |
| term (≥37weeks | 8(72.7) | 5(100.0) | 0.18 | 2.35 | 0.72-8.55 |
| before term (<37 weeks) | 3(27.3) | 0 | 7 | | |
| **Parity** | | | | | |
| primipara | 22(44.0) | 19(38.0) | | | |
| 1 | 16(32.0) | 20(40.0) | 0.99 | 0.98 | 0.59-1.61 |
| 2 | 7(14.0) | 2(4.0) | 9 | | |
| 3 | 3 (6.0) | 6(12.0) | | | |
| >3 | 1(2.0) | 3(6.0) | | | |

Among the PROM group.11(22%) had a history of PROM in prior pregnancy and in the majority it occured at term. In the control group 5(10%) had a prior history of PROM and in all of them it occured at term.

Majority of the participants were of low parity with 38(76%) of PROM group being para 1 or less while 39(78%) of the control group were para 1 and below.

There is no statistical difference in the PROM and control groups with regard to history of prom and past obstetric history.

**Table 3: current obstetric history (n=100)**

| Current history | prom | control | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| **Gestation (weeks)** | | | | | |
| 32-34 | 13(26.0) | 0 | | | |
| 35-36 | 9(18.0) | 7(14.0) | 0.764 | 0.92 | 0.46-1.64 |
| ≥37 | 28(56.0) | 46(86.0) | | | |
| **ANC Profile** | | | | | |
| Yes | 45(90.0) | 50(100.0) | 0.746 | 1.00 | 0.24-4.15 |
| No | 5(10.0) | 0 | | | |

Majority of PROM occurred at term 28(56%). While 5(10%) of the PROM group had no antenatal profile there was no statistical difference between the two groups

**Table 4: Characteristics of PROM**

| Factors | Frequency | Percentage |
|---|---|---|
| Duration of rupture | | |
| Hours (<24) | 44 | 88.0 |
| Days (>24hrs) | 6 | 12.0 |
| **Diagnosis** | | |
| Speculum exam | 40 | 80 |
| Pooling/valsalva | 10 | 20 |
| **Antibiotics** | | |
| Yes | 33 | 66 |
| No | 17 | 34 |
| If yes type of antibiotic | | |
| Xpen | 10 | 20.0 |
| Gentamycin | 9 | 18.0 |
| Flagyl | 16 | 32.0 |
| Erythromycin | 10 | 20.0 |
| Augmentin | 11 | 22.0 |
| Other | 2 | 4.0 |

Majority of the participants 44(88%) had rupture of membranes less than 24hours prior to admission in hospital while 12% had drained for more than 24 hours..

60% of the PROM group had been given some antibiotic in the labour ward.

**Table 5:Investigations done**

| investigations | prom | control | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| **Ultrasound** | | | | | |
| Done | 11(22) | 23(46) | 0.881 | 1.00 | 0.53-1.87 |
| Not done | 39(78) | 27(54) | | | |
| **ANC profile** | | | | | |
| Yes | 45(90) | 50(100) | 0.746 | 1.00 | 0.24-4.15 |
| No | 5(10) | 0 | | | |

There was no statistical difference among the two groups with regard to investigations done.

Table 6: Fetal outcome

| Outcome | prom | control | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| **Apgar score at 5'** | | | | | |
| <7 | 5(10.0) | 0 | 0.746 | 1.00 | 0.24-4.15 |
| >7 | 45(90.0) | 50(100.0) | | | |
| **Birth weight(g)** | | | | | |
| <1500 | 3(6.0) | 0 | | | |
| 1501-2499 | 10(20.0) | 0 | 0.851 | 1.00 | 0.45-2.22 |
| 2500-3999 | 36(72.0) | 48(96.0) | | | |
| ≥4000 | 1(2.0) | 2(4.0) | | | |
| **Fetal admission to NBU** | | | | | |
| Yes | 10(20.0) | 3(6.0) | 0.834 | 1.00 | 0.41-2.46 |
| No | 40(80.0) | 47(94.0) | | | |

While the PROM group had some babies with an Apgar score of less than 7 at 5 minutes none of the babies from the control group had this.

Majority of the babies had birth weight more than 2500g that is 37(74%) and 50(100%) among the PROM and control group respectively.

More babies were admitted to the NBU from the PROM group compared to the control group.

Among the neonates, 6% were macrosomic.

There was no statistical significant difference between the two groups with regard to fetal outcome.

**Table 7: Maternal outcomes (n=100)**

| Outcome | PROM | control | P=value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| **Mode of delivery** | | | | | |
| SVD | 35(70.0) | 24(48.0) | 0.886 | 1.00 | 0.56-1.83 |
| C/S | 15(30.0) | 26(52.0) | | | |
| **Complications at delivery** | 0 | 0 | 0 | Undefined | Undefined |
| **Complications in pueperium** | 0 | 0 | 0 | Undefined | Undefined |
| **Duration of hospital stay** | | | | | |
| 1 | 19(38.0) | 21(42.0) | | | |
| 2-4 | 15(30.0) | 28(56.0) | 0.899 | 1.00 | 0.59-1.69 |
| ≥5 | 16(32.0) | 1(2.0) | | | |

The mean duration of hospital stay for PROM was 3.2 days while that of controls was 2.6days.

Most of the PROM group delivered SVD 35(70%) with 15(30%) undergoing caesarean section. On the other hand among the control group 24(48%) had SVD with 26(52%) undergoing CS.

Other parameters of maternal outcome included complications at delivery (retained placenta, post partum haemorrhage) plus complications in pueperium (fever, foul smell of lochia.) However, none of these were recorded in any participant.

There was no statistically significant difference between the two groups.

**Table 8: Gram stain results (n=100)**

| Results | prom | control | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| **Gram positive** | | | | | |
| Yes | 27(54.0) | 46(92.0) | 0.874 | 1.00 | 0.51-1.96 |
| No | 23(46.0) | 4(8.0) | | | |
| **Gram negative** | | | | | |
| Yes | 7(14.0) | 5(10.0) | 0.828 | 1.00 | 0.39-2.54 |
| No | 43(86.0) | 45(90.0) | | | |

Among the study participants, of the PROM group 27(54%) tested positive on gram stain while 46(72%) from the control group did.

On the other hand 7(14%) were gram negative compared to 5(10%) of the controls.

There was no statistically significant difference between the two groups.

**Table 9: Culture results (n=100)**

| Results | prom | control | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| Positive | 9 (18.0) | 2(4.0) | | | |
| Negative | 41(82.0) | 48(96.0) | 0.822 | 1.00 | 0.38-2.64 |

When the swabs were cultured, 9(18%) of the PROM group had some growth while 2(4%) of the controls recorded some growth.

There was no statistically significant difference in the culture results between the two groups.

**Table 10: Culture isolates (n=11)**

| Organism | PROM (%) N=9 | Control % N=2 | p-value |
|---|---|---|---|
| Enterococcus | 0(0) | 2(100.0) | 0.018 |
| Streptococcus viridans | 1(11.1) | 0(0) | 0.818 |
| Staphylococcus sp. | 1(11.1) | 0(0) | 0.818 |
| Staphylococcus Aureus | 1(11.1) | 0(0) | 0.818 |
| Escherichia coli | 6(66.7) | 0(0) | 0.181 |

From the culture results it is noted that 6(66.7%) were Escherichia coli and 11(22%) 0f study participants had positive culture. Of the pathogenic organisms isolated 6(66.7%) were Escherichia coli. For the control group enterococcus was isolated.

**Table 11: Antibiotic sensitivity pattern**

| | | Bacteria identified | | | | |
|---|---|---|---|---|---|---|
| | | Entero | e. coli | Strep | Staph | Staph aureus |
| Antibiotic | sensitivity | N=2 | N=6 | N=1 | N=1 | N=1 |
| Augmentin | resistant | 0 | 33.3 | 100 | 0 | 0 |
| | sensitive | 100 | 67.7 | 0 | 100 | 100 |
| Amoxicillin | resistant | 0 | 0 | 100 | 0 | 0 |
| | sensitive | 100 | 0 | 0 | 100 | 100 |
| Gentamycin | resistant | 0 | 16.7 | 0 | 0 | 0 |
| | sensitive | 100 | 83.3 | 100 | 100 | 100 |
| Nitrofurantoin | resistant | 0 | 0 | 0 | 0 | 0 |
| | sensitive | 100 | 0 | 0 | 0 | 0 |
| Vancomycin | resistant | 0 | 0 | 0 | 0 | 0 |
| | sensitive | 100 | 0 | 0 | 0 | 0 |
| ciprofloxacin | resistant | 0 | 0 | 0 | 0 | 0 |
| | Sensitive | 0 | 100 | 100 | 100 | 100 |
| erythromycin | resistant | 0 | 0 | 0 | 0 | 0 |
| | sensitive | 0 | 0 | 0 | 100 | 100 |
| Cefuroxime | resistant | 0 | 16.7 | 0 | 0 | 0 |
| | sensitive | 0 | 83.7 | 100 | 100 | 100 |
| Minocycline | resistant | 0 | 50 | 0 | 0 | 0 |
| | sensitive | 0 | 50 | 0 | 0 | 100 |
| Ceftazidime | resistant | 0 | 0 | 0 | 0 | 0 |
| | sensitive | 0 | 100 | 0 | 0 | 0 |
| Ceftriaxone | resistant | 0 | 0 | 0 | 0 | 0 |
| | sensitive | 0 | 100 | 0 | 0 | 0 |

Entero = Enterococcus E. coli= Escherichia coli step=Streptococcus viridans

Staph= Staphylococcus species Staph. aureus= staphylococcus aureus

As can be seen from the results above there is resistance to commonly used antibiotics. For instance augmentin has 100% sensitivity against enterococcus and staphylococcus while it has only 66.7% activity against E. coli.

While ciprofloxacin has 100% sensitivity to Escherichia coli its use in pregnancy is contraindicated.

Cefuroxime has 88.3% sensitivity while Ceftriaxone has 100% sensitivity to Escherichia coli. Also Cefuroxime has 100% sensitivity to both staphylococcus species and staphylococcus aureus.

Thus cephalosporins, specifically Ceftriaxone and Cefuroxime would be recommended for use in PROM.

## DISCUSSION.

In this study, one hundred participants were recruited, with fifty in the PROM group and similar number in the control group. The mean age of the participants was 27.9 years, median 28.0 with a range of between 18 and 41 years. There was no statistical significance in the sociodemographic characteristics between the two groups.majority of our participants had formal education. Studies have linked low socioeconomic status with higher incidence of bacterial vaginosis **(16, 17,18)** that predisposes to PROM. However this was not seen in our study.

Prelabour rupture of membranes (PROM) is the occurrence of drainage of liquor before the onset of contractions. It can occur before maturity (<37 weeks) referred to as preterm Prelabour rupture of membranes (PPROM).

Our main objective in this study was to find the microbial pattern of women presenting with PROM. Infection has been associated with its development. Urinary tract infection and bacterial vaginosis implicated.**(23)**

From a study at KNH in 1980 that involved culture of fetal membranes, Wanjala was able to isolate *Escherichia coli, staphylococcus species*, and *proteus* species. The r ate of isolation of pathogenic organism he found to be 28.57%.**(24)** another study at KNH on organisms in women who had Mac Donald stitch insertion and endocervical swabbing and culture done in the three trimesters isolated a mixed flora. Isolated organisms included *peptostreptococcus*, *peptpcoccus*, *fusobacterium* and *bacteroids.* **(25).** The findings in our study are consistent with this as our isolates were Escherichia coli, streptococcus viridans, staphylococcus species and staphylococcus aureus. Our isolation rate was 18% in the PROM group and 4% in the control group. Okiri in a study on post partum infection in women using single dose versus multiple dose antibiotic prophylaxis during elective caesarean section isolated the following organisms *E.coli, klebsiella, proteus, pseudomonas* and *staphylococcus.* **(29)**

Various studies looked at role of antibiotics in the presence of PROM. The largest being the oracle study that compared use of Co-amoxiclav and Erythromycin. The former was associated with high incidence of necrotising enterocolitis. Thus it recommended the use of erythromycin. **(27)** When the isolates were subjected to antibiotic sensitivity, we found that the commonly used augmentin in Kenya had a sensitivity of 66.7% to *E.coli.* resistance was 33.3%. Okiri found a 100% resistance to augmentin. **(29).** Gentamycin had sensitivity of 83.3% while Cefuroxime also had 83.3% sensitivity. Ceftriaxone had 100% sensitivity to *E. coli.*

In regard to maternal and fetal outcomes, the Cochrane reviews looked at various studies with varied interventions **(30, 31).** In the Cochrane reviews, fetal outcomes looked at Apgar score<7 at 5minutes, admission to newborn unit and also length of NBU stay. From the cochrane review **(31)**, apgar score <7 at 5 minutes RR 0.98 (95%CI 0.28, 3.34).These are similar to the parameters in our study, where among the PROM group, 5(10%) had Apgar score<7 at 5minutes while the control group had Apgar score >7 at 5minutes in 100% of the group.In our study with regard to apgar score OR 1.00 (95%CI 0.24, 4.15). This is similar to the cochrane results.As for NBU admission 10% of babies in the prom group were admitted while 6% of controls were. The main indication for NBU admission was respiratory distress syndrome. As for birth weight, 36(72%) of the prom and 48(96%) of the control group had birth weight above 2500g. There was no statistically significant difference between the two groups in terms of Apgar score at 5minutes, birth weight and admission to NBU with p values of 0.746, 0.851 and 0.834 respectively.

As for maternal outcomes, mode of delivery and complications during and after delivery were considered here. In the cochrane review **(31)** various aspects of maternal outcome considered including suspected chorioamnionitis, operative delivery, caesarean section,internal fetal monitoring,epidural analgesia, post partum haemorrhage, length of hospital stay and some more. Use of antibiotics statistically significant resulted in statistically significant reduction in endometritis also reduction in maternal and neonatal stay in hospital. In the prom group 35(70%) delivered SVD while in the control group

26(52%) were delivered by caesarean section. There were no recorded complications at and after delivery. The duration of hospital stay was also considered with prom group staying mean 3.2 days while controls stayed 2.6 days.There was no statistically significant difference in the mode of delivery between the PROM and control groups. Though in absolute numbers the PROM group stayed longer in hospital. The mode of delivery p value 0.886. An explanation for the findings of no complications especially after delivery in our study could be the finding that 88% of the prom participants presented to hospital with hours of membrane rupture that is less than twenty-four hours and were also put on antibiotics.

## CONCLUSIONS.

1. There was no difference in the sociodemographic features of the two groups. The mean age was 27.9years. Majority were also of low parity.there was no association with PROM.
2. There was no statistically significant difference in fetal outcome between the PROM and control groups.
3. *Escherichia coli* was the most commonly isolated organism in PROM.
4. Ceftriaxone and Cefuroxime were found to be the most sensitive to organisms isolated in our study.
5. There was no difference in maternal outcomes between the PROM and control groups.

## RECOMMENDATIONS

1. We recommend the use of Cefuroxime and Ceftriaxone in PROM.
2. Regular institution assessment of antimicrobial resistance pattern to advice on choice of antibiotics to use.
3. Future studies can be done to look further at fetal outcomes with regard to duration of NBU stay, any complications there and even neonatal mortality.

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**Questionnaire.**

1. Identification code----------

**Demographic characteristics.**

2. age ----------

3. educational background

a) primary

b) Secondary

c) College

d) None

4. Employment history

a) Employed

b) Unemployed

5. Nature of employment

a) Manual work

b) Office work

6. Marital status

a) Single

b) Married

c) Divorced

d) Widowed

**Past obstetric history**

7. history of prom in prior pregnancy

- yes
- no

8. if yes in 7 above at what gestation did prom occur?

9. Parity ----------

10. Any complications at last delivery----------

. **Current obstetric history**

11. Gestation in weeks----------

12. Antenatal clinic attendance a) yes
b) No

13. Antenatal profile a) HIV test and result
b) Hemoglobin level
c) VDRL
d) Urinalysis

14. Duration of membrane rupture prior to admission a)hours
b)days

15 Duration from rupture of membranes to delivery ----------

16. Diagnosis of prom
a) Speculum examination
b) pooling/valsalva

17) cervical length (in centimeters)

18) Any evidence of chorioamnionitis: a) fever
b) Tachycardia
c) Others specify.

19. Investigations done
a) Ultrasound
b) Cervical swab .

20.) Antibiotics given: specify

21.) Steroid given: yes or no.

**Fetal outcomes**

22.) Mode of delivery----------

23.) APGAR score at five minutes----------

24.) Birth weight ----------

25.) Fetal admission to new born unit ----------

26.) Indication for 25 above ----------

27.) Duration of NBU stay----------

**Maternal outcomes.**

28.) Mode of delivery

29.) Complications at delivery

a) retained placenta

b) postpartum haemorrhage

c) Others

30.) Complications in pueperium.

a) fever

b) foul smell of lochia

c) Others

31.) Duration of hospital stay after delivery

**Microbial pattern of patients presenting with PROM at labour ward KNH**
**Laboratory request form.**

Serial number IP NO

1. Age (years)

2. Gestation (weeks)

3. Parity

4. Gross appearance of liquor

5. Other details (any odour, smell)

6. Report

6.1 Gram stain of swab

- gram positive
- gram negative

6.2 Culture results (any growth obtained)

- yes
- no

6.3 Identities of organisms grown (cultured)

6.4 Antibiotic and antibiotic sensitivity patterns

- sensitive
- Resistant

**Consent**

**Introduction.**

My name is **DR. KENNEDY ODOYO ONYANGO** a postgraduate student undertaking the study on "microbial patterns of patients presenting with PROM at KNH labour ward." as part fulfillment for the award of the degree of Master of Medicine in Obstetrics and Gynecology by the university of Nairobi. My contacts are **mobile no: 0723881932.**

My supervisors are led by **DR. WANYOIKE GICHUHI**, of the department of Obstetrics and Gynaecology, university of Nairobi..

The second supervisor is **DR. JOHN ONGECH**, of the department of obstetrics and Gynaecology, **Kenyatta national hospital**...

As the study has been approved by the KNH ethics and research committee, any questions or issues regarding the study could also be addressed to:

The chairperson, KNH-ERC

P.O. BOX 20723,

NAIROBI.

Tel: 2726300-9.

The ERC chairperson is **Prof. K.M.Bhatt.**

This study involves mainly pregnant mothers who have the birth water bursting before the onset of labour. As infection has been attributed to be one of the main causes of this occurrence that leads to delivery of babies before their time and its attendant complications. Studies done elsewhere have shown that use of antibiotics does improve the maternal outcomes. Therefore this study is undertaken to help decide the antibiotics that can be used in our setup.

It will involve filling of a questionnaire and an examination for obtaining material to be grown in the lab. This shall entail the use of a special tool called speculum to help expose

the entrance into the womb where the material shall be taken from. The procedure should not be painful but can cause mild discomfort. At other times the process can induce early labour.

As part of standard practice at the hospital mothers are put on some antibiotic treatment when they have drainage of liquor. If the results from the laboratory suggest the need to change the antibiotics being used thus shall be done accordingly.

Incase of further or any questions the principal investigator or any of above individuals can be contacted.

It is also important that the results of this study may be published in scientific journals and also presented at scientific symposiums. Also the specimen taken shall not be used for any other test other than the culture and gram stain. No specimen shall be transported out of the country.

I ---------- do hereby accept to participate in the study having been explained to me the purpose and procedures involved I have not been given financial inducement or any other promise in order to participate in the study.

Signature ----------

Witness ----------

Date----------

Mimi **Dkt. KENNEDY ODOYO ONYANGO** ni mwanafunzi wa utaaluma ya wakina mama. Ninafanya utafiti kuhusu kuwekom kwa infection wakati maji yanapomwagika kabla ya uchungu wa kuzaa kutokezea. Utafiti sehemu zingine za ulimwengu umeonyesha matumizi ya madawa hufanya watoto wanbapozaliwa hawana uvamizi wa viini kwa wingi. Utafiti huu utaonyesha ile aina ya madawa yanayofaa kutumiwa hapa kwetu.

Kwa maswali yoyote nambari langu la simu ni **0723881932.**

Wasimamizi wangu waongozwa na **Dkt. WANYOIKE GICHUHI** wa chuo kikuu cha nairobi

Wapili ni **Dkt. JOHN ONGECH** wa hospitali kuu ya kenyatta Pia kuna kamati kuu inayosimamia utafiti na maswala ya kisayansi katika hospitali kuu ya kenyatta mwenyekiti wake akiwa **Prof. K.M. Bhatt.**

Hawa wote wanaweza kujulishwa ikiwa kuna swali lolote kuhusu utafiti huu.

Mimi ---------- naapa kwamba baada ya kuelezwa utafiti unaofanywa nimekubali kushiriki. Sijapewa fedha au ahadi yoyote.

Sahihi----------

Mshuhudia----------

Tarehe----------

**Budget**

Stationery---------- 15,000.

Antibiotic discs---------- -20,000.

Swabs ---------- 5000.

Assistant allowances ---------- 20,000.

Culture/sensitivity laboratory costs ---------- 40,000.

Contingency---------- 10,000.

**TOTAL----------110,000**

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Ref: KNH-ERC/ A/07

22nd July 2008

Dr. K. O. Onyango
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr Onyango

RESEARCH PROPOSAL: "CURRENT MICROBIAL PATTERN OF PATIENTS PRESENTING WITH PRELABOUR RUPTURE OF MEMBRANES (PROM) AT LABOUR WARD IN KENYATTA NATIONAL HOSPITAL" (P58/03/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your revised research proposal for the period 22nd July 2008 – 21st July 2009.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Obs/Gynae, UON
Supervisors: Dr. Wanyoike Gichuhi, Dept. of Obs/Gynae, UON
Dr. J. Ongech, Dept. of Obs/Gynae, UON