

Preterm Labour, Pprom, Prom And Neonatal Outcomes Associated With Vaginal Infection: A Prospective Study

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Abstract

Purpose

1. To find the incidence of preterm labor, preterm premature rupture of membranes (PPROM) and premature rupture of membranes (PROM) in relation with vaginal infection.
2. Use of high vaginal swab to detect the organism in relation with vaginal infection.
3. Role of an appropriate antibiotic therapy for vaginal infection.

Materials and Methods: A total of 90 patients with gestational age above 28 weeks till term were included in the study. Women who presented with signs of PROM, PPRM and preterm labor were enrolled in study. The diagnosis of spontaneous rupture of the membranes was confirmed by inspection of the cervix for flow of amniotic fluid from the cervical canal, if leakage is not present than patient is asked to cough and leak is noticed. The amount, colour and smell of the fluid were assessed. Based on the findings of cervical dilatation and uterine contractions patients were categorized as preterm labor (uterine contractions 4/20"/10', cervical dilatation ≥ 3 cm in multi and >1.5 cm in primi, effacement 30%) or threatened preterm labor (uterine contractions 3-4/< 20 /10, absent of cervical dilatation). Swab from the posterior fornix of the vagina were taken and sent for Gram's staining and Culture and sensitivity. All the patients were monitored for sign of chorioamnionitis.

Results: Preterm delivery (Birth prior to 37 WOG) occurs in 7-11 %, Delivery occurs prior to 34 WOG, neonatal mortality found in 75% (1/3rd) and 50% (1/2) developed neurological impairment as a long term sequel. Approximately 25-30% of preterm delivery found to be due to PPRM, among them 25-40% were associated with intrauterine infection.

Conclusions: This study help us to find the microbiological correlation of preterm labour, PROM, PPRM in western part of Nepal, So that we can plan our treatment and prevent from neonatal mortality and other complications like neurological deficit.

Keywords: Vaginal infection, Preterm labour, PROM, PPRM, Antibiotic

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I. Introduction

Preterm delivery, by Definition according to WHO preterm birth contributes prior to delivery of a baby prior to completed 37 WOG by upper limit and 20 WOG in lower limits contributes incidence approximately 5-13 % worldwide^{1,2}, delivery occurs prior to 34 WOG accounts 75% (1/3rd) neonatal mortality and 50% (1/2) neurological impairment as a long term morbidity and high cost for its management³⁻⁵. Most of the preterm labor which is associated with preterm delivery contributes 25-30% with PPRM, among them 25-40% associated with intrauterine infection⁶. Preterm delivered babies contributes 75% of neonatal mortality associated with prematurity who delivered extreme premature consist high mortality and consumes more resource taken as a burden for even developed countries. Who survives after efforts remains high risk > 50% for neurological impairment. Preterm labor – sign of labor it means regular progressive contraction with cervical dilatation and effacement with vaginal show starts prior to 37 completed WOG as an upper limit and lower limit for that after completion of 20 WOG. Premature rupture of membranes (PROM) it's a spontaneous rupture of membranes after term pregnancy prior to the onset of regular uterine contractions, cervical dilatation and effacement and show. Preterm prelabor rupture of membranes (PPROM) is spontaneous rupture of membranes prior to 37 WOG and after completion of period of gestation after viability it means minimum 20 WOG, without sign of labor. More than 50% of women with PROM or PPRM go into spontaneous onset of labor within 24 hrs. Outcomes of preterm labor, PROM, PPRM is often associated with adverse maternal and neonatal outcomes due to infection which is directly proportion to delivery time and duration of rupture of membrane and also associated with period of gestation¹⁻⁶. Estimated that 10% of perinatal deaths are directly or indirectly associated with PROM worldwide. The causes of most preterm labor, PPRM, PROM is not known, but too many conditions

have been associated with an increased risk of preterm delivery. Among multiple cause, infection is one of them, among infection vaginal infection with a common vaginal syndrome in women of reproductive age, has been associated with high risks for prematurity and premature rupture of membranes⁷⁻¹². When histologically examination performed, main cause for rupture of membranes is associated with decrease or loss of tensile strength of the fetal membranes. The collagens are main structural component of the fetal membranes which helps the maintain tensile strength. Infection related PPRM, PROM and preterm labour are mainly associated with the production of prostaglandins and matrix-degrading enzymes which is produced by microbial endotoxins and pro-inflammatory cytokines (e.g. IL-8, IL1 β , TNF α), which are released after the binding of microorganisms to pattern-recognition receptors⁷.

Finally it lead to increase enzyme metalloproteinase, that's enzyme responsible for collagen degradation, which lead to decrease in the tensile strength of fetal membranes and ultimately leads to rupture of the fetal membranes. Prostaglandins especially PGE1, PGE2 acts as major role in initiating and stimulating uterine contractions, while degradation of the extracellular matrix in foetal membranes is implicated in PPRM. However, infection caused by ascending microorganisms may also associate with secondary to PPRM, which increases maternal and neonatal mortality and morbidity. Hypothesis is that several normal micflora that are commonly present in the vaginal flora, including group E. coli, B streptococci, Staphylococcus aureus and microorganisms that cause Bacterial Vaginosis, secrete proteases that degrade collagen and which ultimately decrease the tensile strength of fetal membranes leads to preterm labor, PPRM and PROM. Intrauterine infection has been demonstrated in >50% of cases. Recent data suggest that hematogenous route of microbes may invade the amniotic cavity from the bloodstream after dissemination from remote sites, e.g. from the gastrointestinal tract or urinary tract¹³⁻¹⁴. One of the greatest threats to infant with preterm labor, PPRM and PROM is respiratory distress syndrome (RDS), necrotizing enterocolitis and other prematurity related complication even sepsis. Prematurity contributes one of the single risk factor approximately 70% of perinatal mortality in India¹⁵. There is increased incidence of perinatal mortality associated with complication related with prematurity, congenital anomalies, death also may be associated with cord accidents, intracranial haemorrhage, trauma, necrotizing enterocolitis are more common in premature baby. In preterm baby there are immature blood brain barrier makes them more vulnerable to directly crossing bacteria and its toxin which leadsTo brain damage ultimately leads poor neurological development. Preventive measures can prevent the above risk factor, ultimately keeping this thing in mind the present study was undertaken to find out the role of vaginal infection in preterm labor, PPRM and PROM.

II. Material And Methods

This was a prospective study conducted at Nepalgunj Medical College Teaching Hospital, Kohalpur. Duration of the study was 1 year from May 2015 to May 2016. Written informed consent were obtained from enrolled women. Patients with gestational age above 28weeks till term were included in the study. Women who presented to the labor room and delivery unit with complaints suggesting of sign of PROM, PPRM and preterm labor were enrolled as cases in study.

Patients with maternal complications and already treated with antibiotics for PROM, PPRM and preterm labor were excluded from the study. Period of gestation up to 28 weeks has poor survivals in our hospital, so excluded from our study. Complete history, general physical and obstetrical examinations completed. Enrolled women were evaluated using a sterile speculum examination. The diagnosis of spontaneous rupture of the membranes was confirmed by inspection of the cervix for flow of amniotic fluid from the cervical canal if leakage absent than asking the patient to cough. The amount, colour and smell of the fluid were assessed. Based on the findings of cervical dilatation and uterine contractions patients were categorized as preterm labor (uterine contractions 4/20"/10', cervical dilatation ≥ 3 cm in multi and >1.5 cm in primi, effacement 30%) or threatened preterm labor (uterine contractions 3-4/< 20 /10, absent of cervical dilatation). Swab from the posterior fornix of the vagina was taken and sent for Gram's staining and culture sensitivity. All the patients were monitored for sign of chorioamnionitis. The neonatal out come in patients who delivered was noted.

Microbiological analysis- Vaginal swabs were obtained from cases and sent to the Microbiology lab. The Gram's staining was done followed by inoculation of material in petri dish as per standard protocols. After overnight incubation, plates were checked for growth. Identification of pathogen was done and the significant pathogen was then evaluated for antimicrobial susceptibility testing using commonly used antibiotics for aerobic microflora.

III. Results

Out of the 90 cases of high vaginal swab culture study, 60 cases were positive & 30 cases were sterile

Table 1 High vaginal swab showing number of growth

Positive	Negative
60(66.66%)	30(33.33%)

Among 90 cases, 60 (66.66) were culture positive and 30 (33.33%) samples were negative.

Table 2: Total number of cases diagnosed at time of admission.

Threatened preterm	17(18.88%)
Preterm labour	36(40%)
PROM	26(28.88%)
PPROM	11(12.22%)

Out of 90 patients enrolled in study at time of admission diagnose as 17(18.88%) was threatened preterm, 36(40%) preterm labour, 26(28.88%) PROM and 11(12.22%)PPROM.

Table 3: Threatened preterm conservatively managed

Conserved	Delivered
12(70.58%)	5(29.42%)

12(70.58%) Delivered 5(29.42%) Total 17 Out of 17 cases, 10cases of positive culture in threatened preterm labour, 12(70.58%) cases were conserved and 5(29.42%) had pre- term delivery. This suggests that if the infections are promptly treated preterm delivery can be avoided. Most of the patients studied were between 32– 37 weeks 50 cases (55.55%).

Table 4: incidence of cases enrolled in study according to gestational age.

Gestational age	No. (%)
28-32	15(16.66)
32-37	50(55.55)
37-40	21(23.33)
>40	4(4.44)

Above table shows maximum number 32-37 weeks 50(55.55%) followed by 37-40 weeks 21(23.33%) 28-32 weeks 15(16.66%) >40 weeks 4(4.44%).

Table 5: High vaginal swab culture positive in patient studied.

	Positive culture	Negative culture
Threatened preterm(17)	10(58.82%)	7(41.18%)
Preterm labour (36)	30(83.33%)	6(16.67%)
PROM(26)	12(46.15%)	14(53.85%)
PPROM(11)	8(72.72 %)	3(17.28%)

Cases presented Culture positive in threatened preterm 10(58.82%) out of 17, preterm labour 30(83.33%) out of 36, PROM 12(46.15%) out of 26 and 8(72.72 %) PPRM out of 11

E. coli found the largest group of positive culture study 16 (26.66%). The next organism isolated was Candida albicans 12(20%) followed by Klebsiella in 7 (11.66%), Staph. Aureus and staph epidermidis 6(10%) each, Enterobacter and pseudomonas 4 (6.66%) and proteus, acinetobacter, citrobacter,diphtheroids and pseudomonas 1(1.66) each of the cases. Shows in figure 1.

Figure 1: High vaginal swabs growth in patients studied. Vaginal swab growth Number No growth 30(50%) Growth 60(50%)

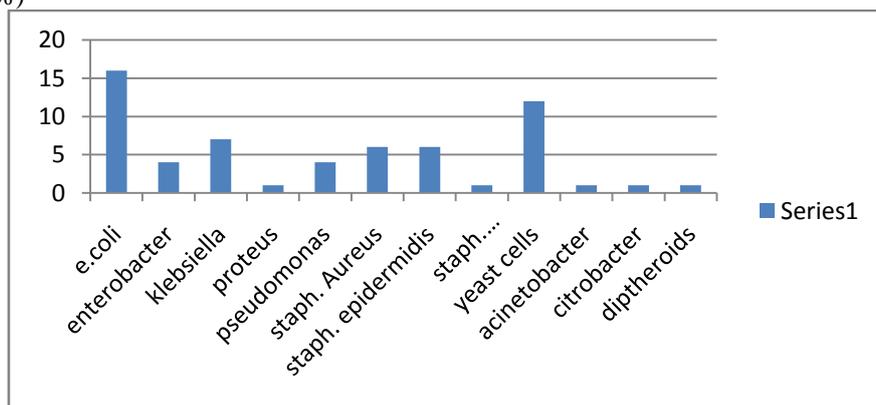
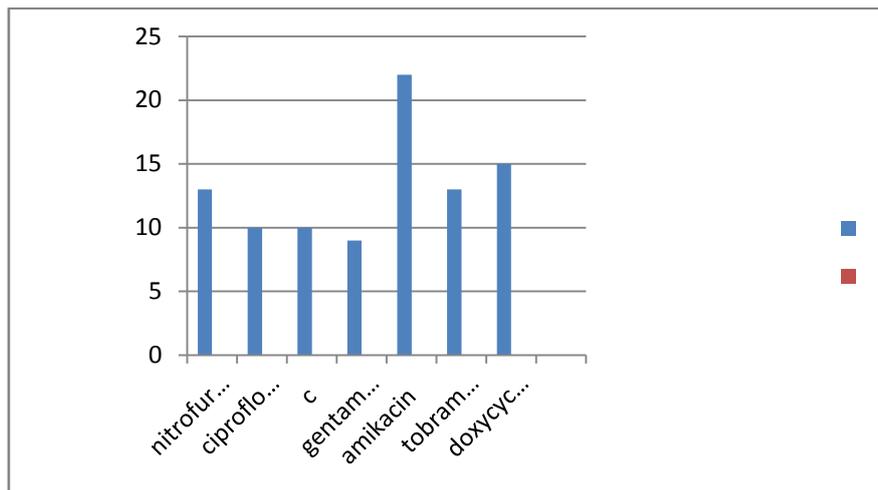


Figure II: Antibiotics sensitivity in high vaginal swab culture positive patients.



Antibiotics Sensitivity Amikacin 22 (36.66%) doxycycline 15 (25%) nitrofurantoin and tobramycin 13 (21.66%)

IV. Discussion

In this observational study, we performed lower genital tract culture by taking swab from upper part of vaginal canal, in pregnant women who admitted with diagnosis of PPRM, PROM, and threatened preterm and preterm labour. Studied the vaginal infection and their antibiotic sensitivity and maternal and neonatal outcome is the major concern of this study. Most common isolated bacteria were E.colli followed by candida. In resource limited settings like our set up, where microbiological evaluation of amniotic fluid is not possible, identification of bacteria in high vaginal swab can guide antibiotic therapy in women with preterm labour or PPRM, PROM. Previous studies have shown good correlation between genital tract flora and organism grown in amniotic fluid or blood of neonates with early onset sepsis. Study conducted by Naeye et al, McDonald et al and Das et al^{16, 17, 18} showed that infection was 2 -3 times more common in patients with rupture of membranes before 37 weeks of gestation compare to ruptures of membrane at term. In our study 8 (72.72%) cases out of 11 cases of PPRM, 12 (46.15%) cases out of 26 cases PROM, 10 cases (58.82%) out of 17 threatened preterm, and 30 (83.33%) cases out of 36 cases were culture positive. E-coli was the most commonest organism isolated in the study done by Sharma¹⁹ Das et al¹⁸ (44%), Raunt et al and Agarwal et al^{20, 21}. In our study also shows that most commonest bacteria was isolated E.coli contribute 16 (26.66%) positive culture sample. The next organism isolated was Candida albicans 12 (20%). In a study done by Lanier Jr et al, the incidence of chorioamnionitis after PROM is 20%²², in our study there was no case diagnosed as clinically chorioamnionitis. This probably was because all the patients in the study were given prophylactic antibiotics and were delivered before 24 hrs from the onset of PROM, PPRM. A study done Swati Pandey, where neonatal sepsis was seen in 25% of the cases.²³ In our study, incidence of neonatal sepsis was 5.12% (4 out of 78 delivered) and all mothers of these four neonates had grown microorganism in vaginal swabs suggesting vaginal infection. The incidence of neonatal sepsis was less as the neonate after birth received injectable antibiotics. Antibiotic therapy in PPRM has been associated with significant reduction in incidence of chorioamnionitis, birth within one week of starting antibiotics and improved neonatal outcomes. Dudley J et al²⁴, concluded from his study where difficulty in obtaining amniotic fluid samples and various reports indicating mixed bacterial growth in amniotic fluid cultures, broad spectrum antibiotics ampicillin and metronidazole are prescribed during expectant management of PPRM a good alternative. We also practising same antibiotic prior to culture report, drug was changed after culture report. According to ACOG guidelines recommended a 7 day course oral or parenteral of Ampicillin or Amoxicillin and Erythromycin in pregnant women with PPRM who are remote from term.²⁵

V. Conclusion

Preterm delivery and its outcome contribute one of the important problems in obstetrics. Vaginal infection being a one of common cause of preterm labor, PROM and PPRM, so, timely detection and treatment is important to avoid prematurity, associated neonatal morbidity and mortality. Our study provides data about microbiological correlation of threatened preterm, preterm labour, PROM, PPRM in our pregnant women. Most of pathological agents, isolated in our study, were sensitive to amikacin, doxycycline, nitrofurantoin and tobramycin.

VI. Recommendation

Large multicentral study required for further sensitivity and bacteriological examination for prevention of PPRM,PROM, Preterm labour

VII. Limitation of The Study

Most of patient took antibiotic prior to sending Culture and sensitivity excluded from study and culture costs.

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IX. Conflict of Interest

There is no conflict of interest.

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