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, PPROM 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 then 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 4/20ʺ/10ʹ, cervical dilatation ≥3cm in multi and >1.5cm 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% (1/3⁴) and 50% (1/2) developed neurological impairment as a long term sequel. Approximately 25-30% of preterm delivery found to be due to PPROM, among them 25-40% were associated with intrauterine infection.

Conclusions: This study help us to find the microbiological correlation of preterm labour, PROM, PPROM 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, PPROM, 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 ¹², delivery occurs prior to 34 WOG accounts 75%(1/3⁴) neonatal mortality and 50%(1/2) neurological impairment as a long term morbidity and high cost for its management¹³⁻⁴. Most of the preterm labor which is associated with preterm delivery contributes 25-30% with PPROM, among them 25-40% associated with intrauterine infection⁵. Preterm delivered babies contributes 75% of neonatal mortality associated with prematurity who delivered extreme prematurity 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 labor 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 PPROM go into spontaneous onset of labor within 24 hrs. Outcomes of preterm labor, PROM, PPROM 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 gestation¹⁴⁻⁶. Estimated that 10% of perinatal deaths are directly or indirectly associated with PROM worldwide. The causes of most preterm labor, PPROM, PROM is not known, but too many conditions

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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 membranes\(^7\). 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 PPROM, 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, IL1β, TNFα), which are released after the binding of
microorganisms to pattern-recognition receptors\(^8\).

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 PPROM.
However, infection caused by ascending microorganisms may also associate with secondary to PPROM, which
increases maternal and neonatal mortality and morbidity. Hypothesis is that several normal micrflora 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
take decrease the tensile strength of fetal membranes leads to preterm labor, PPROM 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 tract\(^1\). One of the greatest threats to infant with preterm labor, PPROM 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 India\(^2\). There is increased incidence of perinatal mortality associated with complication related with
prenaturity, 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, PPROM 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, PPROM and
preterm labor were enrolled as cases in study.

Patients with maternal complications and already treated with antibiotics for PROM, PPROM 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 ≥3cm in multi and >1.5cm 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
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.**

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threatened preterm</td>
<td>17</td>
<td>18.88%</td>
</tr>
<tr>
<td>Preterm labour</td>
<td>36</td>
<td>40%</td>
</tr>
<tr>
<td>PROM</td>
<td>26</td>
<td>28.88%</td>
</tr>
<tr>
<td>PPROM</td>
<td>11</td>
<td>12.22%</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Status</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conserved</td>
<td>12</td>
<td>70.58%</td>
</tr>
<tr>
<td>Delivered</td>
<td>5</td>
<td>29.42%</td>
</tr>
</tbody>
</table>

12(70.58%) Delivered 5(29.42%) Total 17 Out of 17 cases, 10 cases 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.**

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-32</td>
<td>15(16.66)</td>
</tr>
<tr>
<td>32-37</td>
<td>50(55.55)</td>
</tr>
<tr>
<td>37-40</td>
<td>21(23.35)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>4(4.44)</td>
</tr>
</tbody>
</table>

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.**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Positive culture</th>
<th>Negative culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threatened preterm (17)</td>
<td>10(58.82%)</td>
<td>7(41.18%)</td>
</tr>
<tr>
<td>Preterm labour (36)</td>
<td>30(83.33%)</td>
<td>6(16.67%)</td>
</tr>
<tr>
<td>PROM (26)</td>
<td>12(46.15%)</td>
<td>14(53.85%)</td>
</tr>
<tr>
<td>PPROM (11)</td>
<td>8(72.72%)</td>
<td>3(27.28%)</td>
</tr>
</tbody>
</table>

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%) PPROM 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, diptheroids 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%)
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 PPROM, 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.coli 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 PPROM, 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 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 PPROM, 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 Sharma (44%), Raunt et al and Agarwal et al. 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%, 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, PPROM. A study done Swati Pandey, where neonatal sepsis was seen in 25% of the cases. 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 PPROM has been associated with significant reduction in incidence of chorioamnionitis, birth within one week of starting antibiotics and improved neonatal outcomes. Dudley J et al, 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 PPROM 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 PPROM who are remote from term.

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 PPROM, 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, PPROM in our pregnant women. Most of pathological agents, isolated in our study, were sensitive to amikacin, doxycycline, nitrofurantin and tobramycin.

VI. Recommendation
Large multicentral study required for further sensitivity and bacteriological examination for prevention of PPROM, 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.

VIII. Acknowledgments
Thanks to our Prof. C.R. Das, Prof. M. Srivastav, dept. of microbiology and our patients who cooperate in our study. Without our department member and without help of dept. of microbiology cannot be completed this study. At last my family member who encourage to me and gives continuous support to complete the study.

IX. Conflict of Interest
There is no conflict of interest.

References