J. of Obst. & Gyn. of India Vol. 51, No. 2: March/April 2001 Pg 83-85

A One Year Case Control Study to Evaluate the Incidence of Infection as the Cause of Premature Rupture of Membranes

B. R. Desai, Shobhana S. Patted, Richa Sharma

Department of Obstetrics & Gynaecology, Jawaharlal Nehru Medical College, Nehrunagar, Belgaum – 590 010.

Summary:

The present prospective case control study was undertaken to evaluate the incidence of subclinical infection with P.R.O.M. and to see the maternal & perinatal outcome in P.R.O.M. with relation to infection. Both cases & controls were subjected to a battery of investigations & the hypothesis of infection as the cause of P.R.O.M. was proved. This was supported by obtaining statistically significant maternal CRP value which is a good predictor of sub clinical infection. Urinary tract is the likely focus of infection predisposing to PROM, but there is no significance of cervical swab, placental culture & sensitivity and placental histopathological examination in diagnosing infection. Neonates of PROM mothers required more NICU admission. A negative predictive value of CRP assures a healthy neonatal outcome. None of the patients in this study clinically developed post partum endometritis.

Introduction:

PROM is perhaps one of the most common accompaniment of premature delivery and its neonatal complications requiring admission to a neonatal intensive care unit. Various factors have been implicated in the causation of PROM, of which infection of the maternal genital tract plays a major role.

The pathogenesis of PROM remains uncertain. Infection has long been recognized as a complication of PROM for both the newborn and mother, due to ascent of organisms through cervicovaginal flora. Infection of the chorioamnion and lower uterine segment has been proposed as an important factor in the pathogenesis of PROM and / or preterm labour.

The present study was conducted at District hospital and K.L.E.S Hospital and MRC, Belgaum to evaluate the role of infection as an etiological factor in PROM. This is a prospective case control study conducted over a period of one year.

Material and Method

Women with PROM beyond 28 gestational weeks were considered eligible for study group and women without PROM but in labour beyond 28 weeks were included in control group. PROM was confirmed by noting the presence of liquor on per speculum examination. Patients not included in study were the ones with overt evidence of systemic infection, outside handled cases and those who came with malpresentations, twins or hydramnios.

30 study and 30 control cases were subjected to various investigational procedure which comprised of evaluating CRP (by slide agglutination method) of mother at admission, urine & cervical swab for c/s, cord blood for CRP estimation, placenta for c/s and

histopathological examination. Both the mothers and neonates were observed post delivery for evidence of infection. No special protocol was used for diagnosing infection in these cases. It was thought that the use of such a protocol might lead to over diagnosing clinically unimportant conditions. The main parameters analysed were maternal fever 24 hours after delivery, unhealthy lochia, subinvolution, and neonates requiring NICU admissions.

Results:

It was found that CRP is a good predictor for detecting subclinical infection in PROM. The p value for CRP positive cases was < 0.001 obtained by using X^2 test (Table I) which is statistically significant. Therefore in clinical practice it would seem that CRP could be used to predict infection especially for those patients who are preterm and not in labour, where thought is given for conservative line of management.

Table I
Comparison of maternal CRP values in both case and control groups

	Cases	Control
Positive for CRP	16	5
Negative for CRP	14	25
Using X2 test	p<0.001	

To find out the reservoir of infection, cultures were taken from various sites, the purpose was to see if patients with PROM grew more organisms and if ascending infection was responsible for PROM by isolating the same type of organisms from the cervix and placenta. Urine c/s showed a significant statistical correlation between PROM and UTI. (Table II) but cervical swabs and placental c/s results on the other hand were of no significance (Table III & IV). Here we have excluded the vaginal commensal positive cases as the criteria for diagnosing infection requires isolation of pathogenic organisms which were grown in excess on the culture media as compared to others. Anaerobic organisms were not cultured in the present study. Placental histopathological examination for evidence of inflammatory changes suggestive of an infective process yielded insignificant results (Table V).

Table II
Urine culture and sensitivity in case and control group.

	Cases	Control
Organisms grown	8	1
No organisms grown	22	29
Using Z test	p<0.02	

Table III
Comparison of cervical culture positive patients

	Cases	Controls
Positive for organisms	7	5
Negative for organisms	23	25
Applying Z test	p>0.05	

Table IV
Positive placental culture reports in cases and controls.

	Cases	Controls
Positive for organisms	10	11
Negative for organisms	20	19
By Z test	p > 0.05	

Table V
Results of histologically evident placental chorioamnionitis

	Cases	Controls
Positive for inflammatory changes	5	1
Negative for inflammatory changes	25	29
Using Z test	p > 0.05	

Baby's cord blood was subjected for CRP estimation but there is no statistical correlation between CRP mothers having a CRP positive baby (Table VI). A raised maternal CRP was not a reliable predictor of perinatal infectious morbidity and should not be used in isolation to predict neonatal outcome and a search should be made for other parameters that could be used in conjunction with CRP for detecting the risk of infection. Therefore CRP positive mothers can be put on a conservative line of management but with a higher vigilance due to the already lurking subclinical infection and such patients require antibiotic cover. Nevertheless negative predictive value of CRP is greater as none of the CRP negative mothers gave birth to CRP positive babies. A significant correlation was found between PROM and increased NICU admissions (Table VII). 9 preterm and 2 term babies were admitted. Out of these 2 neonatal deaths encountered were due to prematurity and inborn error of metabolism and not due to infection per se. On observing the post natal course of these women – none of them in the present study developed endometritis.

Table VI
CRP positive baby's in cases and control.

	Cases	Control
CRP positive	4	-
CRP Negative	26	30
X2	p > 0.05	

Table VII
Perinatal outcome

	Cases	Control
NICU admission	11	-
By χ^2 test	$p < 0.001$	

Discussion:

- The hypothesis that infection is the cause of PROM stands proved. This is supported by obtaining statistically significant maternal CRP values which is a good predictor of subclinical infection. Krohn et al (1990) got 79% sensitivity and 80% specificity in the predictive effectiveness of CRP as a marker of infection. In a study by Ismail et al (1985) CRP was found to be more sensitive in identifying clinical chorioamnionitis as compared to fever / WBC/ foetal tachycardia. According to. Ernest et al (1987) elevated CRP values before delivery predict infectious morbidity in only 8% - 29% of patients, and upto 18% patients with serious infections may be misdiagnosed as having normal CRP values before delivery.
- Urinary tract is the likely focus of infection predisposing to PROM. Malee (1992) holds the view that if urine culture comes as a positive for micro-organisms, patients should be treated adequately and that evaluation of a febrile patient with PROM must include a search for extrauterine source of infection and urinary tract infection is found with greatest frequency.
- In general the criteria for diagnosing infection requires isolation of pathogenic organisms and demonstration of an associated tissue reaction. Unfortunately from the results of the present study, we can say that these parameters have limited significance in clinical obstetrics, as neither the presence of bacteria in cervical swab or placental culture nor inflammation of placenta accurately predict maternal and neonatal outcome.
  Also no correlation was found on comparing the organisms grown in urine, cervical swab and placental culture. According to a prospective study of 97 patients with PROM conducted by Carroll et al (1996) they found that lower genital tract cultures were poor predictors of intrauterine infection. According to Seo, et al (1994) culture obtained between amnion and chorion demonstrated increased recovery of ureaplasma urealyticum as well as aerobic and anaerobic microorganisms associated with bacterial vaginosis after preterm delivery. Greater recovery of cervico-vaginal micro-organisms within foetal membrane than in the amniotic fluid suggests that cervico-vag organisms associated with preterm and PROM ascend through the cervix into the lower uterine segment, where thay can infect membrane and decidua without causing amniotic fluid infection. Examination of placenta is controversial in confirming the diagnosis of chorioamnionitis as 30 - 40% of term vaginal deliveries will have placentas with histopathology consistent with chorioamnionitis and no clinical evidence of infection. Furthermore placental pathology only confirms the diagnosis at best in retrospect, Garite et al (1982)
- Negative predictive value of CRP is more important if neonates are taken into account that is more of the CRP positive mothers had CRP positive babies, which means, that if mother is CRP negative, then one can be sure of a healthy neonatal outcome and such patients (if preterm) are ideal for conservative line of management.
- But PROM mothers do pose an increased risk to the outcome as observed by more neonatal admission to ICU and such mothers were CRP positive too.
  Three babies were admitted due to birth asphyxia, this can be explained on lines with Bada et al (1977) study who observed that birth asphyxia was the major cause which led to NICU admission probably because intrauterine foetal respiratory movements could be detrimentally affected by loss of amniotic fluid in PROM, resulting in delay or failure to take the first breath.
- None of the patients in our study clinically developed post-partum endometritis

References

1. Bada. S. Henrietta, Leticia C. Alojipan and Billy I Andrews. Paed. Clinics of North America. Vol. 24. No. 3, Pg. 491, Aug 1977.
2. Carroll – S.G, Papaioannou – S, Ntumazah – I : Philpott – Howard – J. Nicolaides – K.H.: Br. J. Obst. Gyn Vol 103 (1), Pg: 54, Jan 1996.
3. Ernest. J. M, Melissa Swain, R.N., Steven M. Block, Lewis H. Nelson, Christos G. Hatjis and Paul J. Meis. Am. J. Obst. Gyn. Vol: 156, Pg 449, 1987.
4. Garite J. Thomas and Roger K. Freeman Obstet Gynecol. Vol 59, Pg 539, 1982.
5. Ismail A. Mahmud, Michael J. Zinaman, Richard I. Lowensohn and A.H. Moawad. Am. J. Obst. Gyn. Vol 151, Pg 541, 1985.
6. Krohn, Pahnke – VG, Albrecht – K, Trams – G, / Geburtshilfe. Prenatol Vol 194 (5) Pg 208, 1990
7. Malee P. Maureen, OBG clinics of North America. Vol. 19. No. 2, 310. June 1992.
8. Seo Kyung, James A Mc. Gregor, Janice I French, Management of high risk Pregnancy – Queenan (Text). 3rd ed, 1994, Pg 476, Blackwell Scientific Publications, Boston.