

COMPARISON OF ACTIVE VS EXPECTANT MANAGEMENT OF PRELABOR PREMATURE RUPTURE OF MEMBRANES BETWEEN 34-37 WKS OF GESTATION MATERNAL AND FETAL OUTCOME

Qudsia Qazi¹, Farzana Nawaz², Fouzia Afridi³, Saima¹, Nazia²

ABSTRACT:

Objectives: To compare induction of labor, in prelabor preterm rupture of membranes between 34 and 37 weeks of gestation, with expectant management in terms of NICU admission, chorioamnionitis and mode of delivery.

Study Design: Randomized controlled trial

Place and Duration of Study: Department of obstetrics and gynaecology, Hayatabad medical complex Peshawar from January 2014-August 2014.

Methodology: A total of 384 gravid women at > 34 weeks 0 days and < 36 weeks 6 days of gestation with PPPOM were included in the study and divided into two groups of 192 each. Participants were randomly allocated by lottery method in a 1:1 ratio to induction of labor(IOL) or expectant management(EX).

Results: Outcome measures included mode of delivery, cesarean section rate, hyperbilirubinemia, NICU admission and chorioamnionitis. A total of 50(13%) patients underwent c/s. Out of these 33 were from actively managed group and 13 were from conservative group. Hyperbilirubinemia was seen in 58(30.3%) of active and 32(16.6%) of expectant group. Chorioamnionitis occurred more often in expectant group 8(4.1%) and maternal hospital stay was also prolonged in this group. No serious adverse events were reported.

Conclusion: Aggressive management of preterm premature rupture of membranes at > 34 weeks of gestation by induction of labor is safe and avoids maternal – neonatal infectious complications.

Key Words: Preterm premature rupture of membranes, induction, chorioamnionitis.

INTRODUCTION

Pre labor rupture of membranes (PROM) is the rupture of the fetal membranes with a latent period before the onset of spontaneous uterine activity prior to 37 weeks of gestation and leads to one third of preterm birth¹. The latent period, the time from membrane rupture until delivery, is inversely proportional to the gestational age at which PROM occurs. Intact fetal membranes with normal amniotic fluid are necessary for normal fetal growth and development. Membranes also serve as a barrier that separates the sterile fetal environment from the bacteria colonized in vagina. PPROM is an important clinical problem and a dilemma for the gynecologist.

The reported incidence of prelabor rupture of the membranes averages from 6% to 10% and about

20% of these cases occur before 37 weeks' gestation². PPROM complicates 1%–5% of all pregnancies and accounts for 30%–40% of all preterm deliveries³. One of the most common complications of preterm PROM is early delivery.

Multiple factors predispose certain patients to preterm PROM such as a) Black patients are at increased risk of preterm PROM compared with white patients, b) lower socioeconomic status, c) when intrauterine pressure overcomes membrane resistance as a result of weakening of membrane either congenital or acquired (smoking and vitamin C deficiency), or because of damaging factors, either mechanical (amniocentesis or amnioscopy) or Failure of mechanical support such as cervical dilatation, d) physical-chemical damage by Chorio decidua infection⁵ as Trichomonas, group B Streptococci, bacterial vaginosis, sexually transmitted infections, e) have had a previous preterm delivery, f) have vaginal bleeding, or g) have uterine distension (e.g., polyhydramnios, multifetal pregnancy)⁶.

The most favorable approach in dealing with preterm premature rupture of the membranes at 34 weeks 0 days to 36 weeks 6 days of gestation, however, remains the most conflicting area. Balancing the risk of ascending infection and cord prolapse against the hazards of prematurity is a complex process about

¹ Department of Gynae, LRH, Peshawar

² Department of Gynae, KTH, Peshawar

³ Department of Gynae, HMC, Peshawar

Address for correspondence:

Dr. Qudsia Qazi

Department of Gynae B Unit, LRH, Peshawar

Cell: 0336-0096618

Email: qudsiakamran@gmail.com

which there is little consensus². Even when the state of the cervix is unfavourable, the majority of women labour spontaneously within 24 hours. However, if the woman does not labour within 24 hours, labour may be delayed up to seven days after membrane rupture, with longer latent periods in nulliparous women⁸. Management involves waiting for labour to occur (Expectant) or induction of labour. Whether or not to induce labour may depend on the state of the cervix, with an insufficiently ripe cervix resulting in increased length of labour and if induction fails option is caesarean section. Induction of labor after rupture of the membranes, particularly in gravid women with an unfavorable cervix, may be associated with increased rates of cesarean delivery. Women with active management have shorter PROM to delivery interval as compared with the expectant group and mostly women prefer active management.

Women with PPROM who are managed expectantly beyond 34 wk of gestation are counseled about the increased risk of chorioamnionitis, longer hospitalization duration, instrumental vaginal delivery and cesarean section⁷. Expectant management of PROM has been associated with maternal infections such as chorioamnionitis (inflammations of the membranes) or endometritis (generally a postpartum infection).

Prematurity leads to a number of perinatal and neonatal complications, including a 1 to 2 percent risk of fetal death. When PROM occurs too early, surviving neonates may develop sequelae such as malpresentation, cord compression, oligohydramnios, necrotizing enterocolitis, neurologic impairment, intraventricular hemorrhage, and respiratory distress syndrome⁴.

Physicians caring for pregnant patients should be versed in the management of preterm PROM because rapid diagnosis and appropriate management can result in improved outcomes. Moreover IOL increases cost of medical care compared to spontaneous labor and such excess cost can be justified, if the indication for IOL alleviate a risk to mother or fetus.

The purpose of this study was to investigate differences in maternal and neonatal morbidity associated with active versus expectant management of premature rupture of membranes at 34 weeks 0 days to 36 weeks 6 days of gestation.

METHODOLOGY

A randomized controlled study was conducted with the objective of comparing the fetal and maternal morbidity and mode of delivery in conservative and actively managed PPROM at 34-37 weeks of pregnancy. All pregnant patients in Obstetrics and Gynecology C department for a period of 8 months, admitted with the complaint of gross vaginal fluid loss constituted the study group (consecutive) and then allocated into two groups.

EXCLUSION CRITERIA

1).Advanced labor 2).Patients with complications of labor 3).Patients not fit for conservative Mx. i.e. intra uterine fetal death or pre eclampsia, eclampsia, ante partum hemorrhage, maternal diabetes. 4).patients not fit for vaginal delivery. i.e. having cephalopelvic disproportion, previous two or more cesarean sections, malpresentation or placenta previa.

Informed consent was taken from all eligible and counseled participants. Rupture of membranes was diagnosed by attending staff based on history and clinical finding i.e. Amniorrhesis was confirmed by visualization of pooling fluid in the posterior vaginal fornix through the cervix during sterile speculum examination. Gestational age was confirmed by a reliable last menstrual period, early dating sonogram.

Patients allocated to IOL were induced according to the national guidelines and counseled that induction of labor might be associated with failure where emergency cesarean section would have to be performed. After vaginal examination labor was induced with prostaglandin. Maternal pulse, temperature and color of liquor maintained four hourly. Monitoring of uterine contractions and fetal heart rate auscultation with the help of CTG was done every half hour. Women randomized to EM were monitored according to local protocol until spontaneous delivery.

Monitoring was consisted of at least four hourly fetal heart rate, maternal pulse and temperature monitoring and twice weekly blood sampling for maternal leukocyte count and C-reactive protein measurement. They were advised rest and i/v antibiotic 24 hrs after onset of PPROM for seven days or earlier if they developed any maternal or fetal complication. The total leukocyte count (TLC) was performed on daily basis. Among expectantly managed patients those who developed chorioamnionitis were induced while those with fetal distress without labor underwent emergency cesarean sections. Clinical chorioamnionitis was defined, in the absence of other causes of hyperpyrexia, by a temperature of $>100.4^{\circ}\text{F}$ with either uterine tenderness (or contractions), leukocytosis, maternal or fetal tachycardia, or a foul-smelling vaginal discharge. Intrapartum maternal hyperpyrexia or clinical findings suggestive of neonatal infection resulted in admission to the neonatal intensive care unit for a sepsis evaluation. The diagnosis of neonatal sepsis was made only in neonates with positive blood cultures. However, all babies with suspected sepsis received empiric broad-spectrum antibiotic therapy until cultures returned and were negative (usually 3 days). Antibiotic therapy was continued for 7 to 10 days in those neonates with culture-proved sepsis. In patient where labor started spontaneously without any complications, delivered vaginally.

Postpartum neonatal and maternal outcome measures were recorded on a written proforma, including

maternal and neonatal length of stay in hospital. All randomized patients remained in their assigned group and were included in the statistical evaluation by using chi square test (SPSS version 19) at the completion of the study. SPSS version 19

RESULTS

During the 8 months study period 192 women were randomized to either active or expectant management. The demographic and clinical characteristics of each group are shown in Table 1 and 2. Of 192 patients managed conservatively 44.7% were primigravidae and 55.2% were multigravidae while in conservatively managed group 33.3% were primis and 66.6% were multigravidae. Majority (58.3%) of actively managed group belonged to 20-30 yrs of age and 66.1% of conservatively managed group were in age group of 30-40 yrs. Majority of pts belonged to lower and middle socioeconomic group. The total cost of stay in hospital and management was greater in induced group. More than 95% of the women in each group were admitted to the hospital within 24 hours of membrane rupture. A total of 3520 deliveries were recorded in the period of study and 384 pts presented with PPROM. Thus incidence of PROM was 10%. In conservative group patients delivered normally within 24 hrs were 69.7% and those of active group were 87.9%. The average PROM delivery interval was shorter in the induction group (Table 3) i.e. 11.9% of actively managed group delivered from 24-48 hrs as compared to 30.3 % of conservatively managed group with statistically significant difference between two groups i.e. p-value of 0.01. Regarding mode of delivery no statistically significant

difference was obtained for vaginal delivery among two groups i.e. 68.7% of actively managed and 77% of conservative group delivered normally. The rest i.e. instrumental delivery and c-section had no difference between two groups with p value of 0.1. In induced group 7.2% delivered by vacuum, 6.7 % by forceps and 17.1% by c-section as compared to 7.8%, 6.2 % and 8.8% in conservative group (Table 4). The incidence of cesarean delivery was lower than 20% incidence noted in obstetric population. All cesarean deliveries were performed either for non reassuring fetal status or secondary arrest of labor. Clinical chorioamnionitis was seen in 4.1% of conservatively managed and 0.5% of actively managed cases with p value of 0.2 as expected, the latency from admission to delivery was prolonged in observation group (Table 5). Pyrexia (p value 0.02) was seen significantly more often in expectant group while postpartum hemorrhage (p value 0.07) showed no difference between two groups. Similarly maternal hospitalization was prolonged for expectant group, with these women having an additional 3 days in hospital compared with patients who underwent induction of labor. Thus maternal and neonatal morbidity can be reduced by delivering pts within 24 hrs.

Hyperbilirubinemia was seen significantly more often in IOL group (p value 0.005) while Hypoglycemia (p value 0.3) showed no difference between two groups. Neonates born in IOL group stayed 2 days longer in hospital than those of expectant group and 7.8% of them got admitted to NICU (0.2). Newborns admitted to NICU born with low APGAR score of < 6 at 1 and 5 minutes i.e. p value 0.6 showed no difference between

Table 1: Gravidity Distribution in Two Groups n=384

Total %	Active Mx(192)		Conservative Mx(192)	
	No	%Age	No	%Age
Primi 39	86	44.7	64	33.3
Multi 60.9	106	55.2	128	66.6

Table 2:

AGE	Active Mx		Conservative Mx	
	No	%Age	No	%Age
20-29Yrs	112	58.3%	57	29.6%
30-39Yrs	69	35.9%	127	66.1%
>40Yrs	11	5.7%	08	4.1%

Table 3: Time Between Presentation of Pprome and Delivery

	Active Mx		Conservative Mx	
	No	%Age	No	%Age
<12Hrs	83	43.2	73	38.0
12-24 Hrs	86	44.7	61	31.7
>24Hrs	23	11.9	58	30.2

Table 4: Mode of Delivery

	Active Mx		Conservative Mx	
	No	%Age	No	%Age
Normal vaginal	132	68.7	148	77
Vacuum	14	7.2	15	7.8
Forceps	13	6.7	12	6.2
C/section	33	17.1	17	8.8

Table 5: Maternal outcome

	Active Mx		Conservative Mx	
	No	%Age	No	%Age
Pph	03	1.5	07	3.6
Pyrexia	7	3.6	25	13
Hospital stay>24 hrs	42	21.8	35	18.2
Chorioamninitis	1	0.5	8	4.1

Table 6: Fetal outcome

	Active Mx		Conservative Mx	
	No	%Age	No	%Age
Admission to nicu	15	7.8	24	12.1
Low apgar score (at 1 and 5 min)	28	14.5	32	16.6
Hypoglycemia	40	20.8	23	11.9
Hyperbilirubinemia	58	30.3	32	16.6

two groups {14.5% newborns of IOL group and 16.6% of expectantly managed group}. There were no stillbirths or neonatal deaths in the 384 pts.

DISCUSSION

Preterm prelabor rupture of the membranes is a dilemma for the obstetricians. On the one hand, awaiting spontaneous labor may lead to an increase in infectious disease for both mother and child, on the other hand induction of labor leads to preterm birth with an increase in neonatal morbidity due to prematurity. In this study the incidence of PROM between 34 and 37 weeks was 10% which is comparable to incidence of 5-10% in most studies^{10,11}. In our study groups were similar with respect to gestational age at delivery and dose of prostaglandin used but dissimilar in terms of mother's age and obviously gravidity and in length of latent period. Our findings suggested lower incidence of PROM in the nulliparous than in the multiparous patients. This is similar to report of Eslamian and Asadi, though other reports had also shown higher incidences in multiparous patients^{12,13}.

In our study there was reduced latent period when induced with prostaglandin E2 but in spite of this hospital stay was prolonged in induced group due to increased incidence of failed induction and c-section rate. Caesarean section rate in the study group was

13%. We found an increase in abdominal delivery after active management with induction of labor, as suggested by studies of premature rupture of the membranes at term¹⁷ with a caesarean section rates of 12%, Peleg et al¹⁴ in their review concluded that strong predictors of caesarean delivery after PROM at term included nulliparity, long labor and epidural anesthesia.

Prostaglandin E2 vaginal tablet have been used safely in our community for IOL in both normal and complicated pregnancies. There are also reports which suggest its use in grand multiparas¹⁵ however we can't draw conclusions from this result because of small sample size, also we have not used prostaglandin E2 in grandmultiparas in our study. However what has probably been less reported in the literature is the use of prostaglandin E2 in grandmultiparas with previous caesarean section who had PROM.

In this study, prophylactic antibiotic was used in all patients 24 hrs after PROM which is supported by published reports emphasizing role of antibiotics in management of PROM¹⁶. This may have contributed to the low occurrence of chorioamnionitis (4.6%), still births and no occurrence of early neonatal deaths recorded in this study.

Decisions to electively deliver a fetus preterm however, requires grounding in good clinical evidence

as mild prematurity is associated with a significant health burden. Delayed induction of labor after hospital admission was linked to worsened perinatal outcome, in a multicentre international study of PROM. Clinical chorioamnitis and maternal colonization with group B streptococcus were identified¹⁸. Mercer et al found a 52% increase in maternal infectious morbidity (29.8% vs 19.6%, not significant) with expectant management but a similar incidence of abdominal delivery and neonatal infection. In our study intrapartum pyrexia was 13% in expectant group as compared to 3.6% in induced group. PPH was 3.6% in conservative group. Our results were comparable with those of a study conducted in Lahore at Allama Iqbal medical college showing a decrease in intrapartum pyrexia, PPH and instrumental delivery in induced than in conservative group¹⁹. Therefore it appears that the relative benefits and risks of active versus expectant management after premature rupture of membranes in near-term gestation have not been clearly elucidated²⁰.

Induction of labour may shorten the length of hospital stay but there is insufficient evidence to suggest that it is harmful or beneficial for the baby²¹. However, expectant management in both groups and more importantly in the extended latency period of the late preterm PROM group increased NICU admission. This can be explained by the fact that some of the neonates were admitted on account of prematurity, low birth weight or presumed neonatal sepsis following prolonged latency period. In more recent studies [PPROMEXIL and PPROMEXIL- 2], it was reported that induction of labour did not significantly reduce the incidence of neonatal sepsis or improve pregnancy outcome compared with expectant management in late preterm PROM²². Hypoglycemia and hyperbilirubinemia were seen more often in the IOL group. For other neonatal outcome measures, there were no significant differences between the two groups.

CONCLUSION

In PPROM at 34 -37 weeks, active management reduces the risk of chorioamnionitis without reducing the rate of cesarean section and fetal distress therefore it is the preferred mode of management.

REFERENCES

1. Meis PJ, Ernest JM, Moore ML. Causes of low birth weight births in public and private patients. *Am J Obstet Gynecol* 1987;156:1165-8.
2. Maxwell GL. Preterm premature rupture of membranes. *Obstet Gynecol Surv* 1993;48:576-83.
3. Mercer BM, Goldenberg RL, Meis PJ, Moawad AH, Shellhaas C, et al. (2000) The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. The National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 183: 738-745.
4. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL, et al. Induction of labor compared with expectant management for prelabor rupture of the membranes at term. *N Engl J Med* 1996;334:1005-10.
5. Bendon RW, Faye-Petersen O, Pavlova Z, Qureshi F, Mercer B, Miodovnik M, et al. Fetal membrane histology in preterm prematurity rupture of membranes: comparison to controls, and between antibiotic and placebo treatment. *Pediatr Dev Pathol* 1999;2:552-8.
6. American College of Obstetricians and Gynecologists. Premature rupture of membranes. Clinical management guidelines for obstetrician-gynecologists. ACOG practice bulletin no. 1. *Int J Gynaecol Obstet* 1998;63:75-84.
7. Royal College of Obstetricians and Gynaecologists (2006) Preterm prelabour rupture of membranes. Guideline No. 44. Available: <http://www.rcog.org.uk/files/rcog-corp/uploaded-files/GT44PretermPrelabourRupture2006.pdf>. Accessed 1 September 2011.
8. Conway DL, Prendiville WJ, Morris A, Speller DC, Stirrat GM. Management of spontaneous rupture of the membranes in the absence of labor in primigravid women at term. *Am J Obstet Gynecol*. 1984 Dec 15;150(8):947-51. (Conway 1984).
9. Meikle SF et al. A retrospective review of efficacy and safety of prostaglandin E2 with premature rupture of membranes at term. *Obstetrics and gynaecology*, 1992, 80(1):76-9.
10. ACOG Practice Bulletin No. 80: premature rupture of membranes. Clinical management guidelines for obstetrician and gynecologists. *Obstet Gynecol*. 2007 Apr; 109(4):1007-19.
11. Semczuk-Sikora A, Sawulicka-Oleszczuk H, Semczuk M. Management in Premature Rupture of Membranes (PROM)222 at term- own experiences *Ginekol Pol* 2001; 72 (10): 756-64.
12. Eslamian L, Asadi M. The Caesarean section rate in cases with Premature Rupture of Membranes (PROM) at 36th week of pregnancy or later. *Acta Medica Iranica*. 2002; 40 (2): 83-87.
13. Zamzami T. Y. Prelabour rupture of membranes at term in low-risk women: induce or wait. *Arch Gynecol Obstet*. 2006 Feb; 273 (5): 278 – 82.
14. Peleg D et al. Predictors of caesarean delivery after prelabor rupture of membranes at term. *Obstetrics and gynaecology*, 1999, 93(6):1031-5.
15. Yamani YT, Rouzi AA. Induction of labor with vaginal prostaglandin E2 in grandmultiparous women with one previous caesarean section. *International Journal of obstetrics and gynaecology*, 1999, 65(3):251-3.
16. Passos F, Cardoso K, Coelho AM, Graça A, Clode N, Mendes da Graça L. Antibiotic prophylaxis in premature rupture of membranes at term: a randomized controlled trial. *Obstet Gynecol*. 2012 Nov; 120(5):1045 - 51. doi:<http://10.1097/AOG>.

17. Kappy KA, Cetrulo CL, Knuppel RA, Ingardia CJ, Sbarra AJ, Scerbo JC, et al. Premature rupture of the membranes at term: a comparison of induced and spontaneous labors. *J Reprod Med* 1982;27:29-33.
18. Seaward PG et al. International multicenter term PROM study: Evaluation of predictors of neonatal infection in infants born to patients with premature rupture of membranes at term. *American journal of obstetrics and gynaecology*, 1988;179:635-9.
19. Javaid MK, Hassan S, Tahira T. Management prelabour rupture of membranes at term, induction of labour compared with expectant. *Professional Med J* 2008;15:216-9.
20. Mercer BM, Crocker LG, Boe NM, Sibai BM. Induction versus expectant management in premature rupture of membranes with mature amniotic fluid at 32 to 36 weeks: a randomized trial. *Am J Obstet Gynecol* 1993;169:775-82.
21. Hartling L, Chari R, Friesen C, Vandermeer B, Laczko-Masmonteil T. A systematic review of intentional delivery in women with preterm prelabour rupture of membranes. *J Matern Fetal Neonatal Med*. 2006 Mar;19(3):177-87.
22. van der Ham DP, van der Heyden JL, Opmeer BC, Mulder AL, Moonen RM, van Beek JH, et al. Management of late preterm premature rupture of membranes: the PPROMEXIL-2 trial. *Am J Obstet Gynecol*. 2012 Oct;207(4):276.e1-10. doi: 10.1016/j.ajog.2012.07.024. Epub 2012 Jul 20.

ONLINE SUBMISSION OF MANUSCRIPT

It is mandatory to submit the manuscripts at the following website of KJMS. It is quick, convenient, cheap, requirement of HEC and Paperless.

Website: www.kjms.com.pk

The intending writers are expected to first register themselves on the website and follow the instructions on the website. Author agreement can be easily downloaded from our website. A duly signed author agreement must accompany initial submission of the manuscript.