PERINATAL AND MATERNAL OUTCOME IN PRELABOUR RUPTURE OF MEMBRANES

Nesam Susana Minnalkodi¹

¹Professor and HOD, Department of Obstetrics & Gynaecology, Government Chengalpattu Medical College.

ABSTRACT

Prelabour Rupture of Membranes (PROM) is one of the most common complications of pregnancy that has major impact on fetal and maternal outcome. It occurs in 1 out of every 10 pregnancies; 80% of women who present with PROM are term. It is also one of the commonest event where a normal pregnancy can turn into a high risk situation for the mother as well as for the fetus. Despite the relative frequency of this event, clinical management is one issue unresolved by the clinical research till date. A prospective study was designed to know the incidence, etiology, risk factors, fetal and maternal outcomes of prelabour rupture of membrane in Government Chengalpattu Medical College Hospital. One hundred mothers with singleton pregnancy in the age group of 19 to 35 years with leaking per vaginum and without maternal complications interfering with active management of PROM like heart disease, Pregnancy Induced Hypertension (PIH) were chosen and assessed with a standardized protocol. The data was collected and analysed statistically.

KEYWORDS

Amniorrhexis, PROM, PPROM.

HOW TO CITE THIS ARTICLE: Nesam Susana Minnalkodi. "Perinatal and Maternal Outcome in Prelabour Rupture of Membranes." Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 101, December 17; Page: 16629-16634, DOI: 10.14260/jemds/2015/2481

INTRODUCTION

Prelabour Rupture of Membranes (PROM) is one of the most common complications of pregnancy that has major impact in fetal and maternal outcome. It occurs in 1 out of every 10 pregnancy. 180% of women who present with prom are term. It is also one of the commonest event where a normal pregnancy can turn into a high risk situation for the mother as well as for the fetus. Despite the relative frequency of this event, clinical management is one issue unresolved by the clinical research to date. 2

The maternal problem associated with PROM are risks of infection, cord prolapse and unfavorable cervix for induction.1 The latter is associated with high incidence of dysfunctional labor, chorioamnionitis, an increased rate of cesarean section, post-partum haemorrhage and endomyometritis, while the problem of neonates includes problems of sepsis and postural deformities if the PROM to delivery interval is many weeks. Gestation of less than 34 weeks poses problems of bronchopulmonary dysplasia (If less than 26 weeks) hyaline membrane disease (Leading to respiratory distress syndrome).^{3,4,5} intraventricular hemorrhage, necrotizing enterocolitis and sepsis.5,6,7 Fetal wastage and neonatal mortality and morbidity are high when PROM occurs in pregnancies of less than 32 weeks. The decision for appropriate management depends on the assessment of the gestational age, the likelihood of infection and the availability of neonatal intensive care facilities.

The aim of the modern obstetrics is to have a healthy baby and a healthy mother. Much of the literature available is pertaining to the studies in the developing countries where neonatal salvage rates in preterm deliveries are very high and stringent asepsis is followed.

Financial or Other, Competing Interest: None.
Submission 04-11-2015, Peer Review 05-11-2015,
Acceptance 20-11-2015, Published 16-12-2015.
Corresponding Author:
Dr. Nesam Susana Minnalkodi,
No. 53, Vedhachalam Nagar, Chengalpattu,
Kanchipuram District-603001, Tamilnadu.
E-mail: minniesusan@yahoo.com
DOI:10.14260/jemds/2015/2481

This study is undertaken to identify the etiological factors, maternal and perinatal outcome and also deals with the critical areas of controversies related to the management of PROM and to review the recent literature for clinical research. More recently the use of PGE2 for cervical ripening has been suggested.

AIMS AND OBJECTIVES

- 1. To know the incidence of prelabour rupture of membranes in Chengalpattu Medical College Hospital.
- 2. To evaluate the risk factors of PROM.
- 3. To find out the etiology of PROM.
- 4. To assess fetal and maternal outcome in PROM.

MATERIALS AND METHODS

This present prospective study was conducted in Chengalpattu Medical College Hospital. The cases were selected from Labour Ward.

Inclusion Criteria for Case Selection

- 1. Singleton pregnancy between 37-41 weeks of gestation.
- 2. Primi and multigravida.
- 3. Age group 19-35 years.
- 4. Confirmed cases of leaking with or without membrane.
- a) Leaking from cervix confirmed by speculum examination.
- b) History of leaking per vagina.
- c) Cervix dilatation <3cm.
- d) No uterine contractions.

Exclusion Criteria

- 1. Multiple gestation.
- 2. Maternal complications interfering with active management of PROM like pregnancy induced hypertension, heart disease, previous Cesarean section.

One hundred patients were taken for study with PROM. Similarly 100 patients with intact membranes were taken as control.

ASSESSED WITH HISTORY TAKING

- 1. Age.
- 2. Socio-economic status.
- 3. Obstetric history.
- 4. Time of rupture.
- 5. Amount of liquor drained.
- 6. Any intervention outside.
- 7. History of coitus.
- 8. History of any infection.
- 9. Any prior surgical procedures of cervix.
- 10. History of recurrence of PROM.

CLINICAL EXAMINATION

- 1. Nutritional status/Anemia.
- 2. Vital Signs.
- 3. Abdomen Examination for Gestational Age.
 - Liquor volume.
 - Uterus acting or not.
 - Fetal presentation.
 - · Fetal well-being.
- 4. Speculum Examination.
- To confirm leaking.
- Cervical dilatation.
- Status of membranes.

LAB INVESTIGATIONS

Amniotic fluid for culture and sensitivity (By cervical swab) and other cultures for mother and fetus whenever necessary. All the patients are admitted in labour ward and started 1gm of systemic ampicilin and managed individually. Induction was done in 90% of the cases. Equal number of cases with no prom and no complication are taken as controls. Progress of labour was carefully watched. Depending upon the maternal and fetal condition, labour terminated by natural vaginal/operative methods. After delivery maternal and fetal outcome were studied. Neonates which needed admission were admitted in neonatal intensive care unit and subjected to investigation and followed till discharge. Mother also followed till discharge.

RESULTS AND OBSERVATION

Incidence in Chengalpattu Medical College Hospital – 9.06%. The incidence of PROM ranges from 5%-10% of all deliveries. PPROM occurs in approximately 1% of all pregnancies.

Age	Study	Control
(Years)	(No. of Cases)	(No. of Cases)
<20	4	15
21-29	82	79
>30	14	6
Total	100	100
Table 1: Age Incidence in PROM		

Incidence of PROM is more in the age group of 20-29 yrs. which is around 82%. In the control group 79% of the cases were between age group 20-29 years. There is no relationship between the two factors.

	SOCIOECONOMIC STATUS IN PROM			
	STUDY	CONTROL		
CLASS	(No. of	(No. of		
	Cases)	Cases)	chi sq=5.7	
III	4	1	p=0.06	
IV	5	1	not	
V	90	98	significant	
TOTA L	100	100		
m 11 2 C ' ' C' ' ' PDOM				

Table 2: Socioeconomic Status in PROM

Many studies (Stuart et al., Evans GS, Lin YS boil Reprod. 2005;72;2305) have shown that poor nutritional status causes

defect in the membrane, which is significantly influenced by the Socioeconomic status.⁸ Since the study was taken in a Government Hospital, almost all patients belonged to Class IV and V Socioeconomic status.

	GRAVIDA STATUS				
GRAVIDA	STUDY (No. of Cases)	CONTROL (No. of Cases)	-let 2 44		
1	47	50	chi sq=2.44		
2	34	36	p=0.48 not		
3	17	14	significant		
4	2	-	Significant		
TOTAL	100	100			
Table 3: Parity Incidence in PROM					

The case distribution with regard to parity was not significant in this study and was comparable with the study of Margret B. Ballard.

BOOKED/UNBOOKED			
BOOKED/UNBOOKED STUDY CONTROL (No. of Cases) (No. of Cases)			
BOOKED	61	73	
UNBOOKED	39	27	
TOTAL 100 100			
Table 4: Antenatal Care and PROM			

Thirty nine cases of PROM in this study did not have proper antenatal checkup, poor antenatal booking may be one of the risk factors implicated in PROM.

GESTATIONAL AGE (WEEKS)	STUDY (No. of Cases)	CONTROL (No. of Cases)
37	5	3
38	23	17
39	24	16
40	33	45
41	15	19
TOTAL 100 100		
Table 5: Incidence of PROM in		
Relation to Gestational Weeks		

Incidences of PROM are more in term pregnancies. The incidence in term PROM is 10% and PPROM complicates 3% of all pregnancies.

RUPTURED MEMBRANES			
STATUS	STUDY (No. of Cases)	CONTROL (No. of Cases)	
ABSENT	91	100	
PRESENT	9	0	
TOTAL	100	100	
Table 6: Membrane Status in PROM			

In this study, high rupture of membranes was present in 9 cases. They continue to leak fluid in small amounts, but have adequate amniotic fluid. This has good prognosis. It is caused by tear in the membranes above the lower uterine segment. High leaks may seal spontaneously. They are not associated with fetal or maternal complications.

LIQOUR			
COLOUR	STUDY (No. of Cases)	CONTROL (No. of Cases)	
CLEAR	93	100	
MECONIUM STAINED	7		
TOTAL 100			
Table 7: Colour of the Liquor in PROM			

Among 100 cases of PROM, in this study 93 cases had come with clear liquor and 6 cases had meconium stained

liquor with fetal distress which went for cesarean section. One case had thin meconium stained liquor and was induced and delivered.

PRESENTATIONS			
PRESENTATIONS	STUDY	CONTROL	
	(No. of Cases)	(No. of Cases)	
VERTEX	97	100	
BREECH	3	0	
UNSTABLE	0	0	
TOTAL	100	100	
Table 8: Fetal Presentation and PROM			

In this study group, 97% of the cases had cephalic presentation and about 3 cases of mal-presentation in the study group could be one of the contributing factors to cause PROM. In the control group, 100% of the cases had cephalic presentation

	COITUS			
COITUS	STUDY (No. of Cases)	CONTROL (No. of Cases)		
PRESENT	20	0		
ABSENT	80	100		
TOTAL	100	100		
Table 9: Coitus as a risk factor				

In this study, coitus within the preceding one month was found to be 20%. It frequently leads to PPROM.

ETIOLGICAL FACTORS	PERCENTAGE	
INFECTIONS	20	
PRIOR SURGICAL PROCEDURES	15	
H/O RECURRENCE	15	
COITUS	9	
MALPRESENTATIONS	3	
NOT KNOWN	38	
TOTAL	100	
Table 10: Etiological Factors in PROM Study Group		

Among the etiological analysis of PROM in the study group, most cases are caused by idiopathic causes. Infection caused 20% of all cases of PROM.

INFECTION	FREQUENCY	
NIL	80	
E.COLI	11	
KLEBSIELLA	4	
P.AERUGINOSA	1	
PROTEUS	3	
S.AUREUS	1	
TOTAL	100	
Table 11. Pactoriological Study of Amnietic Fluid in		

Table 11: Bacteriological Study of Amniotic Fluid in PROM

Amniotic fluid analysis showed 20 positive cases. Organisms grown were E. Coli, Klebsiella, Proteus, Pseudomonas, Staph Aureus and the remaining did not show any organisms. Infection causes 20% of all the cases of PROM.

PROM REC	STUDY (No. of Cases)	CONTROL (No. of Cases)
ABSENT	85	100
PRESENT	15	0
TOTAL	100	100
Table 12: PROM Recurrence		

In the study group, about 15 cases had recurrence of PROM. PROM in prior pregnancy has a definite association and has significant recurrence risk. P value is significant.

PRIOR SURGICAL PROCEDURES				
ABORTION STUDY PERCENTAGE				
1 D&C 17 17%				
2 D&C	1	1%		
Table 13: Prior Surgical Procedures in PROM				

Prior surgical procedures of cervix has significant effect of PROM. In this study, about 17 cases had one D and C and one case had two D and C. P value is significant.

LATENCY PERIOD		
DURATION (HOURS)	NO.OF CASES	
<6 HRS	53	
6-12 HRS	47	
>12 HRS NIL		
TOTAL 100		
Table 14: Latency Period in PROM		

In this study, all the cases were intervened and none were allowed to go beyond a latency period of >12 hrs. Preterm gestations will have longer latency period.

About 53 cases had latency period of <6 hrs. It is inversely proportional to the gestational age.

PGE2 AND MISOPROSTOL		
STUDY	FREQUENCY (No. of Cases)	
PGE2	46	
MISO	44	
SPONTANEOUS	10	
TOTAL	100	
Total 15: Induction in PROM		

Forty four cases were given induction in this study using misoprostol while 46 were induced using PGE2. Immediate induction using ripening agents misoprostol/PGE2 appears to be beneficial in multiparae and nulliparae with poor Bishops Score.

DELIVERY			
PGE2/MISOP	ROSTOL	FREQUENC Y (No. of Cases)	PERCENTA GE
	NORMAL	42	91.30%
PGE2	CESAREA N SECTION	4	8.70%
	TOTAL	46	100%
	NORMAL	41	93.20%
MISOPROSTOL	CESAREA N SECTION	3	6.80%
	TOTAL	44	100%
Total 16: Induction in PROM and Nature of Delivery			

In PGE2 induction group out of 46 cases 42 cases delivered normally, while 4 cases went for Cesarean Section. In misoprostol induction group, 41 patients delivered normally out of 44 while 3 cases delivered through Cesarean Section.

DELIVERY			
DELIVERY	STUDY (No. of Cases)	CONTROL (No. of Cases)	
NORMAL	87	90	
CESAREAN SECTION	19	10	
TOTAL	0	100	
Total 17: Mode of Delivery			

Eighty seven cases were delivered vaginally with or without induction (Miso or PGE2) and 13 cases were delivered by Cesarean Section. In no induction group about 4 cases delivered vaginally and 6 cases had Cesarean delivery mostly for fetal distress.

BIRTH WEIGHT(KG)	STUDY (No. of Cases)	CONTROL (No. of Cases)	
2.0-2.5 KG	6	2	
>2.5 KG	94	98	
TOTAL	100	100	
Total 18: Baby Birth weight in PROM			

Since the study group only included term PROM the average birth weight of babies in both study and control group was not much different. Previous study by Allen 1991 also found that 60-80% PROM occurs in term pregnancies.

5 MINUTES APGAR SCORE			
APGAR (10)	STUDY (No. of Cases)	CONTROL (No. of Cases)	
7	11	4	
8	57	41	
9	32	55	
TOTAL	100	100	
Total 19: 5 Minute Apgar score in PROM			

Low APGAR in PROM in this study is mainly due to infection and meconium staining, which also contributes to increased morbidity.

FETAL OUTCOME					
PGE2	FREQUENCY (No. of Cases)	PERCENT (%)	MISOPROSTOL	FREQUENCY (No. of Cases)	PERCENT (%)
NORMAL	45	90	NORMAL	35	70
RD#	5	10	RD#	14	28
EXPIRED	0	0	EXPIRED	1	2
TOTAL	50	100	TOTAL	50	100
Table 20: Comparison of Fetal Outcome Using PGE2 and MISO					

#RD-RESPIRATORY DISTRESS: Though Misoprostol group had a shorter induction time, the respiratory distress is comparatively higher than in the PGE2 group. This is attributed significantly due to more uterine tachysystoles.⁹

FETAL OUTCOME		
STUDY	FREQUENCY (No. of Cases)	
NIL	80	
RESPIRATORY DISTRESS	13	
BIRTH ASPHYXIA	4	
NEONATAL SEPSIS	2	
DEATH DUE TO MENINGITIS	1	
TOTAL	100	
Table 21: Fetal Outcome		

A 20% of the babies in the study group had various morbidities like birth asphyxia, respiratory distress and one mortality was due to meningitis. But only 4 cases had morbidities in the control group.

MATERNAL OUTCOME		
OUTCOME	STUDY	
	(No. of Cases)	
NIL	79	
PUERPERAL FEVER	9	
POST PARTUM HAEMORRHAGE	11	
WOUND INFECTION	1	
TOTAL	100	
Table 22: Maternal Morbidity in PROM		

Clinical features of chorioamnionitis are nil, but bacteriological study showed positive cultures for 20 cases. This is attributed to intrapartum use of antibiotics. The study had 9 cases of puerperal fever, 11 cases of post partum haemorrhage and 1 case of wound infection.

DISCUSSION

PROM contributes to significant maternal and neonatal morbidity. The obstetrician is faced to challenge the situation. The option for management includes expectant management vs. immediate intervention. The exact etiology is poorly understood. Infective, biochemical, mechanical pathways are included in this process. At term, the programmed cell death and activation of catabolic enzymes such as collagens and mechanical forces result in ruptured membranes.

This study was done in Govt. CHMC Hospital taking into account of 100 patients with PROM and 100 patients as control without PROM. Overall, incidence at CHMC Hospital was found to be 9.06% General Incidence varies from 2-18% (GLIIIH et al. 1970) 2.7 to 17% (Arias). 11

The incidence of PROM is high in low socio-economic group. This is attributed to poor nutritional status due to deficiency of vitamins and minerals. In this study group, 96% of the patients were in the low Socio-economic group.

Sixty one cases of PROM patients were getting proper antenatal care among 100 cases of PROM when compared to 73 cases getting proper antenatal care in control group. Poor antenatal care may be one of the risk factors for PROM.

In this study, 47% were primi and 34% were multi. Distribution of cases with regard to parity was not significant in this study and was comparable with the study of Margret B. Ballard who did not find any difference in parity distribution.

But Calvin from his extensive studies showed increased incidence in multigravida.

In 80% of the cases, PROM occurs in term. This study included only term gestation. Among 100 patients in the study group, 91 patients were with absent membranes and leaking liquor and 9 patients had intact membranes with leaking

liquor (HROM). In control group all patients had intact membranes and with no leaking. In study group who had leaking 93% had clear liquor and 7 had meconium stained liquor and none of them had blood stained liquor.

Taking malpresentation as one of the risk factor for PROM in the study group, three cases were presented with breech presentation while in control group all presented with vertex presentation Coitus being one of the major risk factor for PROM. 12 coitus within the preceding one month was found to be 20% in the study group (Raybum and Wilson 1980) Naeye (1987) reported that preterm delivery due to PROM were 11 times more frequent with coitus. Digital vagina examination should be avoided until labour is initiated as it may have an impact on neonatal infections and endometritis in PPROM.

In 38% of PROM the cause and risk factors could not be elicited. ¹³ The remaining 20 cases had bacteriological evidence of infection. ¹² They showed positive cultures for E. coli, Klebsiella, pseudomonas aeruginosa, staph. aureus and proteus. Specific culture for chlamydial infection could not be done due to lack of facility and cost effects.

Regarding the latency period no cases in study group had >12 hrs. latency. When the gestational age is smaller, the latency period is longer. The mean total duration of labour in multipara in study group was almost more than >6hrs, while in control group it was <6 hrs. No significant differences on the total duration of labour in nullipara in both groups.

At present the management of PROM lies with immediate stimulation of labour rather than waiting for spontaneous onset of labour. Immediate stimulation with PGE2, Misoprostol is a good approach in all term PROM with unripe cervix. Prostraglandin induction shortens the time to delivery and decreases the risk of infection and Cesarean section rate is not increased. 14,15

After taking into consideration fetal presentation, parity, gestational age, cervical favorability, presence of signs/risk factors for chorioamnionitis and by exclusion of fetal distress, Cephalopelvic Disproportion, labour is induced at the time of presentation. Thirteen cases of Cesarean section in study group were done for fetal distress and failed induction and 10 cases of Cesarean section was done in control group.

The major maternal complication of PROM is chorioamnionitis. Clinical evidence of infection has not been noticed in any of the patients in study group, but bacteriological evidence of infection showed 20%, 9 patients in study group had fever in the immediate postpartum period and 1 case had wound infection and 11 cases went in for postpartum haemorrhage. Complications due to infection are reducing now a days. This may be attributed to regular use of intrapartum antibiotics. 17,18

High perinatal morbidity in PROM is attributed to respiratory distress in this present study, one case of perinatal mortality due to meningitis and its complications. ^{3,4,6}

Among 21 cases of perinatal morbidity, 13 cases of respiratory distress, 4 cases of birth asphyxia has been documented. 6

With good neonatal intensive care, strict asepsis, prophylactic antibiotics, immediate induction policy, the maternal and neonatal morbidity due to infection is grossly reduced.

SUMMARY AND CONCLUSION

PROM term is now managed by inducing labour at the time of presentation. This study shows that careful antenatal monitoring for risk factors and etiology detection and prompt treatment of infection and pelvic examination under aseptic precautions and appropriate therapy are important factors in the prevention of PROM.

 Abnormal labour and operative procedures have increased in PROM. Failed induction and fetal distress are the common indications for caesarean section in induction group. Use of vaginal prostaglandins offered better results in this study. PGE2 is safe shortens labour and has no effect on Cesarean section rate.

- Expectant line of management is beneficial for preterm PROM patients without signs of infection.
- Early interventions with proper care with strict asepsis and with prompt delivery and with good neonatal setup mortality due to sepsis, respiratory distress and birth asphyxia have been decreased.
- Neonates treated with prophylactic antepartum and intrapartum antibiotics definitely has fewer complications and an improved long term outcome.
- Use of corticosteroid helps to improve the outcome in PPROM between 28-32 weeks.
- Even though PROM occurs more at term the perinatal morbidity and mortality is mainly due to PPROM research is needed to identify the etiologies and prevention of PROM, especially in the preterm gestation.
- This study coincides with other studies and shows that the most important risk factors associated with PROM are low socioeconomic status, nutritional deficiency and improper antenatal care.
- To conclude with improvement in SE status, nutritional supplement and proper antenatal care will definitely reduce the incidence of PROM.

BIBLIOGRAPHY

- 1. Lee T, Silver H. Etiology and epidemiology of preterm premature rupture of the membranes. Clin Perinatology 2001;228:721-734.
- ACOG practice bulletin No. 80: premature rupture of membranes. Clinical management guidelines for obstetrician-gynaecologists. Obstet. Gyn. A/N. 2007;109(4);1007-19.
- 3. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH consensus statement. 1994:12;1-24.
- 4. NIH consensus development panel. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH consensus panel on the effect of corticosteroids for fetal maturation on perinatal outcomes. JAMA Feb! 1995;273(5):413-8.
- Egarter C, Leitich H, Karas H, Weiser F, Hussain P, Kaider A, et al. Antibiotic treatment in premature rupture of membranes and neonatal morbidity: a meta-analysis. American Journal of Gyn 1996;174:589-97.
- Roberts O, Daniel S. Antenatal corticosteriods for accelerating fetal lung maturation for women at risk of preterm birth, Cochrane update. Obs Gyn 2007;109(1):189.
- ACOG committee opinion no. 475; Antenatal corticosteroid therapy for fetal maturation obs Gyn Feb 2011;117(2pt1);422-4.
- 8. Stuart et al., Evans GS, Lin YS. Boil Reprod. The incidence and management outcome of PPROM in a Tertiary Hospital in Nigeria American journal of clinical medicine research 2014;2(1): pp14-17.
- Tan BP, Hannah ME. Prostaglandins versus oxytocin for prelabour rupture of membrane at or near term. Cochrane database Sys Rev 2001; issue 4.
- 10. Mercer BM. Preterm premature rupture of membranes; current approaches to evaluation and management, Obs gyn clin North Amer Sep 2005;32(3);411-28.
- 11. Arias F, Victoria A, Cho K, et al. Placenta histology and clinical characteristics of patients with preterm premature rupture of membranes. Obs Gyn 1997;89:265-71.

12. Harger JH, Hsing AW, Tuomala RE, et al. Risk factors for PROM – A multicentric case control study Am J Obstet Gynaecol 1990;163:130-37.

- 13. Gunn GC, Mishell Dr Jr, Morton Dg. Premature rupture of the fetal membranes. A review AM Jobslet Gynecol 1970;106:469-83.
- 14. Meike SF, Bissel ME, Freedman WL, et al. A retrospective review of the efficacy and safety of PGE2 with PROM at term Obstet Gyn 1992;80:76-9.
- 15. Chung TM, Rogers H, Gordon, et al. "Prelabour rupture of the membranes at term and unfavourable cervix; a randomized placebo controlled trial on early intervention with intravaginal PGE2 gel." AVST N2 Obst Gyn 32(1992):25-7.
- Hannah ME, Ohsson A, Farine D, Hewson SA, Hodnet ED, Myhr TL, et al. Induction of labour compared with expectant management for the prelabour rupture of membranes at term. N Eng Journal Med 1996;334:1005-10.
- 17. American College of Obstetrician and Gynaecologist. Premature rupture of membranes. Clinical management guidelines for obstetricians and gynaecologists. ACOG practice Bulletin No. 1. Int Journal of Gyn Obs 1998;63:74-84.
- 18. Kenyon SL, Taylor DJ, Tarnow- Mordi W, et al. Broad spectrum antibiotic for preterm, prelabour rupture of fetal membranes; the ORACLE I randomized trial. Lancet 2001;357:979.