ORIGINAL ARTICLE

Prolonged Pre-Labour Rupture of Membranes in Infants at Term with Early-Onset Neonatal Sepsis

AMBREEN NASIR¹, MUHAMMAD NASIR RANA², SABA ILYAS MALIK³, SHABANA KHOKHAR⁴, HUMAIRA DURRANI⁵, WAJIHA RIZWAN⁶, SHEHNAZ KAUSER⁷

^{1,3-7}Rahber Medical and Dental College, Lahore

²The Institute of Child Health/Children's Hospital, Lahore

Correspondence to: Dr. Ambreen Nasir, 136-I.H. Street 20., PAF Falcon Society, Gulberg-3, Lahore, Email: drnasirrana@yahoo.com, Mob: +92 321 844 7009

ABSTRACT

Aim: To find the association of prolonged pre-labour rupture of membranes in infants at term with early-onset neonatal sepsis.

Study design: It is a descriptive case series study

Place study: Department of Gynecology and Obstetrics, Rahber Medical and Dental College and Pakistan Rangers Hospital, Lahore.

Methodology: A written informed consent was taken from all the patients who were included in the study. Study was continued for six months. 100 mothers were enrolled in the study. Non-probability convenience sampling technique was used.

- Inclusion criteria:
- Mothers withrupture of membranes 24 hours before labor and
- Gestational age between 37 to 42 weeks.
- Exclusion criteria: Mothers with following risk factors were excluded;
- Infants having any congenital anomaly and
- > Mothers taking antibiotics prior to admission

Results: A total of 100 patients were enrolled in the study. Mothers were classed into different groups according to their ages. According to gravidity (G), mothers were divided into 4 groups. Mothers were divided in 4 groups on the basis of parity (para). Blood culture reports were retrieved. Staphylococcal aureus was detected in 25% of cases (25/100). Klebsiella and coagulase negative staphylococcus in 5% each. Acinobacter species and pseudomonas were detected in 3% of cases each. Enterococci were present in 2% of cases (2/100). Enterobacter species and streptococci were detected in 1% each.

Conclusion: Prolonged PROM leads to neonatal sepsis

Keywords: PPROM promneonatal sepsis chorioamnionits

INTRODUCTION

Premature rupture of membranes (PROM) refers to a patient who is beyond 37 weeks' gestation and has presented with rupture of membranes (ROM) prior to the onset of labor. Preterm premature rupture of membranes (PPROM) is rupture of fetal membranes with leakage of amniotic fluid prior to 37 weeks of gestation. Spontaneous preterm rupture of the membranes (SPROM) is ROM after or with the onset of labor occurring prior to 37 weeks¹. Prolonged ROM is any ROM that persists for more than 24 hours and prior to the onset of labor. The incidence of term PROM is 8%. Spontaneous labour follows term PROM at 24, 48 and 96 hours in 70%, 85% and 95% of women, respectively. It's always important to manage it as it has many risks for the newborns. The immediate risks of rupture of membranes include cord prolapse, cord compression and placental abruption. Delayed risks include maternal and neonatal infection. PPROM has many significant complications. It may be the cause of one-third of all preterm deliveries.Matter of concern is that PPROM is often complicated by infections leading to inflammation. Its severitydepends on the type of bacteria and its -----

Received on 21-04-2020 Accepted on 13-08-2020 numbers. A number of risk factors have been identified for PPROM. Factors are both maternal and uteroplacental as well as fetal². Maternal factors includes a previous PPROM, antepartum bleeding, prolonged use of steroids, connective tissue disorders or any direct trauma on abdomen. Other important factors include; cigarette smoking, illicit drug use, anemia and unmarried mothers.

PPROM leads to neonatal sepsis, which is a major cause of neonatal mortality³. Implementation of sustainable development goals (SDG) began in 2016. Its target is to reduce under 5 mortality rate to less than 25 per 1000 live births in every country of the world by 2030. To achieve this target, we have to analyze the important causes ofmortalities in this age group. In fact, a large groupof mortality occurs in neonatal period and sepsis and prematurity are two most important causes.

MATERIALS AND METHODS

It is a descriptive case series study, conducted in department of Gynecology and Obstetrics, Rahber Medical and Dental College and Pakistan Rangers Hospital, Lahore.A formal approval was taken from institutional review board of the college before the commencement of the study. A written informed consent was taken from all the patients who were included in the study. Studywas continued for six months. 100 mothers were enrolled in the study. Non-probability convenience sampling technique was used. Mothers with the following risks were admitted, Rupture of membranes 24 hours before labor and Gestational age between 37 to 42 weeks. Mothers with following risk factors were excluded; Infants having any congenital anomaly and Mothers taking antibiotics prior to admission.

Inclusion criteria:

- Mothers withrupture of membranes 24 hours before labor and
- Gestational age between 37 to 42 weeks.

Exclusion criteria:

- Mothers with following risk factors were excluded;
- Infants having any congenital anomaly and
- Mothers taking antibiotics prior to admission

Predesigned proforma was filled for each patient used to collect data. Mothers were managed according to their conditions. Mothers had different clinical signs and symptoms, e.g., vaginal leak, vaginal bleeding and pelvic pressure. Important findings enumerated were; fever, tachycardia, uterine tenderness and foetal tachycardia. Some of the mothers were induced with prostaglandin E-1 others E-2, whereas many went into spontaneous labor. Some of the mothers were augmented with oxytocin. Some of the patients ended up in caesarean sections due to different indications. Labor room as well the operation theatres of the hospital are according to approved standards. All the normal deliveries were conducted by trained obstetricians, whereas caesarean sections were either done or supervised by consultants. Anesthetists are also qualified and properly trained.

Blood samples of all newborns were taken by aseptic measures. 2ml blood was taken and immediately sent to laboratory for blood culture sensitivity, along with other necessary investigations. Newborns were given appropriate treatment by the qualified neonatologist.

All the data was collected by using predesigned proforma and entered in SPSS vr 21 for analysis.

RESULTS

A total of 100 patients were enrolled in the study. Mothers were classed into different groups according to their ages. Group one was less than 20 years, having 12 mothers in it. Group 2,3,4 and 5 had age ranges from 21 to 25 years, 26 to 30 years, 31 to 35 years and above 35 years. The number of mothers in these groups were 43, 29, 11 and 5 respectively.

Table	1:	One	minute	APGARS	SCORE
rabic	۰.	One	minute	AI OAIO	OOONE

Sr. no.	1-Minute	Cases	Percentage
1.	0-3	NIL	NIL
2.	4-7	52	52%
3.	8-10	48	48%

Table-2: 5-minute APGARS SCORE

Sr. no.	1-Minute	Cases	Percentage
1.	0-3	NIL	NIL
2.	4-7	46	46%
3.	8-10	54	54%

According to gravidity(G), mothers were divided into 4 groups. Primigravida(49/100), G-2 and G-3 (34/100), G-4 to

G-5 (12/100) and more than G-5 (5/100).Mothers were divided in 4 groups on the basis of parity(para). Para-1(18/100), Para-2 and Para-3(16/100), Para-4 and Para-5(8/100) and more than Para-5(2/100).Different babies had different Apgar scores (Table-1,2) According to number of miscarriages, mothers were divided into 3 groups. Mothers with one abortion were placed in group-1(13/100), with 2 to 3 abortions group-2(6/100) and more than 3 abortions in group-3(nil). 62% patients were booked, means having 2 or more antenatal visits. Gestational age was divided into 4 groups (Table-3).

Table-3: Groups of Gravi

Sr No.	Gravidity	No. of Patients	%Age
1.	Primigravida	49	49%
2.	G-2 TO G-3	34	34%
3.	G-4 TO G-5	12	12%
4.	MORE THAN G-5	5	5%

Newborn's gender was documented. 54% were males and 46% were females. Newborns were also grouped according to their weight into 6 groups. Group-1 was with weight less than 1.5 kg(3/100), group-2 with weight 1.6 to 2 kg(3/100), group-3 with weight 2.5 to 3.0 kg(29/100), group-4 with 3.1 to 3.5 kg(44/100), group-5 with weight from 3.6 to 4.0 kg (18/100) and group-6 with weight more than 4.0 kg (3/100). Presentation was quite variable. Some presented with per vaginal leaking of amniotic fluid(100/100), some with per vaginal bleeding (16/100), some vaginal discharge (13/100) and pelvic pressure (21/100). Time duration of per vaginal leaking was further categorized according to time duration (Table-4).

Clinically different mothers presented differently. 18% presented with tachycardia, 9 % with temperature, 11% with uterine tenderness, 22% with foetal tachycardia, whereas 42% had no sign of chorioamnionitis. 66 percent women went into labour spontaneously, whereas, 18% were induced with prostaglandin E-1 and 16% were induced with prostaglandin E-2. Augmentation of labour with oxytocin was done in 26% mothers, whereas, 74% progressed normally. Mode of delivery was different in different mothers.

Table 4. Daration of Vaginar Leaking			
Sr. No.	Duration of per vaginal leaking (in hours)	Number of patients	% Age
-	Š ,		
1.	24hrs – 36hrs	24	24%
2.	37hrs – 48hrs	40	40%
3.	48hrs – 60hrs	17	17%
4.	61hrs – 72hrs	13	13%
5.	72hrs and above	16	16%

Normal vaginal delivery was in 34% (34/100), outlet forceps delivery in 9% (9/100), vacuum extraction in (4/100), vaginal delivery after cesarean section 6% (6/100) and cesarean sections 47% (47/100). Causes of cesarean sections were multiple. Failure of induction 6%(6/100), cervical dystocia7%(7/100), foetal distress17%(17/100), chorioamnionitis9%(9/100) and previous 2 to 3 cesarean sections3%(3/100). APGAR score was variable (Table-). Blood culture reports were retrieved, showing different microorganisms. Staphylococcal aureus was detected in 25% of cases (25/100). Klebsiella and coagulase negative staphylococcus in 5% each. Acinobacterspecies and pseudomonas were detected in 3% of cases each. Enterococci were present in 2% of cases (2/100). Enterobacter species and streptococci were detected in 1% each.

DISCUSSION

Preterm prelabor rupture of membrane is one of the complications in pregnancies. In about 30-35% of the cases, it leads to premature deliveries. Though the amniotic fluid is sterile but once membranes are ruptured, it becomes a ready source of infection. Once infected it leads to chorioamnionitis. PPROM is one of the main causes of premature deliveries. This is one the major cause due to which Pakistan, as well as some countries of the world was unable to achieve the target of Millennium Development Goal no. 4, in which these countries had target of a two-third reduction from 1990 to 2015. It's important to prevent deaths caused by pneumonia and diarrhea, but mortalities in neonatal period must be decreased by controlling premature births, septicemia and birth asphyxia⁴.

Each year approximately 4 million babies die in the first month of life. A large number had stillbirths and almost 500,000 mothers die due to pregnancy related issues. Almost 3/4th of all neonatal deaths occur in the first week of life and maximum on the first day of delivery. Unfortunately, 99% of neonatal deaths occur in the developing countries. These countries have done little improvement in last decade in decreasing the mortality rates of newborns. Significant causes of deaths in newborns are; premature deliveries, sepsis and birth asphyxia. These three diseases are responsible for more than 75% of all neonatal deaths⁵.

In our study, we have doneinductionwith prostaglandins, whereas, in another study they have found that both oxytocin and prostaglandins are effective and safe in PROM⁶. In a study, conducted by Alamet al has observed the incidence of term PROM in 8 %7. There are a number of risk factors of chorioamnionitis. One of the important is maternal obesity8. Researchers and clinicians are always in search of predictors of chorioamnionitis, so that all such cases can be managed well in time. As procalcitonin is a good predictor of sepsis, but in a study its usefulness could not be proved⁹. However, maternal genital colonization with mycoplasma has found some association with chorioamnionitis¹⁰.

It's always difficult to treat choroamnionitis, so different regimes have been tried from time to time to treat it. In one of the combination therapy, they have found of ceftriaxone. combination clarithromvcin and metronidazole a useful therapy in perinatal outcome¹¹it's a routine that whenever premature delivery is expected, corticosteroids are given to mother for better outcome of baby. However, in a study, they conducted in women with PPROM at 32 to 33.6 weeks; they could not establish any significant difference^{12,13}. Different studies and centers report variable ratio or proportion of complications. In one of the study, clinical chorioamnionitis was present in 16% of the patients. Whereas, if we combine all three parameters, i.e., clinical, microbiological and histological, then it is 70%¹⁴. It is commonly observed that there is increased association of neonatal sepsis in babies born to mothers with PPROM. However, in one of the study, they have observed that there is no such increase¹⁵. In one of the study, they have observed that common morbidities in newborns are sepsis, bronchopulmonary dysplasia and respiratory distress syndrome¹⁶. Inanotherstudy, researchers have studied about increased risk of cerebral palsy in newborns of PPROM mothers. They could not find any association ¹⁷.

Management by different modes can decrease the outcome of newborns. Apart from other treatment options, researchers in one of the study found that vaginal probiotics along with antibiotics had improved the outcome in the newborns¹⁸.It's a usual practice to give steroids in expected premature deliveries. Normally, single course is given. However, sometimes, two courses are also given. There is apprehension, that two courses may increase the risk of chorioamnionitis as well neonatal mortalities. To evaluate these risks, a study was conducted. They studied 1652 woman with PPROM receiving steroids, and 145 women received 2nd dose of steroids as well. They had the conclusion that there is no increased risk factor for chorioamnionitis or neonatal mortality¹⁹. In a review article 23 studies were included. In total 8615 women at 37 weeks or more were enrolled. It was concluded that planned early birth after PPROM in mothers is useful in decreasing the risks of infectionin mothers and there was same percentage of cesarean sections²⁰. Howeverneonatal infections were reduced. Premature rupture of membranes is always a risk factor for newborns. Although, if it's not infected it can be spontaneously stopped. However, different treatment modalities have been tried from time to time. Important ones are; injecting clotting factors locally, the tablets that may induce the body's immune system. Some have tried placement of the sponges and like materials. However, there are no case-controlled studies to compare different modalities. As there are limited studies, so currently it may be difficult to decide about efficacies of these studies ²¹.

CONCLUSION

- Prolonged PROM leads to neonatal sepsis
- Staphylococcus aureus is the commonest organism.
- Shortening the interval between PROM and delivery can reduce risk of neonatal sepsis.

Recommendations: PPROM is one of the causes of neonatal sepsis, so there should be a high index of suspicion for its diagnosis and proper management.

REFERENCES

- Assefa N E, Berhe H, Girma F, Berhe K, Berhe Y Z,Gebrehet G. Risk factors of premature rupture of membranes in public hospitals at Mekele city, Tigray, a case control study. BMC Pregnancy and Childbirth (2018) 18:386
- Pharande P, Abdel-Latif M E, Barbara Bajuk B, LuiK, Bolisetty S. Preterm infant outcomes in relation to the gestational age of onset and duration of prelabour rupture of membranes: a retrospective cohort study *BMJ Paediatrics Open* 2017;1:e000216. doi:10.1136/bmjpo-2017-000216.
- 3. Ocviyanti D, Wahono W T. *Risk Factors for Neonatal Sepsis in Pregnant Women with Premature Rupture of the Membrane.* Journal of Pregnancy Volume 2018, Black

Article ID 4823404, 6 pages https://doi.org/10.1155/2018/4823404

- R E, Shibuy k, Boschi-Pinto C, Bryce J. WHO estimates of the causes of death in children. Volume 365, Issue 9465, 26 March–1 April 2005, Pages 1147-1152.
- Zupan J, Cousens S, ELawn J. 4 million neonatal deaths: When? Where ?Why? Volume 365,Issue 9462, 5–11 March 2005, Pages 891-900.
- Mahomed K, Wild K, Weekes C R. Prostaglandin gel versus oxytocin – prelabour rupture of membranes at term – A randomised controlled trial. Aust N Z J ObstetGynaecol2018; 58: 654–659
- Alam M M, Saleem A F, Shaikh A S, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. J Infect DevCtries2014; 8(1):067-073
- Hadley E E, Discacciati A, Costantine M M, Munn M B, Pacheco L D, Saade G R, Chiossi G. Maternal obesity is associated with chorioamnionitis and earlier indicated preterm delivery among expectantly managed women with preterm premature rupture of membranes.
- Thornburg L L, Queenan R, Griffith B B, Pressman E K. Procalcitonin for prediction of chorioamnionitis in preterm premature rupture of membranes.
- Stirling K.M, Hussain N, Sanders M.M, Campbell W. Association between maternal genital mycoplasma colonization and histologic chorioamnionitis in preterm births Journal of Neonatal-Perinatal Medicine, vol. 9, no. 2, pp. 201-209, 2016.
- Lee J H, Romero R, Kim S M, Chaemsaithong P, Park C W, Park J S, Jun J K, Yoon B H. A new anti-microbial combination prolongs the latency period, reduces acute histologic chorioamnionitis as well as funisitis, and improves neonatal outcomes in preterm PROM The Journal of Maternal-Fetal & Neonatal Medicine . Volume 29, 2015 -Issue 5
- Sheibani L, Fong A, Henry DE, Norton ME, Truong YN, Anyikam A, Laurent LC, Rao R, Wing DA. Maternal and neonatal outcomes after antenatal corticosteroid administration for PPROM at 32 to 33 6/7 weeks gestational

age. J Matern Fetal Neonatal Med. 2017 Jul; 30(14):1676-1680.

- Marel VD, deJonge R, Duvekot J, Reiss I, Brussé I. Maternal and Neonatal Outcomes of Preterm Premature Rupture of Membranes before Viability. Klin Padiatr. 2016 Mar; 228(2): 69-76.
- Arora P, Bagga R, Kalra J, Kumar P, Radhika S, Gautam V. Mean gestation at delivery and histological chorioamnionitis correlates with early-onset neonatal sepsis following expectant management in PPROM. J Obstet Gynaecol. 2015 Apr; 35(3):235-40.
- Drassinower D, Friedman AM, Običan SG, Levin H, Gyamfi-Bannerman C.Prolonged latency of preterm premature rupture of membranes and risk of neonatal sepsis.Am J Obstet Gynecol. 2016 Jun; 214(6):743.
- Sim WH, Araujo Júnior E, Da Silva Costa F, Sheehan PM. Maternal and neonatal outcomes following expectant management of preterm prelabour rupture of membranes before viability. J Perinat Med. 2017 Jan 1;45(1):29-44.
- 17. Drassinower D, Friedman AM, Običan SG, Levin H, Gyamfi-Bannerman C.Prolonged latency of preterm premature rupture of membranes and risk of cerebral palsy. J Matern Fetal Neonatal Med. 2016 Sep;29(17):2748-52.
- Daskalakis GJ, Karambelas AK. Vaginal Probiotic Administration in the Management of Preterm Premature Rupture of Membranes. Fetal Diagn Ther. 2017; 42(2):92-98.
- Brookfield KF, El-Sayed YY, Chao L, Berger V, Naqvi M, Butwick AJ. Antenatal corticosteroids for preterm premature rupture of membranes: single or repeat course? Am J Perinatol. 2015 May; 32(6):537-44.
- Middleton P, Shepherd E, Flenady V, McBain RD, Crowther CA. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more).Cochrane Database of Systematic Reviews 2017, Issue 1.
- 21. Crowley AE, Grivell RM, Dodd JM. Sealing procedures for preterm prelabour rupture of membranes. Cochrane Database of Systematic Reviews 2016, Issue 7.