

Evaluation of the perinatal results of pregnant with preterm premature rupture of membrane

Orkun Çetin¹, İpek Dokurel Çetin², Cihat Şen³, Seyfettin Uludağ³, Begüm Aydoğan³, Abdullah Tüten³

¹Department of Obstetrics and Gynecology, Süleymaniye Obstetrics and Gynecology Training and Research Hospital, Istanbul, Turkey

²Department of Pediatrics, Cerrahpaşa Medical Faculty, Istanbul University, Istanbul, Turkey

³Department of Obstetrics and Gynecology, Cerrahpaşa Medical Faculty, Istanbul University, Istanbul, Turkey

Abstract

Objective: Evaluation of perinatal outcomes of pregnant with preterm premature rupture of membrane (PPROM) who applied to our clinic.

Methods: The study was designed as a cross-sectional study and performed at the Perinatology Department, Medical Faculty of Istanbul University Cerrahpaşa between January 2009 and July 2011. Forty PROM cases were admitted to our study. Patients were enrolled after written informed consent was obtained. Forty cases diagnosed as PPRM who were between 26th and 37th gestational weeks without any obstetric and maternal pathological symptoms were included into the study.

Results: The mean age of PPRM group was 31.2. In the study, the mean gestational week for PPRM cases was 32.5. The mean gestational week for delivery was 33.5±3.19. The mean follow-up period of the cases was 5.8±2.6 days. The neonatal sepsis incidence was reported as 20% (8/40) in PPRM cases.

Conclusion: The preterm premature rupture of membranes is an obstetric issue affecting perinatal outcomes. The evaluation of patients is crucial. During the assessment of patient gestational week and infectious parameters must be taken into account and an appropriate treatment must be chosen individually. PPRM cases should be followed-up and treated in centers that have neonatal intensive care units.

Key words: Preterm premature rupture of membrane, perinatal outcome, neonatal sepsis.

Preterm erken membran rüptürü olan gebelerin perinatal sonuçlarının değerlendirilmesi

Amaç: Kliniğimize başvuran, preterm erken membran rüptürü olan gebelerin perinatal sonuçlarının değerlendirilmesinin yapılması.

Yöntem: Çalışma, kesitsel bir araştırma olarak planlandı. Çalışmaya katılan olgular, İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Kadın Hastalıkları ve Doğum Ana Bilim Dalı Perinatoloji Bilim Dalı ve Gebe Polikliniğine Ocak 2009 - Temmuz 2011 tarihleri arasında başvuran erken membran rüptürü olan gebeler arasından seçildi. Çalışmaya 26.-37. gestasyonel hafta arasındaki, obstetrik ve maternal patolojik bulgusu olmayan 40 preterm erken membran rüptürü (PEMR) olgusu dahil edildi.

Bulgular: Preterm erken membran rüptürü olan 40 olgunun yaş ortalaması 31.2 idi. Preterm erken membran rüptürü gelişen olguların, membran rüptürünün gerçekleştiği gebelik haftası ortalaması 32.5 idi. İzlem süreleri ortalama 5.8±2.6 gün olan olgularımızın ortalama doğum haftası 33.5±3.19 olarak bulundu. Preterm erken membran rüptürü olgularında neonatal sepsis gelişme sıklığı %20.0 (8/40) olarak bulundu.

Sonuç: Preterm erken membran rüptürü, perinatal sonuçları etkileyen bir obstetrik problemidir. Hastalar çok dikkatli bir şekilde değerlendirilerek gebelik haftası ve enfeksiyon bulguları başta olmak üzere tüm faktörler göz önüne alınmalı ve uygun tedavi yöntemi planlanmalıdır. Özellikle PEMR olguları, yenidoğan yoğun bakım servisinin olduğu ileri merkezlerde takip ve tedavi edilmelidir.

Anahtar sözcükler: Preterm erken membran rüptürü, perinatal sonuçlar, neonatal sepsis.

Introduction

Preterm labor still exists in the obstetrics despite the developments in medicine and technology and it is one of the most significant problems causing perinatal

morbidity and mortality. Although other obstetric complications decrease by the improvement of modern obstetrics approach, preterm labor and the incidence of preterm premature rupture of membrane still have not

Correspondence: Orkun Çetin, MD. Süleymaniye Doğumevi Eğitim ve Araştırma Hastanesi, Telsiz Mah. Kazlıçeşme, İstanbul, Turkey. e-mail: drorkuncetin34@hotmail.com

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been decreased by treatment methods developed so far. Therefore, a relative increase has occurred in the incidences of morbidity and mortality associated with preterm labor.^[1] Mortality rates of infants delivered by preterm labor constitute 85% of perinatal deaths by excluding congenital anomalies.^[2]

Premature rupture of membrane (PROM) is a condition that occurs when fetal membranes are ruptured at least one hour before the onset of labor and amniotic fluid flows out; so, the barrier between fetus and external environment is broken down. If it occurs before 37th gestational week, it is called preterm premature rupture of membrane (PPROM). PROM and PPRM are similar in terms of their etiologies, complications and outcomes; however, it is considered that the actual cause of membrane rupture in PPRM is the infection around choriodesidual region.^[3-7]

While premature rupture of membrane is observed in 10% of all pregnancies, about 60-80% of PROM is observed in term pregnancies and 20-40% of PROM is observed in pregnancies lower than 37th gestational week.^[6] PPRM is observed in 2-3% of all pregnancies and it is the most significant reason for preterm labor.^[8] Spontaneous preterm labors before 32nd gestational week are frequently accompanied by clinical or sub-clinical infection symptoms. It is together with long-term morbidity in newborns. The incidence rate is quite high in subsequent pregnancies.

Spontaneous preterm labors after 32nd gestational weeks are frequently associated with the increase in uterine contraction frequency and with increased uterine volume (polyhydramnios, multiple pregnancies). It is less likely complicated by infection. Microorganisms associated with prematurity are *Neisseria gonorrhoea*, group B streptococci, *Bacteriodes* species and other anaerobes, *Trichomonas vaginalis*, *Chlamydia trachomatis* and microplasmas.^[5,6,9-12] In many studies, bacterial vaginosis has been found as associated with preterm labor and PPRM.^[1,5]

The most significant complications in preterm PROM are prematurity due to preterm labor, hypoxia and asphyxia associated with umbilical cord compression or cord prolapse, pulmonary hypoplasia and fetal deformities.^[4,6]

After PPRM diagnosis is confirmed, maternal and/or fetal indications that will require emergency delivery should be analyzed. The most emergency ones among them are bradycardia associated with cord pro-

lapse and compression for fetal indications, and chorioamnionitis. This wide range is affected by gestational age, latent period duration, accompanying medical and obstetric complications, infection, positive vagina culture, nonreactive non-stress test (NST), variable deceleration and presentation type.^[6] Primary approach in the treatment for PPRM is to prevent premature labor and to decrease infection risk for fetus and mother in the meanwhile, and to prevent amniotic fluid loss and fetal distress development.

In our study, we analyzed perinatal outcomes of pregnant with PPRM who applied to our clinic.

Methods

The study was designed as a cross-sectional study. Cases included into the study were chosen among pregnant with PPRM who applied to Perinatology Department, Cerrahpaşa Medical Faculty of Istanbul University between January 2009 and July 2011. Pregnants who were between 26th and 37th gestational weeks and without any obstetric and maternal pathological symptoms were included into the study. The study was not continued in the presence of maternal (diabetes mellitus, cardiac disease, preeclampsia-eclampsia, ablatio placentae, multiple pregnancy, polyhydramnios, acute pyretic disease) and fetal (severe intrauterine growth retardation, dead fetus, near-fatal fetal anomaly) factors.

Preterm PROM diagnosis has been made by considering anamnesis of patient and by observing active water break during dry vaginal speculum examination. The diagnosis was made in patients, who had no active water break, through pH measurement by vaginal litmus paper. Additionally, the diagnosis in all patients was confirmed by conducting AmniSure test which is more precise (AmniSure, N-Dia Inc., New York, NY, USA; it is a single-step *immunoassay* test. The test is done by using monoclonal antibody pairs in order to determine placental alpha microglobulin [PAMG-1] protein which is less on cervicovaginal region after membrane rupture. PAMG-1 is a protein defined by the cell on desidual section of placenta. PAMG-1 is within amniotic fluid during pregnancy). If patients were on active labor or if clinical findings of chorioamnionitis were detected during admission, such patients were not included into the study. Gestational week was determined according to last menstrual period.

Additionally, last menstrual period was confirmed by the measurement of crown-rump length (CRL) performed on first trimester.

All patients were informed about the study by informed consent prepared previously. All patients admitted to the hospital and followed-up in the maternity ward for vital symptoms, uterine sensitivity and daily NST.

Four g/day ampicilline was administrated to all patients empirically. Antibiotics were changed according to antibiogram results for the patients who had over 100,000 colonies according to urinary colony count. Antibiotherapy was maintained uninterruptedly for seven days. 2 doses of 12 mg betamethasone were administered intramuscularly in order to provide fetal lung maturation in all pregnant who below 34th gestational week.

When active labor began, fetal distress condition was observed and chorioamnionitis findings were confirmed (maternal fever over 38 °C, uterine sensitivity, malodorous discharge, maternal tachycardia, fetal tachycardia 'above 160 beat/minute', elevated white blood cell count '15,000 leucocyte/microliter and above', increased CRP), conservative approach was ended. Patients were delivered by normal delivery, normal delivery with induction and cesarean according to obstetric indications. Delivery data of patients (age and parity of pregnant, PPRM time, PPRM follow-up period, whether induction was performed or not, delivery type, cesarean indication, birth weight, 1st and 5th minute Apgar scores of baby, gender of baby) were recorded after delivery. Neonatal sepsis diagnosis was made by the presence of clinical symptoms (paleness, lethargy, irritability, apnea, respiratory distress, bradycardia, hypotension, vomiting, fever) and/or positive blood and gastric aspirate culture. Percentage, average, standard deviation, minimum and maximum values were used in the descriptive analysis.

Results

In our study, 40 patients with PPRM were taken into clinical gestational follow-up. Mean age of our cases was 31.2 ± 5.3 , mean gravida was 2.1 ± 1.3 and mean parity was 0.7 ± 0.3 (Table 1). Mean gestational week where membrane rupture occurred in PPRM cases was 32.5 ± 3.3 (min.: 26.0 – max.: 36.0). Mean labor week of our cases was 33.5 ± 3.19 (min.: 27.0 – max.: 37.0) (Table 1). Mean follow-up period of PPRM cases was 5.8 ± 2.6 (min.: 3.0 – max.: 15.0) days.

Table 1. Distribution of preterm premature rupture of membrane (PPROM) cases according to their demographic data.

Distribution of PPRM cases (mean values)	
Age	31.2
Gravida	2.1
Parity	0.7
Birth weight	2,184.4
Delivery week	33.5

Maternal CRP was high in 75.0% of PPRM cases (n=30). Elevated white blood cell count was present in 80.0% of cases (n=32).

Among PPRM cases, 57.5% of them were delivered by normal delivery with induction, 12.5% of them by normal delivery and 30% of them by cesarean (Table 2). While 41.7% of cesarean indications were fetal distress, 33.3% of them were old cesarean and 25.0% of them were head-pelvis incompatibility.

When PPRM presence was analyzed according to genders of babies, PPRM rate was found as 59.1% in male babies and as 43.8% in female babies. There is statistically no significant difference between baby genders in terms of PPRM presence ($p=0.186$).

Table 2. Distribution of preterm premature rupture of membrane (PPROM) cases according to their delivery types.

		Count	%
Delivery type	Delivery with induction	23	57.5
	Normal delivery	5	12.5
	Cesarean	12	30.0
Total		40	

Mean birth weight of our cases was 84.38 ± 757.8 (min.: 400.0 – max.: 3280.0) (**Table 1**). Mean 1st and 5th minute Apgar scores were found as 5.74 and 7.25, respectively. Neonatal sepsis frequency was found as 20.0% (8/40) in PPROM cases.

Discussion

Premature rupture of membrane is an obstetric problem which has indeterminate etiology and is difficult to diagnose, associated with critical maternal, fetal and neonatal risks, and has various and controversial approach strategies.

Although PROM is seen in most of the cases after 37th gestational week, it is considered that 10% of all pregnancies usually have it.^[13] Preterm PROM is seen in about 2% of all pregnancies.^[14-16] PPROM incidence rate registered for any hospital is associated with perinatal care level provided and this incidence rate may be about 5% of all pregnancies who deliver for a hospital who accept fetal-maternal cases.^[17] The situation frequently occurring in PROM cases is the continuous or intermittent sudden vaginal discharge at less or high amounts. It is not so easy to diagnose only by anamnesis. Examination by sterile speculum, Valsalva maneuver and nitrazine test applications may help the diagnosis. Digital examination should be avoided as much as possible.^[18-20] In our study, the diagnosis was tried to be made by anamnesis and speculum examination. In doubted cases, the diagnosis was confirmed by AmniSure (single-step immunoassay test).

The most significant factor increasing perinatal morbidity and mortality associated with PPROM is prematurity. It has been shown in many studies that even the slightest changes in gestational week significantly affect mortality and morbidity of newborn.^[21] While delivery begins within first 24 hours following membrane rupture at a rate of 90%, the rate is 50% in deliveries between 28th and 34th gestational weeks and 80-90% of them begin within one week.^[22-24] In our study, mean follow-up period of patients was observed as 5.8 ± 2.6 days (min.: 3 days – max.: 15 days).

In latest studies, the rate of reported neonatal sepsis incidence is between 2% and 4% for PPROM cases.^[25-27] The rate of neonatal sepsis incidence was found as 20% (8/40) in our study. When compared with the literature, it was found that the rate of our clinic is higher. It is considered that the result of our study is associated with some subjective criteria (pale-

ness, lethargy, irritability, apnea, vomiting, fever, etc.) we used when diagnosing neonatal sepsis and with low gestational week of our cases.

When we analyzed the demographic data of our cases, we observed that the mean age was higher in PPROM cases while they had low gravida and parity. It was seen that PPROM cases were averagely at their 32nd gestational week (minimum: 26th week - maximum: 36th week) (**Table 1**). In our study, 65% of fetus were male while 35% of them female in PPROM cases. No significant difference was observed between fetus genders in terms of PPROM ($p=0.186$). When fetuses with neonatal sepsis were analyzed according to their genders, the rate of neonatal sepsis incidence was 27.3% in male fetuses while it was 0% in female fetuses. There was statistically a significant difference between genders in terms of the neonatal sepsis presence ($p=0.001$). We associated this result with the low gestational week of PPROM male fetuses.

Hospitalization of patients with PPROM includes keeping mother and fetus under clinical observation. The role of bed rest is controversial but it may help diagnosis by making amniotic fluid to pond within posterior fornix. It is asserted to examine fetal well-being by cardiotocography (non-stress test) and biophysical profile.^[28] In our study, we performed the follow-up of all PPROM cases by hospitalizing them and the follow-up of fetal well-being by non-stress test.

There are valid evidences that corticosteroids should be administered before 34th gestational week in order to provide fetal lung maturation in PPROM treatment.^[29] However, using corticosteroids at recurrent doses on PPROM cases with prolonged latent phase is controversial.^[30] In our study, as a routine protocol of our clinic, we applied two doses corticosteroid treatment as twelve hours apart to all PPROM cases before 34th gestational week.

When tocolytic agents are taken into account, tocolysis can be done at least for 48 hours if maternal corticosteroid is required and if there is no apparent infection. However, there is no sufficient evidence supporting this approach. Under these conditions, physicians should be cautious and suspicious in terms of intrauterine infection if tocolytic treatment will be initiated. Using tocolytics are supported in order to facilitate maternal-fetal transfer to a suitable tertiary center. However, evidences we have are limited.^[30-33]

In our study, tocolytic treatment was not applied to any case diagnosed as PPRM in accordance with the routine practices of our clinic. Administering antibiotics to mother cures neonatal outcomes by preventing infectious morbidity in fetus and perhaps prolonging latent period. Primary target of antibiotic use in PPRM during conservative treatment is to prevent neonatal morbidity and mortality which poses a significant risk in this group. Prophylactic antibiotics cause gestational period to be prolonged since both they protect newborn against infection in antenatal and postnatal periods, and they prevent intrauterine desidual infection development.^[34-36] It was found in the latest Cochrane compilation related with the antibiotic use in PPRM.^[37] that there is a decrease in maternal infection, a delay in labor, a decrease in neonatal infection and a decrease in the newborn number requiring surfactant or oxygen treatment within 28 days. However, no decrease was observed in necrotising enterocolitis, major cerebral abnormality, respiratory distress syndrome, stillbirth or neonatal death rates. In our study, antibiotherapy was applied to all cases beginning the day when PPRM was detected. It is considered best to deliver by cesarean in PPRM cases, when especially there is breech presentation, gestational age is below 32nd week and estimated fetal weight is below 1,500 gram.^[38] 30% of PPRM cases in our study were delivered by cesarean.

Conclusion

In conclusion, PPRM is an obstetric problem affecting perinatal outcomes. Patients should be examined carefully and all factors, especially gestational week and infection symptoms, should be taken into consideration and appropriate treatment method should be planned. PPRM cases should be followed up and treated especially in advanced centers which have neonatal intensive care units.

Conflicts of Interest: No conflicts declared.

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