remature rupture of the membranes (PROM) is an unpredictable event, which constitutes one of the most important dilemmas in obstetric practice.¹ It is defined as rupture of fetal membranes more than 6 hours before the onset of uterine contractions. When PROM occurs before 37 week of gestation, it is named as preterm premature rupture of the membranes (PPROM).² At term, PROM complicates about 8-10% of all pregnancies, however PPROM incidence is 2-3% only.³⁴ Premature rupture of the membranes is the leading identifiable cause of preterm delivery and accounts for approximately 34% of all premature births.⁵ It is more common in low socio-economic groups, teenagers, single women, smokers and those having sexually transmitted organisms cultured from cervix or vagina in the first half of pregnancy.⁵⁻⁹ Premature rupture of membranes can result from a wide array of mechanisms acting individually or jointly.¹⁰⁻¹² Although the exact mechanism is not known but the mounting evidence implicates the inflammation of chorionic membranes.¹³⁻¹⁵ Inherent weakness of membranes (altered collagen III), urinary tract infections, incompetent cervix, smoking, polyhydramnios, multiple gestation, antepartum hemorrhage/vaginal bleeding, previous PROM delivery and poor nutrition are some of the contributing factors.²⁻⁵⁻⁹⁻¹⁶⁻¹⁹ The fetal matrix

Objective: To study the outcomes of pregnancies complicated with preterm premature rupture of the membranes (PPROM) between 26-36 week gestation.

Methods: A retrospective study of 36670 pregnancies registered and managed in the Department of Obstetrics and Gynecology, King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia (KSA) from March 1993 to February 2003.

Results: Two hundred and twenty cases of PPROM (0.6%) were registered and treated expectantly out of 36670 total pregnancies registered during the study period. The majority of the cases (38.6%) were delivered within 72 hours of premature rupture of the membranes (PROM). Only 2.3% of the cases were prolonged to a latency period of more than one month. Maternal morbidity included chorioamnionitis (20.9%), postpartum endometritis (6.8%), abruptio placenta (4%) and septicemia (0.5%). The prenatal survival rate was 94.5% whereas neonatal outcomes included neonatal mortality (5.5%), respiratory distress (15.9%), sepsis (7.7%), and necrotizing enterocolitis (3.1%). Our study showed a positive correlation between increasing maternal age and cesarean section; increased maternal and neonatal infection rates with prolonged latency; and increased risk of neonatal infection among mothers having chorioamnionitis.

Conclusion: The incidence of PPROM in KSA is low. Ultimate goal of therapy must be safety of the mother first. Expectant management should be the rationale if fetal immaturity exists. Induction of labor in PPROM patient ≥ 34-week-gestation is a logical approach to minimize maternal infectious morbidity.
Metallo-proteinases (MMPs) are involved in membrane growth in response to growing pregnancy, which under certain pathological conditions are overactivated, leading to membrane destruction and rupture before term.\textsuperscript{20-25} The structural weakness of membranes may result from raised inflammatory cytokines, calcium and prolactin in amniotic fluid and shearing forces generated by the uterine contractions in response to prostaglandin E2 and fetal calcitroic hormones.\textsuperscript{10,26} Labor, almost always, follows PROM and approximately 50-90\% of these patients enter spontaneous labor within 24 hours, however, the delay between PROM and the onset of labor varies.\textsuperscript{5} The chances of infection increase as the time between PROM and labor increases.\textsuperscript{14} Pre-term premature rupture of the membrane leads to premature delivery, infections of mother or fetus and compression of umbilical cord.\textsuperscript{27-36} Considering such serious consequences of PPROM, we decided to find out the outcome of conservative management of pregnancies with PPROM between 26-36 weeks of gestation.

Methods. Two hundred and twenty singleton pregnancies complicated with PPROM between 26-36 weeks of gestation and managed expectantly, were studied retrospectively in the Department of Obstetrics and Gynecology, King Khalid University Hospital, Riyadh, KSA, from first March 1993 through 28th February 2003.

Inclusion criteria. All patients with documented evidence of PPROM between 26-36 weeks gestation were included in the study.

Exclusive criteria. Any complications other than PPROM, involving maternal or fetal outcomes, such as, intrauterine growth reduction (IUGR), diabetes, pre-eclampsia, fetal malformations and others, were regarded as exclusion of that case from the study group.

Diagnosis. Diagnosis of PPROM cases was confirmed by visualization of amniotic fluid (ferning/arborization and nitrazine positive) in vaginal vault and ultrasound confirmation of oligohydramnios.

Management. All cases of PPROM were monitored in the labor room for at least 24 hours. Then stable patients without evidence of infection or labor were transferred to antenatal ward for observation, strict bed rest, serial ultrasound examination and frequent monitoring for infection and premature labor. Evaluation of fetal well-being was carried out by the biophysical examination. Expectant management (bed rest, prophylactic antibiotics, corticosteroids, tocolytics, surveillance for infection) in hospital was the rationale if pregnancy found to be less than 32 week or fetal lung immaturity existed.

In a selected group of patients (cervical dilatation <4 cm and gestational age <34 week) having spontaneous preterm labor but no infection, vaginal bleeding or fetal distress, the tocolytic agents were used to delay the delivery for 36 week gestation (at least 48 hours), and corticosteroids were injected to enhance fetal lung maturity. Indications for delivery included advanced labor, fetal distress, fetal death, failed tocolysis, vaginal bleeding or chorioamnionitis. Chorioamnionitis was treated with intravenous antibiotics during labor or prior to cesarean section.

Results. Among the total 36670 deliveries, 220 (0.6\%) singleton pregnancies complicated with PPROM were registered and treated conservatively.

\begin{figure}
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\includegraphics[width=\textwidth]{figure1.png}
\caption{Latent period exhibited by preterm premature rupture of membranes patients in expectant management.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Neonatal morbidity in expectant management of PPROM patients between 26-36 week gestation. (PPROM - Preterm premature rupture of membranes, RDS - Respiratory distress syndrome, IVH - Intra-ventricular hemorrhage, NEC – Necrotizing enterico-colitis).}
\end{figure}
during 10-year study period. Age of the patients ranged from 16-45 years with a mean of 30.5 year, however the mean gestational age at PPROM was 31.8 ± 3 week.

Maternal outcomes. Seventy-three (33.2%) patients were primigravida, whereas 127 (57.8%) had one or more children. Eighty-five (38.6%) patients delivered within 72 hours of PPROM, 52 (23.6%) patients delivered within 7 days, 45 (20.5%) patients within 2 weeks and 33 (15%) patients within one month. Only 5 (2.3%) deliveries were prolonged to a latency of more than one month (Figure 1). One hundred and forty-seven patients (66.8%) were delivered by vaginal delivery, 70 patients (31.8%) had lower segment cesarean section (LSCS) and only 2 needed instrumental vaginal delivery. High vaginal swab (HVS) culture was positive in 42% (93 patients) and negative in 58%. Forty-six (20.9%) patients had amnionitis, 15 (6.8%) postpartum endometritis, 9 (4%) abruption of placenta, and only one (0.5%) patient with chorioamnionitis developed septicaemia before delivery. No maternal death was encountered in present study.

Neonatal outcomes. The prenatal survival rate was 94.5% (208 out of 220). Thirty-five (15.9%) infants delivered at 26-28 weeks, with survival rate of 41%, 56 (25.5%) delivered at 29-31 weeks with survival rate of 85%, 89 (40.5%) infants delivered at 32-34 weeks, the survival rate was 98%, whereas, 40 (18.2%) infants delivered at 35-36 weeks gestation had a 100% survival rate. Out of 12 (5.5%) neonatal deaths recorded in this study, only 3 died of β-hemolytic streptococcal sepsis acquired within 72 hours of birth. The relative proportion of neonatal morbidity factors is shown in Figure 2.

Discussion. The management of patients with PPROM remains controversial. Immediate delivery entails the risks of prematurity in the infant, whereas conservative observation raises the concern of placing the mother and fetus both at risk of sepsis. Such patients should be counseled regarding the potential neonatal risks involved and they must be observed and managed at a tertiary care hospital with adequate neonatal intensive care unit (NICU) facilities. Multiple options for management are available in the absence of fetal distress, overt intrauterine infection and maternal indications for delivery. Unlike the PROM at term, management of PPROM is considerably more complicated and requires a thorough evaluation of gestational age, fetal position, presence of infection and feto-maternal well-being. All these variables are important contributors to the final outcome. Although the gestational age and presence or absence of chorioamnionitis determines the initial management of the patient, the overall goal is to manage the patient expectantly until she has reached a gestational age beyond, which neonatal morbidity and mortality is minimal and to achieve delivery before mother or fetus become infected. In expectant management the institution of antibiotics is advantageous in prolongation of pregnancy and reduction of fetal and maternal morbidity. In accordance with earlier studies, the use of antibiotics in our study reduced the incidence of chorioamnionitis to 21% and postpartum endometritis to 6.8%. Perinatal mortality in early PPROM (26-32 week gestation) results from the complications of prematurity but in late cases (32-36 week gestation) the relative contribution of infection becomes more important. Prophylactic antibiotics reduced neonatal morbidity in present study, example, respiratory distress syndrome (RDS) (15.9%), sepsis (7.7%) and necrotizing enterocolitis (3.1%). National Institute of Health (NIH) recommends the use of steroids for women with PPROM prior to 30-32 week gestation in the absence of clinical chorioamnionitis.

Corticosteroids administration is an effective intrapartum obstetric intervention to promote fetal pulmonary maturation before delivery of the preterm infant and in reducing perinatal morbidity. Approximately 75% of the PPROM patients managed expectantly deliver within one week. In our study, 20% of women having amnionitis delivered within the first 72 hours of rupture of the membranes and the use of steroids did not increase the incidence of maternal infection. These results confirm the earlier findings reported by Haque. In present study, the incidence of postpartum endometritis was 2%, which is less than the previous reported studies. We observed only one incidence of maternal septicaemia, whereas no maternal death was encountered. The neonatal survival rate in this study was fairly high, however no clinically significant neonatal advantage to expectant management of PPROM at 32-34 weeks gestation was achieved and induction with oxytocin with shorter duration of labor appeared to reduce the risk of neonatal infections. Although the cause of PROM is not known, however our study shows a positive correlation between increasing maternal age and cesarean section, increased maternal and neonatal infection rates with prolonged latency and increased risk of neonatal infection among mothers having clinical chorioamnionitis.

In conclusion, the ultimate goal of therapy must be safety of the mother first, then consideration for optimum neonatal outcome. Majority of the PPROM patients have infection or advanced labor within 3-7 days of PROM, thus, forcing the obstetrician to accomplish delivery despite fetal immaturity. In the remaining patients, the timing of delivery is a difficult decision for obstetricians. Aggressive attempts to delay delivery may expose
the mother to severe morbidity. In present study, we found that neonatal mortality and morbidity reaches a minimum at 32-34 weeks gestation. Therefore, induction of labor in patients who presented with PROM at or beyond 34 week gestation is a logical approach in order to minimize maternal infectious morbidity, as neonatal mortality and morbidity have already reached minimum levels at that stage of gestation. However, at earlier stages of gestation, conservative management with careful surveillance for infection and fetal distress is a rational approach to the problem, to achieve further in utero fetal maturation. The obstetrician and neonatologist should work as a team to ensure optimal care for mother and fetus. Future studies are wanted to identify the optimal methods for prolongation of latency interval while avoiding compression deformities, infection and pulmonary hypoplasia. 

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Outcome of pregnancies with PPRM ... Khashoggi