Outcome of pregnancies with preterm premature rupture of membranes

Tariq Y. Khashoggi, *ABOG, M.Med.*

ABSTRACT

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 placentae (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.

Saudi Med J 2004; Vol. 25 (12): 1957-1961

Premature 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.[3-4] Premature rupture of the membranes is the leading identifiable cause of preterm delivery and accounts for approximately 34% of all premature births.[4-5] 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 chorioamnionic 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

From the Department of Obstetric and Gynecology, King Khalid University Hospital, King Saud University, Riyadh, *Kingdom of Saudi Arabia.*

Received 14th April 2004. Accepted for publication in final form 24th August 2004.

Address correspondence and reprint request to: Dr. Tariq Y. Khashoggi, Associate Prof. of Obstetrics and Gynecology, PO Box 81, Riyadh 11411, *Kingdom of Saudi Arabia*. Tel. +966 (1) 5910000 ext. 3840/3848. Fax. +966 (1) 5910000 ext. 3855. E-mail: khashoggit@ngha.me.sa

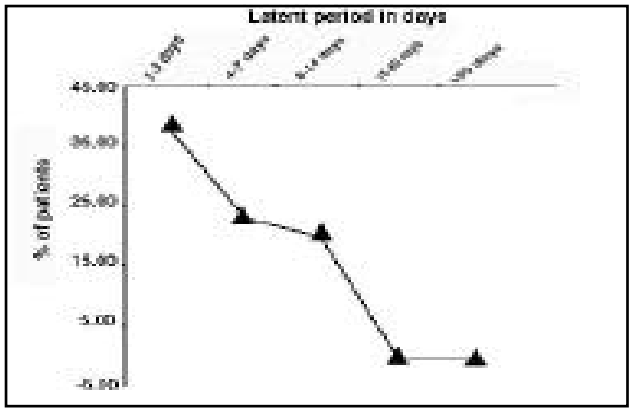

Figure 1 - Latent period exhibited by preterm premature rupture of membranes patients in expectant management.

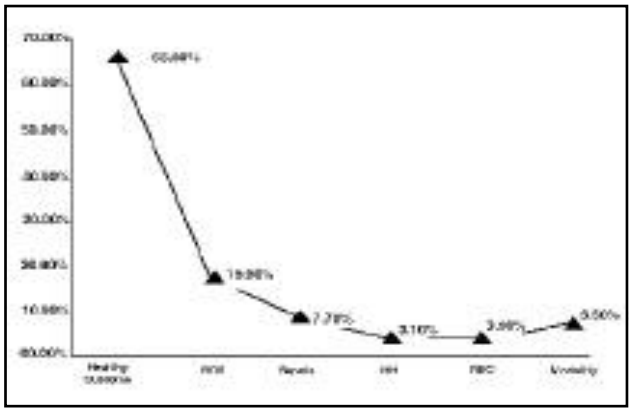

Figure 2 - Neonatal morbidity in expectant management of PPROM patients between 26-36 week gestation. (PPROM - Preterm premature rupture of membranes, RDS - Respiratory distress syndrome, IVH - Intra-ventricular hemorrhage, NEC – Necrotizing entero-colitis).

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.[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.[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.[5] The chances of infection increase as the time between PROM and labor increases.[14] Pre-term premature rupture of the membrane leads to premature delivery, infections of mother or fetus and compression of umbilical cord.[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

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 septicemia 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.[37-38] 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.[2,5,7,18] 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.[39-44] 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.[45-46] In expectant management the institution of antibiotics is advantageous in prolongation of pregnancy and reduction of fetal and maternal morbidity.[45,47] In consistence with earlier studies, the use of antibiotics in our study reduced the incidence of chorioamnionitis to 21% and postpartum endometritis to 6.8%.[47-50] 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.[51-52] 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.[53] Corticosteroids administration is an effective intrapartum obstetric intervention to promote fetal pulmonary maturation before delivery of the preterm infant and in reducing perinatal morbidity.[54-58] Approximately 75% of the PPROM patients managed expectantly deliver within one week.[56,49] 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.[59] 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 septicemia, 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.[40] 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.[60-61]

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 rationale 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.

Acknowledgment. The author would like to thank Prof. Abdul Aziz Al-Meshari and Dr. Muhammad Saeed Shafi for technical contribution and Miss Denden Ponsaran for secretarial assistance.

References

1. Gibbs RS. Premature rupture of membranes. In: Scott JR, Gibbs RS, Karlan BY, Haney AF, editors. Danforth's Obstetrics and Gynecology. 9th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2003: 191-201.
2. Toth PP, Jothivijayarani A. Concise definitions, diagnosis and management for family practice physicians on PROM. ***Obstet Gynecol Clinics North Am*** 1992; 19: 339-351.
3. Ventura SJ, Martin JA, Curtin SC, Mathews TJ. Report of final natality statistics, 1995. Monthly vital statistics report; Vol 45, no. 11, supp. Maryland: National Center for Health Statistics, 1997.
4. Smith JF. Premature rupture of membranes. Dr. Josef F. Smith Med Library, 2004. Available from URL: http://www.mommyguide.com/prom/2003.
5. Wilkes PT, Galen H. Premature rupture of membranes. Emedicine, 2002. Available from URL: http://www.emedicine.com.med/topic3246.html.
6. Naeye R. Factors that predispose to premature rupture of membranes. ***Obstet Gynecol*** 1982; 60: 93.
7. Keirse MJNC, Ohlsson A, Treffers PE, Kanhai HHH. Prelabour rupture of membranes preterm. In: Chalmers I, Enkin M, Keirse MJNC, editor. Effective care in pregnancy and childbirth. Oxford (UK): Oxford University Press; 1989. p. 666-693.
8. Harger JH, Hsing AW, Tuomala RE, Gibbs RS, Mead PB, Eschenbach DA, et al. Risk factors for preterm premature rupture of fetal membranes: a multicenter case-control study. ***Am J Obstet Gynecol*** 1990; 163: 130-137.
9. Hadley C, Main D, Gabbe S. Risk factors for preterm premature rupture of fetal membranes. ***Am J Perinatol*** 1990; 7: 374-379.
10. French JI, McGregor JA. The pathobiology of premature rupture of membranes. ***Semin Perinatol*** 1996; 20: 344-368
11. Schucker JL, Mercer BM. Midtrimester premature rupture of the membranes. ***Semin Perinatol*** 1996; 20: 389-400.
12. Parry, Samuel, and Jerome F. Strauss III. Premature rupture of the fetal membranes: mechanisms of disease. ***N Engl J Med*** 1998; 338: 663-669.
13. McGregor JA, French JI. Evidence-based prevention of preterm birth and rupture of membranes: infection and inflammation. ***J SOGC*** 1997; 19: 835-852.
14. Lamont RF. The role of infection in preterm labour and birth. ***Hosp Med*** 2003; 64: 644-647.
15. Goldenberg RL, Culhane JF. Infection as a cause of preterm birth. ***Clin Perinatol*** 2003; 30: 677-700.
16. Kanayama N, Terao TYK. Collagen types in normal prematurely ruptured amniotic membranes. A***m J Obstet Gynecol*** 1985; 153: 899.
17. Vadillo-Ortega F, Gonzalez-Avilla G, Karclimen S. Collagen metabolism in premature rupture of amniotic membranes. ***Obstet Gynecol*** 1990; 75: 84-90.
18. Pernoll ML. Premature Rupture of Membranes. In: DeCherney AH, Martin L, Pernoll ML, editors. Current Obstetric and Gynecologic Diagnosis and Treatment. Norwalk (CT): Appleton and Lange; 1994. p. 326-339.
19. Odunsi K, Rinaudo P. Premature rupture of membranes. Hygeia 2004; 2: 1-6. Available on URL: http://www.hygeia.org/poems16.htm
20. Fortunato SJ, Menon R, Lombardi SJ. Expression of a progelatinase activator (MT1-MMP) in human fetal membranes. ***Am J Reprod Immunol*** 1998; 39: 316-322.
21. Athayde N, Edwin SS, Romero R, Gomez R, Maymon E, Pacora P, Menon R. A role of matrix metalloproteinases-9 in spontaneous rupture of the fetal membranes. ***Am J Obstet Gynecol*** 1998; 179: 1248-1253.
22. Fortunato SJ, Menon R, Lombardi SJ. Presence of four tissue inhibitors of matrix metalloproteinases (TIMP 1, 2, 3 and 4) in human fetal membranes. ***Am J Reprod Immunol*** 1998; 40: 395-400.
23. Athayde N, Romero R, Gomez R, Maymon E, Pacora P, Mazor M, et al. Matrix metalloproteinases-9 in preterm and term parturition. ***J Matern Fetal Med*** 1999; 8: 213-219.
24. Fortunato SJ, Menon R. Screening of novel matrix metalloproteinases (MMPs) in human fetal membranes. ***J Assist Reprod Genet*** 2002; 19: 483-486.
25. Fortunato SJ, Menon R. IL-1 beta is a better inducer of apoptosis in human fetal membranes than IL-6. ***Placenta*** 2003; 24: 922-928.
26. Shaarawy M, El-Minawi AM. Prolactin and calcitropic hormones in preterm premature rupture of membranes. ***Int J Gynaecol Obstet*** 2004; 84: 200-207.
27. Gabbe SG, Ettinger BB, Freeman RK. Umbilical cord compression associated with amniotomy: Laboratory observations. ***Am J Obstet Gynecol*** 1976; 26: 353-358.
28. Nimrod C, Varela-Gittings F, Machin G. The effect of very prolonged membrane rupture on fetal development. ***Am J Obstet Gynecol*** 1984; 148: 540-546.
29. Nimrod C, Davies D, lwanick S. Ultrasound prediction of pulmonary hypoplasia. ***Obstet Gynecol*** 1986; 68: 495-500.
30. Rotschild A, Ling EW, Puterman ML. Neonatal outcome after prolonged preterm rupture of the membranes. ***Am J Obstet Gynecol*** 1990; 162: 46-50.
31. Seo K, Mc Gregor JA, French JI. Preterm birth is associated with increased risk of maternal infection. ***Obstet Gynecol*** 1992; 79: 75-80.
32. Vergani P, Ghidini A, Locatelli A. Risk factors for pulmonary hypoplasia in second trimester premature rupture of membranes. ***Am J Obstet Gynecol*** 1994; 170: 1359-1364.
33. Lauria MR, Gonik B, Romero R. Pulmonary hypoplasia: pathogenesis, diagnosis, and antenatal prediction. ***Obstet Gynecol*** 1995; 86: 466-475.
34. Ananth CV, Savitz DA, Williams MA. Placental abruption and its association with hypertension and prolonged rupture of membranes: a methodologic review and meta-analysis. ***Obstet Gynecol*** 1996; 88: 309-318.
35. Kilbride HW, Yeast J, Thibeault DW. Defining limits of survival: lethal pulmonary hypoplasia after midtrimester premature rupture of membranes. ***Am J Obstet Gynecol*** 1996; 175: 675-681.

36. Merenstein GB, Weisman LE. Premature rupture of membranes: Neonatal consequences. ***Semin Perinatol*** 1996; 20: 750-801.
37. Naef RW, Albert JR, Ross EL. Premature rupture of membranes at 34 to 37 weeks' gestation: aggressive versus conservative management. ***Am J Obstet Gynecol*** 1998; 178: 126-130.
38. Edwards RK, Duff P, Ross KC. Amniotic fluid indices of fetal lung maturity with preterm premature rupture of membranes. ***Obstet Gynecol*** 2000; 96: 102-105.
39. Guise JM, Duff P, Christian JS. Management of term patients with premature rupture of membranes and an unfavorable cervix. ***Am J Perinatol*** 1992; 9: 56-60.
40. 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: 1005-1010.
41. Hannah ME, Ohlsson A, Wang E, Myh T, Farine D, Hewson S, et al. Maternal Colonization with Group B Streptococcus and Prelabor Rupture of Membranes. ***Am J Obstet Gynecol*** 1997; 177: 780-785.
42. Novak-Antolic Z, Pajntar M, Verdenik I. Rupture of the membranes and postpartum infection. ***Eur J Obstet Gynecol Reprod Biol*** 1997; 71: 141-146
43. Gareth P, Seaward R, Hannah ME. International multicenter term PROM study: Evaluation of predictors of neonatal infection in infants born to patients with premature rupture of membranes at term. ***Am J Obstet Gynecol*** 1998; 179: 635-639.
44. Mercer BM. Management of preterm premature rupture of the membranes. ***Clin Obstet Gynecol*** 1998, 41: 870-882.
45. Hannah ME, Hodnett ED, Willan A. Prelabor rupture of the membranes at term: expectant management at home or in hospital? The Term PROM Study Group. ***Obstet Gynecol*** 2000; 96: 533-538.
46. Kenyon S, Boulvain M, Neilson J. Antibiotics for preterm rupture of membranes. ***Cochrane Database Syst Rev*** 2003; 2: CD001058.
47. Mercer BM, Miodovnik M, Thurnau GR, Goldenberg RL, Das AF, Ramsey RD, et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes. A randomized controlled trial. ***JAMA*** 1997; 278: 989-995.
48. Duff P. Antibiotic treatment in patients with preterm premature rupture of membranes. ***OBG Management Online*** 2001; 13: 54-66.
49. Mercer BM, Goldenberg RL, Das AF, Thurnau GR, Bendon RW, Miodovnik M, et al. What we have learned regarding antibiotic therapy for the reduction of infant morbidity after preterm premature rupture of the membranes. ***Semin Perinatol*** 2003; 27: 217-230.
50. Fidel P, Ghezzi F, Romero R, Chaiworapongsa T, Espinoza J, Cutright J, et al. The effect of antibiotic therapy on intrauterine infection-induced preterm parturition in rabbits. ***J Matern Fetal Neonatal Med*** 2003; 14: 57-64.
51. Cox SM, Leveno KJ. Intentional delivery versus expectant management with preterm ruptured membranes at 30-34 weeks' gestation. ***Obstet Gynecol*** 1995; 86: 875-879.
52. Farooqi A, Holmgren PA, Engberg S: Survival and 2-year outcome with expectant management of second trimester rupture of membranes. ***Obstet Gynecol*** 1998; 92: 895-901.
53. Wright LL, Verter J, Younis N. Antenatal corticosteroid administration and neonatal outcome in very low birth weight in infants; NICHD Neonatal research network. ***Am J Obstet Gynecol*** 1995; 173: 269-272.
54. Crowley P. Antenatal corticosteroid therapy; A meta-analysis of the randomized trials, 1972 to 1994. ***Am J Obstet Gynecol*** 1995; 173: 322-335.
55. Walling AD. Corticosteroids and Antibiotics for Management of PROM. ***Am Fam Physician*** 1997; 55: 1960 -1965.
56. Whitelaw A, Thoresen M: Antenatal steroids and the developing brain. ***Arch Dis Child Fetal Neonatal Ed*** 2000; 83: 154-157.
57. Vidaeff AC, Doyle NM, Gilstrap LC. Antenatal corticosteroids for fetal maturation in women at risk for preterm delivery. ***Clin Perinatol*** 2003; 30: 825-840.
58. Lee MJ, Davies J, Guinn D, Sullivan L, Atkinson MW, McGregor S, et al. Single versus weekly courses of antenatal corticosteroids in preterm premature rupture of membranes. ***Obstet Gynecol*** 2004; 103: 274-281.
59. Haque KN. Indications for anti-microbial therapy in babies after PROM: the Saudi Arabian experience. ***Postgraduate Doctor Middle East*** 1992; 16: 342-350.
60. Lewis DF, Fontenot MT, Brooks GG: Latency period after preterm premature rupture of membranes: a comparison of ampicillin with and without sulbactam. ***Obstet Gynecol*** 1995; 86: 392-395.
61. Dinsmoor MJ, Bachman R, Haney EI, Goldstein M, Mackendrick W. Outcomes after expectant management of extremely preterm premature rupture of the membranes. ***Am J Obstet Gynecol*** 2004; 190: 183-187.