OBSTETRICS

Expectant management of preterm premature rupture of membranes: is it all about gestational age?

Nir Melamed, MD, MSc; Avi Ben-Haroush, MD, MSc; Joseph Pardo, MD; Rony Chen, MD; Eran Hadar, MD; Moshe Hod, MD; Yariv Yogev, MD

OBJECTIVE: We sought to compare neonatal outcome in cases of uncomplicated preterm premature rupture of membranes (PPROM) (ie, no evidence of clinical chorioamnionitis, placental abruption, or fetal distress) with that of spontaneous preterm deliveries (PTDs) and to determine the effect of the latency period.

STUDY DESIGN: The study group included women with PPROM at gestational age $28^{0/7}$-$33^{6/7}$ weeks (n = 488). Neonatal outcome was compared with a matched control group of women with spontaneous PTD (n = 1464).

RESULTS: Neonates in the uncomplicated PPROM group were at increased risk for composite adverse outcome (53.7% vs 42.0%; $P <$ .001), mortality (1.6% vs 0.0%; $P <$ .001), respiratory morbidity (32.8% vs 26.4%; $P =$ .006), necrotizing enterocolitis, jaundice, hypoglycemia, hypothermia, and polycythemia. Neonatal adverse outcome was more likely in cases of latency period >7 days, oligohydramnios, male fetus, and nulliparity.

CONCLUSION: Consultation regarding prematurity-related morbidity in infants exposed to uncomplicated PPROM cannot be extrapolated from PTDs and should be stratified by the duration of the latency period and the other risk factors identified in the current study.

Key words: latency, neonatal, outcome, preterm premature rupture of membranes

Cite this article as: Melamed N, Ben-Haroush A, Pardo J, et al. Expectant management of preterm premature rupture of membranes: is it all about gestational age? Am J Obstet Gynecol 2011;204:48.e1-8.

Preterm premature rupture of membranes (PPROM) complicates 1-3% of all pregnancies,[1-4] and is associated with maternal and perinatal morbidity and mortality.[2,5] The optimal management of pregnancies complicated by PPROM remains unclear. Specifically, the issue of expectant management vs immediate delivery, especially in cases of PPROM occurring at ≥30 weeks of gestation, is controversial.[6-11]

In cases of preterm labor, perinatal outcome is largely affected by gestational age at delivery. For that reason, the common practice in cases of uncomplicated PPROM (ie, no evidence of clinical chorioamnionitis, placental abruption, or fetal distress) is expectant management, followed by labor induction when the risks of amnionitis exceeds the risk of prematurity, usually at around 32-34 weeks of gestation.

Nevertheless, it has been previously shown that a significant proportion of pregnancies with uncomplicated PPROM may involve subclinical chorioamnionitis.[12-15] Thus, considering the potential unfavorable intrauterine environment in the case of uncomplicated PPROM, it is uncertain whether neonatal outcome in these pregnancies can be directly extrapolated from that of newborns following spontaneous preterm labor at similar gestational age. Furthermore, it is possible that in cases of expectant management of uncomplicated PPROM, it is not only gestational age at delivery that should be taken into consideration, but also the duration of the latency period through which the fetus is exposed to a potentially unfavorable intrauterine environment.

Our aim was to compare neonatal outcome in cases of uncomplicated PPROM with that of spontaneous low-risk preterm deliveries (PTDs) at an equivalent gestational age, and to determine the effect of the latency period on neonatal outcome.

Materials and Methods

We conducted a retrospective cohort study in a single tertiary center from January 1995 through December 2007. The study group included all women diagnosed with PPROM at gestational age of $28^{0/7}$-$33^{6/7}$ weeks (PPROM group). We did not include cases of PPROM at <28 weeks because the controversy regarding expectant management vs immediate delivery in this subgroup is of less relevance. The control group was composed of the women presenting with spontaneous PTD (SPTD) immediately following each of the PPROM cases in the delivery logbook, matched by gestational age at delivery in a 3:1 ratio (SPTD group). Only low-risk women were included in the study and control groups; women with chronic hypertension, pregnancy-induced hypertensive complications, gestational or pregestational diabetes, placenta previa, placental abruption, amnionitis, oligohydramnios (only for the control group), multiple gestations, intrauterine growth restriction at presentation (birthweight <10th percen-

From the Department of Obstetrics and Gynecology, Helen Schneider Hospital for Women, Rabin Medical Center, and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

Presented at the 30th Annual Meeting of the Society for Maternal-Fetal Medicine, Chicago, IL, Feb. 1-6, 2010.

Received April 12, 2010; revised June 20, 2010; accepted Aug. 16, 2010.

Reprints not available from the authors.

0002-9378/$36.00

doi: 10.1016/j.ajog.2010.08.021

TABLE 1
Demographic and obstetric characteristics of women in PPROM and SPTD groups

Characteristic	PPROM group n = 488	SPTD group n = 1464	*P* value
Maternal age, y	29.9 ± 5.0	29.6 ± 5.4	.2
Age >35 y	80 (16.4)	219 (15.0)	.4
Nulliparity	204 (41.8)	948 (64.8)	< .001
Gestational age at delivery, wk	32.5 ± 1.8	32.5 ± 1.8	N/A
28	20 (4.1)	60 (4.1)	N/A
29	32 (6.6)	96 (6.6)	N/A
30	44 (9.0)	132 (9.0)	N/A
31	28 (5.7)	84 (5.7)	N/A
32	60 (12.3)	180 (12.3)	N/A
33	84 (17.2)	252 (17.2)	N/A
34	220 (45.1)	660 (45.1)	N/A
Operative vaginal delivery	12 (2.5)	39 (2.7)	.8
Cesarean section	212 (43.4)	879 (60.0)	< .001
Birthweight, g	1876 ± 431	1869 ± 631	.9
Oligohydramnios[a]	160 (32.8)	N/A	N/A
Latency period, d	8.2 ± 10.0	N/A	N/A
<2	190 (38.9)	N/A	N/A
2-7	124 (25.5)	N/A	N/A
>7	174 (35.7)	N/A	N/A

Data presented as mean ± SD or n (%).
N/A, not applicable; *PPROM*, preterm premature rupture of membranes; *SPTD*, spontaneous preterm delivery.
[a] Amniotic fluid index <50 mm at admission; women with oligohydramnios were excluded from control group.
Melamed. PPROM and neonatal outcome. Am J Obstet Gynecol 2011.

tile), cord pH <7.0, or 5-minute Apgar score <7 were excluded from both groups. The study protocol was approved by the local institutional review board.

Data were collected from patient's hospital charts and from the institutional computerized perinatal database. Neonatal outcome was compared between the study and control groups, stratified by gestational age at delivery and duration of the latency period.

PPROM was defined as spontaneous rupture of membranes occurring before the onset of active labor and $<37^{0/7}$ weeks of gestation. The diagnosis of PPROM was established on the basis of a history suggesting amniotic fluid leakage and a sterile speculum examination demonstrating either amniotic fluid passing through the cervix or fluid accumulation in the posterior vaginal fornix, and was confirmed by nitrazine paper reaction and fern pattern when necessary.

The latency period was defined as the time elapsed between onset of PPROM to spontaneous delivery, labor induction at $34^{0/7}$ weeks, or indicated delivery $<34^{0/7}$ weeks. Gestational age was determined by the patient's last menstrual period and, when available, confirmed by first-trimester ultrasound. Chorioamnionitis was diagnosed on a clinical basis that included maternal fever (>38°C), leukocytosis, fetal tachycardia, uterine tenderness, or foul-smelling amniotic fluid with no other source of infection.

Respiratory morbidity was defined as any of the following: the presence of respiratory distress syndrome, transient tachypnea of the newborn, bronchopulmonary dysplasia (BPD), apnea, or need for ventilatory support. Infectious morbidity was defined as the presence of culture-proven sepsis, meningitis, or pneumonia. Neurologic morbidity included convulsions, hypotonia, intraventricular hemorrhage (any grade), or periventricular leukomalacia (PVL). Composite neonatal outcome was defined as the presence of any of the following: respiratory, infectious, or neurologic morbidity (as defined above); neonatal death; necrotizing enterocolitis (NEC); need for phototherapy; hypoglycemia[16]; or hypothermia.[17]

According to our departmental protocol, all women with suspected PPROM at gestational age $<34^{0/7}$ weeks who are not in active labor and do not have signs of chorioamnionitis or placental abruption are admitted for expectant management, as follows. First, betamethasone is administrated at gestational age $>24^{0/7}$ and $<34^{0/7}$ weeks (12 mg of intramuscular Celestone chronodose [Schering-Plough Lab N.V., Brussels, Belgium] given twice at a 24-hour interval). Second, antibiotic treatment is initiated with intravenous ampicillin (2 g 4 times daily) and oral roxithromycin (150 mg twice daily) for 48 hours, followed by oral amoxicillin (250 mg 3 times daily) and oral roxithromycin (150 mg twice daily) for 5 days. Third, vaginal culture is taken at diagnosis of PPROM, and carriers of group B streptococcus (GBS) are identified and treated during labor.[18] If culture results are unavailable, patients are treated empirically with intravenous ampicillin during labor. Fourth, routine daily follow-up is conducted for evidence of active labor, infection, or well-being. Follow-up includes examination of body temperature, pulse, blood pressure, uterine tenderness, white blood cell count, nonstress test (twice a day), biophysical profile (twice a week), and estimated fetal weight evaluation (every 10-14 days). Vaginal examinations are avoided as long as the patient is asymptomatic and free of contractions. When indicated, sterile visual inspection of the cervix is preferred over digital examination. Fifth, labor is induced at $34^{0/7}$ weeks, either by vaginal prostaglandin E2 tablets or oxytocin. Cesarean section is performed on the basis of obstetric indications. Tocolytic treatment is avoided