



## Assessment of risk factors for survival of neonates born after second-trimester PPRM

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### ABSTRACT

**Objective:** Assess fetal risk factors which impact survival of infants delivered after second-trimester PPRM. **Study design:** Clinical records of 87 patients, who all had second-trimester rupture of membranes between 14+0 and 24+6 weeks of gestation treated January 1998 to July 2005 were reviewed regarding perinatal outcome. This study is based on 25 surviving infants.

**Results:** 13 of these 25 infants died in the hospital. Survivors had a higher birth weight ( $p=0.008$ ) and higher Apgar scores after 5 min ( $p=0.005$ ) than those infants dying. No differences in UA pH, the need of catecholamines and no association between histological verified chorioamnionitis and early onset sepsis were seen between survivors and nonsurvivors.

**Conclusion:** Higher gestational age at birth, higher birth weight, the absence of histologically verified chorioamnionitis and 5 min Apgar scores of  $\geq 6$  have positive prognostic value for survival of neonates delivered preterm after second-trimester PPRM.

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### 1. Introduction

Preterm premature rupture of membranes (PPROM) complicates about a third of all preterm deliveries [1,2] and entails a high risk of fetal and maternal morbidity. The main problems for surviving fetuses are bronchopulmonary dysplasia, cerebral white matter damage, retinopathy and motor and cognitive impairment [3–5]. Several studies have addressed the management of patients with PPRM during pregnancy, but it still remains unclear, which risk factors, especially after delivery, have impact on the survival of infants after PPRM. We analyzed neonatal characteristics that may predict survival. In this study we reviewed the perinatal outcome of pregnancies, which were all complicated by second-trimester rupture of membranes between 14+0 and 24+6 weeks of gestation and managed expectantly with close surveillance. We tried to assess issues that may influence the outcome of these preterm born infants and point out risk factors that might be predictors for survival.

### 2. Patients and methods

The clinical records of a total of 87 patients (Table 1) with preterm premature rupture of membranes at 14+0 to 24+6 weeks of gestation,

treated at the Department of Obstetrics and Gynecology of the Medical University of Graz, were reviewed between January 1998 and July 2005. The present study includes 25 neonates surviving after PPRM. Institutional review board (IRB) was not obtained because the institutional ethics committee does not require IRB approval for these types of retrospective studies. During this study period 20,633 deliveries occurred at our institution, therefore the frequency of women presenting with second-trimester rupture of membranes in this time period was 0.4% (87/20,633). Obstetric, neonatal and pediatric records were reviewed regarding gestational age at membrane rupture, gestational age at birth, signs of clinical chorioamnionitis defined according to the criteria of Gibbs et al. [6], mode of delivery, fetal gender and perinatal outcome. Neonatal morbidities such as intraventricular hemorrhage III–IV, periventricular leucomalacia, early onset sepsis, retinopathy, asphyxia and the need of catecholamines were recorded. Early onset of sepsis was diagnosed by the following parameters:  $I/T$  ratio of neutrophils  $>0.2$ , CRP  $>8$  mg/l and arterial hypotension.

A total of 24 women had to be excluded. Nine patients (10.3%) decided not to continue pregnancy after offering the choice of pregnancy termination. Additional 15 women were excluded, consisting of 4 women with membrane rupture after amniocentesis because of the significantly better perinatal outcome compared with pregnancies complicated by spontaneous preterm premature rupture of membranes at a similar gestational age [7], 7 women with regular uterine contractions indicating onset of labour at booking, 3 patients with clinical signs of chorioamnionitis at admission, and 1 woman with cervical incompetence and cerclage. Therefore the study is

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**Table 1**  
Characteristics of 87 patients with second-trimester rupture of membranes

Characteristics	Patients
Pregnancies	87
Age (years)	30
Excluded	24
PPROM after amniocentesis	4
Regular contractions at admission	7
Cervical incompetence and cerclage	1
Signs of chorioamnionitis at admission	3
Patients' decision to terminate pregnancy	9
Included	63
Multiparous	27
Nulliparous	36
Fetuses	71
Singletons	56
Twins	6
Triplets	1
Outcome	
IUFD and stillbirth	46
Mean latency period (days)	6
Range (days)	0–26
Mean gestational age at PPROM (weeks)	20+4
Mean gestational age at delivery (weeks)	21+4
Live born infants	25
Mean latency period (days)	23
Range (days)	0–118
Mean gestational age at PPROM (weeks)	21+3
Mean gestational age at delivery (weeks)	25+4
Neonates died in hospital	13
Neonates alive at discharge from hospital	12
Histological verified chorioamnionitis	38
Neonates died in hospital	12
Neonates alive at discharge from hospital	5

IUFD = intrauterine fetal death.

PPROM = preterm premature rupture of membranes.

based on 63 pregnancies including 56 singletons, 6 twins and 1 triplet pregnancy resulting in 25 surviving neonates after second-trimester rupture of membranes.

There was no difference in the observation and treatment regimen for multiples and singleton pregnancies. Gestational age was determined on the basis of early ultrasound or menstrual history. When no date of the last menstrual period was available or a discrepancy between the history of the last menstrual period and ultrasound existed, gestational age was based on ultrasound. PPROM was diagnosed by visible loss of amniotic fluid exiting the cervical os (examination with sterile specula) and confirmed by Actim Prom® (Medix Biochemica Ab, Finland), a test for insulin-like growth-factor binding protein 1. Ultrasound examination was performed to confirm gestational age, evaluate amniotic fluid status and to screen for fetal anomalies. Cervicovaginal cultures of all women were taken at admission. All patients were admitted to the hospital and, except in four cases, promptly treated intravenously with broad-spectrum antibiotics (e.g., penicillin, ampicillin/clavulanate, cephalosporine) for seven days. Tocolytics were applied to all infants for 48 h while corticosteroids were given to promote lung maturation after 24+0 weeks of gestation [8]. Ultrasound examination was performed at least once a week for fetal size and amniotic fluid volume; leukocytes and CRP were measured every second day. Fetal heart rate tracings after 24 weeks of gestation were recorded twice a day. Treatment was expectant unless there was clinical or laboratory evidence of intraamniotic infection, changes in cardiotocogram or regular uterine contractions.

Neonatologists attended all deliveries and all surviving infants, except one child (born at 34+4 weeks) who did not need intensive treatment because of its good clinical status, were transferred to the neonatal intensive care unit. All placentas were submitted for histopathology. Histologically verified chorioamnionitis was defined as infiltrate of neutrophils (>10 neutrophils per high-power field) at two or more sites in the chorionic plate and decidual floor. After

discharges from hospital infants were followed by a single neonatologist specialized in developmental assessment at the Department of Pediatrics, Medical University Graz.

Data were entered into a computerized data base and analyzed. Cross tabulations (two tailed Fisher's Exact Test) were used to assess the relationship between categorical data. To determine the statistical significance of group differences in continuous variables we applied the Wilcoxon Rank Sum test. Additionally, regression analysis was used to assess the odds ratios (ORs) for survival versus postpartal death of infants born after second-trimester rupture of membranes. A multiple logistic regression model was built by forward selection of influencing perinatal findings which were previously identified with univariate regression analyses. ORs are presented with a 95% confidence interval (95% CI). All computations were done using the statistical package SPSS version 13 and 16 (SPSS for Windows, Rel. 16.0.2. 2008. Chicago: SPSS Inc.). *p*-values less than 0.05 were considered significant.

### 3. Results

This study is based on 63 pregnancies resulting in 56 singletons, 6 twins and 1 set of triplets. Out of the 71 infants 25 were alive at birth. 13 of these 25 surviving children died in the hospital, the longest time period to death was 31 days (mean latency period 23 days, range 0–118 days).

Mean gestational age at the time of membrane rupture was 22+5 weeks of gestation (range 17+3 to 24+6 weeks) for survivors and 21+6 (range 16+5 to 24+0 weeks) for children who died before discharge. At the time of birth mean gestational age for survivors (27+2; range 24+3 to 34+2 weeks) was statistically significant longer than in the group of children who died (23+6; range 21+2 to 26+2 weeks) (*p*=0.005). Gestational age at birth of the 12 surviving infants and the 13 children who died before discharge are shown in Table 2. Nine of 12 children were female in the surviving group compared to 6 of 13 children in the group of children who died in hospital. Overall 14 children were delivered by cesarean section and 11 were born vaginally. Nine out of the 12 longterm survivors were delivered by caesarian section compared to 5 out of the 13 infants who died in hospital. The mode of delivery showed no statistical significance.

No infant of multiples survived. The mean gestational age of multiples at the time of membrane rupture was 20+2 weeks of gestation (range 17+3 to 23+1 weeks) and 21+1 weeks of gestation (range 18+0 to 23+3 weeks) at the time of delivery. The mean latency period of multiples was 6 days (range 0–15 days).

Antibiotic treatment during pregnancy was as follows: 31 (49%) patients received broad-spectrum penicillin, 20 (32%) amoxicillin/clavulanate, and 8 (13%) a cephalosporine; however, 4 (6%) patients received no antibiotics. The difference in obstetric characteristics such as antibiotic therapy in pregnancy, maternal vaginal infection and reasons of birth induction (contractions, chorioamnionitis, pathological cardiotocogram) were not statistically significant between longterm survivors and those children who died before discharge from hospital. No infant developed a neonatal enterocolitis. All of them, except one child of the surviving group, who was born at

**Table 2**  
Outcome of all surviving infants, 12 longterm survivors (Lt) and 13 children who died after delivery (pp) regarding to gestational age at birth in weeks

Gestational age at birth (weeks)	Surviving infants <i>n</i> =25	
	Lt <i>n</i> =12(100%)	pp <i>n</i> =13(100%)
<23/0–6	0 (0)	7 (54)
24/0–6	3 (25)	2 (15)
25/0–6	4 (33)	2 (15)
26/0–6	0 (0)	2 (15)
>27/0	5 (42)	0 (0)

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