

# Determinants of favourable neonatal outcome after premature rupture of membranes (PROM) before 24 weeks of pregnancy – review of the literature and a case report

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## Abstract

**Objectives:** Premature rupture of the membranes (PROM) in pregnancy refers to rupture of membranes of the amniotic sac and chorion. The aim of the study was to review the literature and analyze the course of pregnancy (primipara) complicated by the premature rupture of the membranes, and consequent loss of amniotic fluid after 19 weeks of gestation.

**Study design:** A 27-year old primiparous patient was admitted to the Gynaecology and Obstetrics University Hospital in Poznań on 9 December 2010, due to suspected premature rupture of the membranes. On presentation, foetal development was at 19 weeks gestation. Standard clinical investigations included ultrasonography, amniotic fluid index measurements and laboratory blood tests.

**Results:** Ultrasonography confirmed the size of the foetus to be normal for the gestational age. However, no amniotic fluid pockets were visible and the amniotic fluid index was 0 cm. The patient was hospitalized on multiple occasions and as a result a decision was made to end the pregnancy prematurely by means of a caesarean section at 32 weeks of gestation. Longer-term observation of the newborn indicated that one year following delivery, the development of the baby was normal, and thus far no neurological injuries or complications have been observed.

**Conclusion:** The pregnancy was ultimately successfully completed with the delivery of a healthy newborn at 32 weeks of gestation. A regime involving rigorous bed rest and antibiotic administration can positively extend the duration of pregnancies complicated by premature rupture of the membranes.

## Key words

Premature rupture of the membranes, infection, pregnancy, prognosis

## INTRODUCTION

Premature rupture of the membranes (PROM) in pregnancy refers to rupture of the amniotic sac and chorion membranes. Pre-term, pre-labour rupture of the membranes (pPROM) occurs in 2.9-3.5% of all pregnancies and is the most common cause of pre-term labour (30-40%) [1]. Pre-term labour, in turn, has been reported to cause ~60-75% of the proportion of mortalities relating to babies born without anatomical and chromosomal defects [2]. Such mortalities are generally associated with pulmonary hypoplasia.

In the event of a PROM, the decision whether to end or continue the pregnancy remains the greatest dilemma for obstetricians. The choice of management, be it conservative, active or invasive, in many cases depends on the clinical situation of the individual at hand. According to the recommendations of the American College of Obstetricians

and Gynecologists of 2007, the pattern of management depends on the maturity of the pregnancy [3]. The available literature suggests that pregnancy with a PROM occurring before 20 weeks gestation is often associated with an unsuccessful outcome. Despite the advances in clinical medical practice, prophylactic and medical treatment of premature amniotic fluid loss, such a pregnancy will not often result in the birth of a healthy newborn [4]. Unfortunately, the survival rate of babies born between 16 – 25 weeks gestation has been documented to be 24.5%, while the survival rate of babies born between 24 – 26 weeks gestation has been observed to range between 50 – 70% [3]. The prognosis in the event of a PROM depends on a number of factors, such as the gestational age at the onset of the PROM, the exact mechanism by which the premature loss of amniotic fluid occurred, and other co-existing pregnancy complications [3, 4].

The aim of the study was to review the literature and analyze the course of pregnancy of a primiparous patient in which the pregnancy was complicated by a PROM, and consequent amniotic fluid loss after 19 weeks of gestation. The pregnancy was successfully managed and completed with the delivery of a newborn at 32 weeks of gestation.

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## MATERIALS AND METHODS

**Gestation at week 19.** A 27-year old primiparous patient, 19 weeks gestation, was admitted to the Gynaecology and Obstetrics University Hospital in Poznań, on 9 December 2010, due to suspected premature rupture of the membranes. The patient reported increased vaginal discharge during the 2 weeks prior to admission, during the same period a metronidazole vaginal suppository administered at bedtime. Gynaecological examination revealed a closed cervix exhibiting normal depth and round shape. A significant volume of vaginal discharge was observed and tests revealed an alkaline vaginal milieu. An ultrasonographic (USG) examination indicated that the size of the foetus was normal for the gestational age. However, no amniotic fluid pockets were visible and the amniotic fluid index (AFI) was 0 cm. Laboratory tests results were as follows: C Reactive Protein (CRP) 5.11 mg/L, toxoplasmosis antibodies IgG 0.15 IU/ml, IgM 0.19 COI (negative), rubella antibodies IgG 134, 10 IU/ml, IgM 0.23 COI (negative), cytomegalovirus antibodies IgG 147, 10 U/ml, IgM 0.21 COI (negative). White blood cell (WBC) morphology count was normal (10.90 G/L). Continuation of vaginal treatment was advised together with Cephalixin 500 mg, 4 times daily.

**Gestation at weeks 23-24.** The patient was hospitalized again between weeks 23-24 of gestation – 28 December 2010 – 5 January 2011, due to observed abdominal tension. Speculum examination revealed loss of amniotic fluid, cough test was positive, and the vagina alkaline. USG revealed a vertex presentation with the head under the symphysis pubis. Foetal biometry was as follows: biparietal diameter (BPD) 55mm corresponding to 22+5 (weeks+day); head circumference (HC) 197mm that correlates with 21+6; abdominal circumference (AC) 160mm corresponding to 21+1; femur length (FL) 32mm which is within the normal values for 20 weeks gestation. Mean foetal age calculated on the basis of biometry results was 21+3 days. Estimated foetal weight was 464g according to the Shepard approach. Placenta in anterior wall of uterus, amniotic fluid index (AFI) = 1.3cm, UmA PI was 1.56, and MCA PI – 1.34. Due to oligohydramnios and the position of the foetal head in the canal, anatomical assessment of the foetus was not possible during the examination. Nevertheless, none of the organs seemed abnormal. Lab tests revealed a WBC count of 14.80 G/L, and CRP of 4.20 mg/L. A urine test indicated normal results. The patient was administered magnesium hydroaspartate 3×2 tablets, and drotaverine hydrochloride 3×1. In addition, betamethasone 2×12mg tablets were administered to promote foetal pulmonary maturation.

The blood morphology prior to hospital discharge (5 January 2011) showed WBC elevated to 25.40 G/L and CRP decreased to 2.88 mg/L. At this time, a general urine test confirmed the presence of numerous bacteria as well as 2-3 leucocytes. During hospitalization, a vaginal smear was taken which revealed that the vagina was infected with *Escherichia coli* (++++). The patient was discharged in a good overall condition, without the presence of uterine contractions. Following discharge, the patient was instructed to follow a rigorous bed rest regime, and to take magnesium hydroaspartate 3×2 tablets, drotaverine hydrochloride 3×1, Amoxicillin 1×1 vaginal insert for 10 days, and a fosfomicin 1×1 sachet.

**Gestation at week 26.** Due to the presence of abdominal tension, the patient was re-admitted at 26 weeks gestation (21 January 2011) for observation and possible treatment modification. USG confirmed an intrauterine limitation of foetal growth with a recorded foetal weight of 760 g, as determined by the Hadlock method. The following laboratory test results were obtained: WBC 13.56 G/L and CRP 5.25 mg/L. A urinary test revealed the presence of numerous bacteria in the urine, as well as the presence of 2-3 leukocytes. Urine and vaginal culture tests resulted in the growth of *Raoultella ornithinolytica* – 5,000 cfu/ml (+++), *Corynebacterium* species – 5,000 cfu/ml (++++), coagulase-negative *Staphylococcus* – 2,000 cfu/ml (+++), and *Lactobacillus* species – 5,000 cfu/ml (++++). Cardiotocography (CTG) indicated the absence of contractions. The patient was instructed to follow a rigorous bed rest regime. In addition, the following medications were administered: magnesium hydroaspartate 4×2 tablets, drotaverine hydrochloride 3×1, cefuroxime vaginal insert 1×1 for 10 days, and amoxicillin 1×1 tablets for 7 days.

**Gestation at week 28.** On 5 February 2011, corresponding to 28 weeks gestation, USG revealed increasing hypotrophy of the foetus, vertex presentation with the head under the symphysis pubis, BPD 72mm – corresponding to 29+0 days, HC 252 mm – corresponding to 27+3, AC 209 mm – correlating with 25+4, and FL 43mm – corresponding to 24+2 weeks gestation. The mean foetal age calculated on the basis of biometry was 25+1 week. The estimated foetal weight was 810g, according to the Hadlock approach. An anterior placenta and complete anhydramnios (0cm) were observed. Doppler flows were normal: *middle cerebral artery* (MCA) pulsatility index (PI) 1.50, umbilical artery (UmA) PI 1.13). Urine culture results were as follows: coagulase-negative *Staphylococcus* – 2,300 cfu/ml; Gould test was negative, and the pH was 5.5). Vaginal cultures indicated the presence of coagulase-negative *Staphylococcus* in 8 colonies.

Betamethasone (2×12 mg) was again administered to promote foetal pulmonary maturation, together with magnesium hydroaspartate 4×2 tablets, drotaverine hydrochloride 3×1, and diazepam 2×2 mg. An oral glucose tolerance test excluded the presence of diabetes in pregnancy. An indirect Coombs test was negative. Doppler USG was performed again and the following results obtained: MCA PI=3.19, resistance index (RI) 1.00; UmA PI 1.13, RI 0.68, and absence of vein pulsatility features. Fluid in the pericardial sac (4mm) was found. The heart to chest area ratio (HA/CA) ratio was normal (0.30). Tricuspid regurgitation (TV) was not observed. Cefuroxime 2×1.5 g intravenous (IV) was administered on day 4 of hospitalization. On day 10, CRP was 4.82 mg/L and intravenous administration of antibiotics was continued. Doppler USG was normal (MCA PI=1.23, UmA PI 0.88). Gynaecological examination revealed a shortened cervix, 1.5 cm dilation, and light bleeding from the genital tract.

On day 17, the antibiotic treatment was stopped with a recorded CRP value of 4.54 mg/L. Doppler USG revealed symptoms of circulatory centralization; umbilical and uterine flows were normal. Tocolysis was stopped on day 21. Laboratory tests indicated a CRP value of 4.38 mg/L, and ampicillin 2×1.0 g IV and metronidazole 2×0.5 g IV were initiated prophylactically. On day 24, CRP was elevated to a value of 12.77 mg/L.



**Gestation at week 31/32.** Due to repeated decelerations on CTG and increasing bleeding from the genital tract, a decision was made to end the pregnancy with a caesarean section on day 24 of hospitalization.

## RESULTS

A male baby (weight 1160 g, Apgar 5.6) was delivered by caesarean section (Pfannenstiel incision) and intubated immediately upon delivery (Fig. 1). Neonatal blood gasometry results were: pH 7.349, pCO<sub>2</sub> 55.7 mmHg, pO<sub>2</sub> 23.2 mmHg, HCO<sub>3</sub> 30.0 mmol/l, BE 2.9 mmol/l, and O<sub>2</sub> sat 36.8%. Following the birth, breathing was supported for approximately 30 minutes. Only a few foci of atelectasis were observed on an X-ray image. The patient was discharged on 4 March 2011 in good overall condition. One year after the delivery, the development of the baby was observed to be normal, and thus far no neurological injuries have been detected (Fig. 2).



**Figure 1.** The child following birth



**Figure 2.** Four months after delivery the development of the baby appears normal and neurological complications absent

## COMMENTS

Unfortunately, the PROM remains a significant problem in contemporary obstetrics and is one of the most common complications in obstetrics, responsible for one third of all preterm labours [5]. The prevalence of a PROM is estimated

to be between 3-4.5% of all pregnancies, and it has been reported as being the most common symptom of pre-term labour [1]. The number of positively-ended gestation cases described in medical literature is very limited.

In a retrospective analysis performed by Falk et al. [6], 108 patients presenting with a preterm PROM (PPROM) prior to week 24 of pregnancy were examined. The period of time between the rupture of foetal membranes and labour was observed to be an average of 6 days [6]. Pre-term labour itself is the cause of 60-75% mortality rate of all babies born without anatomical and chromosomal defects which are the result of immaturity caused by low birth weight and pulmonary hypoplasia [2]. The ultimate consequence of a PROM is that children are born who are not ready to survive outside of the intrauterine environment. Of note is that female babies born prior to 29 weeks of gestation generally have a higher survival rate than their male counterparts [7]. In addition, the survival rate of Afro-American newborns delivered at <29 weeks of gestation is higher than that of Caucasian babies [7].

Undoubtedly one of the largest problems in modern perinatology is the development of intrauterine infection which often accompanies the premature rupture of the membranes. Often, the amniotic fluid is 90% infected 6 hours following rupture, and the intrauterine infection presents yet another challenge for obstetricians. Such a scenario develops in 13-60% of pregnant women affected with a PROM. The foetus, in turn, is infected in 2-13% of cases. The latter has been associated with an increased risk of premature birth and clinical complications, such as septicaemia, pneumonia, bronchopulmonary dysplasia, cerebral palsy, infant respiratory distress syndrome, other types of infections, as well as deformities of the limbs and face. This is the reason why implementation of treatment protocols and antibiotic prophylaxis are important [8, 9, 10]. Premature rupture of the membranes associated with persistently marked oligohydramnions can also lead to Potter's syndrome [3], which has been reported to develop in 50% of infants affected with membrane rupture at 19 weeks of gestation, 25% of newborns at 22 weeks of gestation, and 10% of infants born after 26 weeks of gestation. Pre-term birth remains one of the biggest challenges in modern medicine [3, 11, 12].

A PROM in the second trimester of pregnancy remains a challenge not only to the parents-to-be, but also the entire team of healthcare professionals – gynaecologists, obstetricians and neonatologists. Furthermore, the development of a PROM implies serious medical and ethical issues which require action [3]. According to Mauris et al. [13], only 24% of newborns born >24 weeks of gestation survive the first week of life. According to Haidi et al. [11], only 6.7% of children born < 25 weeks gestation survive following delivery, while 89.4% of newborns survive if they are delivered between 26 – 34 weeks of gestation. The available literature indicates that 27% of babies born <26 weeks gestation die immediately following delivery, and only 38.5% of children survive longer than 28 days.

Of the children who survive delivery, 70% develop in a normal manner [5]. To the best of our knowledge, the available literature presents only a few cases of a PROM at < 20 weeks of pregnancy when premature rupture of the membranes resulted in the birth of a 'healthy' newborn [14, 15]. All the reports, together with the presented study,



are clinical situations where a rigorous bed rest regime and antibiotic therapy based on culture and antibiogram results were introduced immediately following diagnosis. The current case relating to the development of a PROM at 19 weeks of gestation accompanied by other symptoms potentially leading to miscarriage, nevertheless resulting in a successful prolongation of gestation and healthy delivery, is quite surprising. This is especially true in view of all the literature data relating to the survival rate of babies born at <20 and <26 weeks of gestation [11].

The conservative treatment of PPRM before the week 20 of gestation is controversial, and the recommended treatment itself is often deemed ambiguous. This applies especially to those cases where the attitude of the parents to the pregnancy is positive, despite the medical practitioner presenting the risks for the abnormal development of the child. Undoubtedly, this issue requires further studies. The description of similar cases in the population may contribute to the improvement in pre-natal care. The authors therefore believe that the current study may be of educational benefit to obstetricians and neonatologists at large.

In conclusion, a rigorous bed rest regime and relevant antibiotic therapy may extend the gestation period of pregnancies associated with premature rupture of the membranes.

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