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Analysis of the management of preterm rupture of membranes after the 37th week of gestation

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ABSTRACT

Premature rupture of membranes or synonymously prelabor rupture of membranes (PROM) is defined as the outflow of amniotic fluid before the onset of uterine contractions. When it occurs after 37 weeks of gestation, it is called term PROM or tPROM, and its prevalence is as high as 8–10% of pregnancies. tPROM is a significant risk factor for intrauterine infection, which threatens both the pregnant woman and the fetus. This risk increases with the duration of amniotic fluid leakage.

The aim of this study was to retrospectively analyze the management and obstetric outcomes of preterm premature rupture of membranes in women after 37 weeks' gestation.

Keywords: tPROM; CRP; GBS; Apgar score; vaginal delivery; cesarean section.

INTRODUCTION

Preterm premature rupture of membranes (PROM) is defined as the outflow of amniotic fluid before the onset of uterine contractions in labor. Preterm premature rupture of membranes (pPROM) is a similar complication but occurs before 37 weeks' gestation and affects 2–3% of pregnancies [1]. PROM after 37 weeks of gestation, also called term PROM or tPROM, is diagnosed in 8–10% of pregnancies [2, 3, 4]. In practice, tPROM is less problematic and does not cause prematurity and its sequelae, but both pPROM and tPROM carry the risk of intrauterine infection, which increases proportionally to the duration of amniotic fluid leakage and endangers the pregnant woman and the fetus [2, 3, 4, 5, 6]. It seems optimal to try to reduce the duration of amniotic fluid leakage as much as possible in order to minimize the risk. However, it should be taken into account that as many as 60–70% of women with tPROM develop spontaneous labor within 24 h, and even 95% of women with tPROM develop spontaneous labor within 72 h [2, 4]. Waiting seems to be a better option than active and sometimes even prolonged efforts to deliver the baby as soon as possible. Although labor induction is one of the most commonly used procedures in obstetrics, it is not without risk of complications [7]. According to some researchers, it may increase the likelihood of cesarean section for both maternal and fetal indications, but there are also many authors of the opposite opinion [2, 7, 8, 9, 10]. Questions such as the reduction of waiting time with optimal maternal and fetal monitoring, individualization of pre-induction and induction methods, or the use of antibiotics are still under discussion, and definitive answers seem to be elusive.

The aim was a retrospective analysis of procedures and outcomes in women with preterm premature rupture of membranes after 37 weeks' gestation.

MATERIAL

Medical records of women with tPROM admitted to our department between January 1 and December 31, 2022, were analyzed. The study group included 204 participants in at least the 37th week of pregnancy with a definite diagnosis of premature rupture of membranes, with no uterine contractility.

We analyzed the time from the onset of amniotic fluid leakage to delivery according to the results of inflammatory markers, i.e. plasma C-reactive protein (CRP) concentration and culture result for beta-hemolytic streptococci (GBS), mode of delivery, birth status of the newborn, including Apgar score and umbilical cord blood pH, need for antibiotics, and duration of maternal and neonatal hospital stay.

Each participant admitted to the hospital underwent an obstetric examination to assess the cervix and ultrasound and cardiotocography to assess fetal biometry and well-being. All women had their blood count, sodium, chloride, and potassium plasma concentration, activated partial thromboplastin time, prothrombin time and INR (International Normalized Ratio) checked. In case of a positive or unknown streptococcal culture result, they received preventive antibacterial therapy from the beginning of their hospitalization, with ampicillin or clindamycin in those with penicillin intolerance. If the result was negative and a waiting procedure was planned, the pregnant woman received the first dose of antibiotics 12 h after the rupture of the membranes. General condition parameters such as heart rate and body temperature were assessed at least every 4 h and plasma CRP level (concentration) at least every 12 h until delivery.

In the study group, 59 of 204 (28.9%) participants had indications for elective cesarean section, while the remaining 145 (71.1%) were eligible for vaginal delivery.

An interview was conducted with each individual to explain the possible courses of action, including waiting, pre-induction and induction of labor, and their possible consequences. Each participant signed the informed consent form for the procedure.

RESULTS

None of the women eligible for vaginal delivery had clinical signs of intrauterine infection such as fever or maternal and/or fetal tachycardia. Fifteen women (7.8% of the study group) had a C-reactive protein concentration greater than 10 mg/dL, including eleven with CRP between 10–20 mg/dL and four with CRP between 20–30 mg/dL. Of those with elevated CRP, four had unknown streptococcal carrier status and two were GBS positive. The others had negative GBS culture results, but were given prophylactic antibiotic therapy because of their elevated CRP. One participant in this subgroup had symptoms of an upper respiratory tract infection with a negative test for COVID-19.

Seven (46.7%) parturients had a spontaneous vaginal delivery without the need for labor induction. Four multiparas developed uterine contractions and delivered on average 13 h after PROM onset. Neonates were in good general condition, with normal umbilical cord blood pH and Apgar scores of at least 9 at 1 min and subsequent measurements. No neonates required antimicrobial treatment. Most women left the hospital with their infants on the 2nd or 3rd postpartum day, except one whose newborn required an additional day of phototherapy for hyperbilirubinemia.

Three nulliparas were qualified for labor pre-induction with Foley catheter after 7–12 h from the onset of fluid leakage. None of them had a significant increase in CRP concentration during pre-induction (the highest increase was 2.3 mg/L). All women developed regular uterine contractions within 24 h of Foley catheter placement. They delivered neonates in good general condition with normal parameters of cord blood gasometry, who did not require antibiotic therapy, and were discharged home not later than the 3rd day after delivery.

Eight (53.3%) women with initially elevated CRP underwent cesarean section: six (including two after induction of labor using a Foley catheter) for fetal distress and two for non-progressive labor. The general condition of the newborns in this subgroup was also good, with an Apgar score of at least 8 at 1 min and subsequent measurements, and umbilical cord blood pH not lower than 7.13. Most neonates were discharged home at the latest on the 3rd day after birth and none of them required antibiotics. One infant from a pregnancy complicated by class 1 gestational diabetes mellitus with a birth weight of 1900 g at 37+3 weeks of gestation required prolonged hospitalization until day 7 due to fetal growth restriction (FGR) combined with morphologic prematurity.

Two women qualified for vaginal delivery had meconium stained amniotic fluid with CRP concentration less than 5 mg/L and negative GBS culture result. Both were admitted directly to the labour ward for induction of labor with intravenous oxytocin after obtaining informed consent. They delivered vaginally 16 and 17 h after the onset of fluid leakage, one under epidural anesthesia. In both cases the CTG recordings were normal. One infant was born in good general condition, with Apgar scores of 10 at 1, 5, and 10 min and cord blood pH of 7.23, and was discharged home from the hospital on day 3 after delivery. The second infant was born in fair condition, weighing 4000 g, with the cord tightly wrapped around the neck twice. The second stage of labor lasted 68 min, and variable decelerations in CTG were recorded with normal short-term variability. Apgar score was 4/5/6 and cord blood pH was 7.01. Other parameters were: BE – 16.9, pCO2 62 mmHg, HCO3 15.6 mmol/L, lactates 12.1 mmol/L after birth, and then pH was 7.31, BE – 11.7, pCO_2 29 mmHg, HCO_3 14.6 mmol/L, lactates 8.6 mmol/L after 5 h. Discharge from the hospital was on the 7th day.

Neither neonate required antibiotic therapy. Forty-nine participants (24% of the study group) were eligible for induction of labor because of cervical Bishop's score less than 6. The procedure was performed no earlier than 6 h after the onset of PROM. In forty-six cases, a Foley catheter was used, and each participant received antibiotics (ampicillin or clindamycin) according to the preventive regimen, regardless of her GBS carrier status. Vaginal dinoprostone inserts were placed in the remaining three women. Thirty-nine (79.6%) of the inductions were completed by vaginal delivery. In ten cases (20.4%), all after Foley catheter placement, a cesarean section was required, four for fetal distress, two for threatening intrauterine infection, two others for non-progressive labor, one for cervical dystocia, and one for suspected placental abruption.

Twenty-three women (50%) required i.v. oxytocin to induce uterine contractions after labor pre-induction, while twenty (43.5%) developed spontaneous contractility.

None of the women who received prostaglandins needed oxytocin to induce uterine contractions.

The maximum duration from PROM to delivery in the subgroup with induction of labor was 50.5 h. Eight women delivered later than after 48 h, twelve after at least 24 h but not later than 48 h, while the others delivered on average after 14.9 h from the onset of fluid loss.

Three newborns had low Apgar scores, of which two had 3 despite cord blood pH of 7.1 and 7.24, and one had 4 with pH of 7.12. They were evaluated at 1, 8, 9, or 10 min.

None of the neonates required antibiotics. All women and their newborns left the hospital at the latest on the 3rd day after delivery.

Twelve parturients with cervical Bishop's score greater than 6 were eligible for oxytocin induction of labor delivered vaginally. Three were primiparas and nine were multiparas. In all cases, induction was initiated after waiting at least 6 h for spontaneous onset of uterine contractions. The longest time from PROM to delivery was 44 h in a primigravida at 37+1 weeks' gestation who refused to consent to induction. Due to her unknown GBS carrier status, she received prophylactic antibiotic therapy. After the patient's consent was finally obtained, labor was induced 32 h after the PROM. The newborn had an Apgar score of 8/9/9 and its cord blood pH was 7.16. The four-day hospital stay was due to the need for

phototherapy for hyperbilirubinemia. There was no need for antibacterial treatment.

Other women included in this subgroup delivered at an average of 16.9 h after PROM. Three of them were prophylactically treated with antibiotics from the time of hospital admission due to unknown GBS carrier status. The rest of the participants had negative GBS culture results and preventive antibacterial agents were implemented after 12 h from the onset of amniotic fluid leakage. None of them had a CRP concentration above 10 mg/L. Each gave birth to healthy newborns with Apgar scores of at least 8 at the first and subsequent examinations and normal gasometric cord blood results without the need for antibiotics. All left the hospital no later than the 3rd day after delivery.

Eighty-four participants (57.9% of those eligible for vaginal delivery) developed spontaneous uterine activity, but some required augmentation of labor with i.v. oxytocin. Twenty-two women (26.2%) required cesarean section.

Of the sixty-two women (73.8%) who delivered vaginally (including one with the use of a vacuum extractor), thirty-three were primiparas and stated that their priority was to have a natural delivery with minimal medical intervention, including pre-induction and induction of labor. The mean time from PROM to delivery in this subgroup was 13.9 h, 12.2 h in multiparas and 16.3 h in primiparas.

Two women required prolongation of hospital stay to 6 and 7 days, respectively, but the majority spent a maximum of 4 days in hospital and were discharged no later than 3 days after delivery. None required antibiotic therapy.

Three newborns had Apgar scores of 3 at 1 min, two had 4, one had 5, and two had 6 Apgar scores, but all had Apgar scores of 8 or higher at 5 min, while the others had Apgar scores of at least 8 at 1 min and later. All neonates had normal cord blood gas results. One, born after 17 h of PROM and whose mother required prolonged hospitalization, required 5 days of antibiotic therapy for elevated inflammatory parameters.

In 32 cases (22.1%) of waiting for spontaneous vaginal delivery and labor pre-induction or induction, cesarean section was required in eight women because of non-progressive labor, in five because of abnormal mechanism of labor, in 17 because of fetal distress, and in 3 because of threatening intrauterine infection.

All women with suspected chorioamnionitis had initial CRP levels below 10 mg/L and were asymptomatic with respect to fever or maternal and fetal tachycardia. They were primiparas, initially eligible for vaginal delivery, two of whom were GBS-negative, while the GBS status of the last was unknown.

One participant, GBS-negative, was selected for labor pre-induction with Foley catheter due to class 2 gestational diabetes mellitus and had PROM after admission to the hospital before the planned procedure. At her request, the epidural was waived and a Foley catheter was placed. After 9 h from the beginning of pre-induction, fetal tachycardia occurred and persisted for consecutive hours of observation, while the results of pregnancy laboratory tests, including CRP, were normal. Due to persistent fetal tachycardia and unfavorable cervix, cesarean delivery was performed 16 h after tPROM. The newborn had an Apgar score of 10, a cord blood pH of 7.36, and was negative for inflammatory markers. There was no need for therapy, and they left the hospital on the 2nd day after delivery.

In the second case, a woman with an initial CRP of 4.59 mg/L and GBS-negative presented with fever above 38°C and fetal tachycardia during induction of labor with the use of a Foley catheter. A control laboratory test showed an increase in CRP to 13.6 mg/L. The parturient qualified for cesarean section, and 27 h after the onset of fluid leakage and 4 h after the onset of labor pre-induction, a newborn was delivered in good general condition, with an Apgar score of 10 in two tests, but was not tested for umbilical cord gasometry. Laboratory tests of the newborn revealed elevated inflammatory markers, and bacterial culture of blood and ear swabs was positive for *Enterococcus faecalis*. Antibiotic therapy was started with good results. In subsequent measurements, the inflammatory parameters decreased and the control blood culture was negative. The newborn was discharged from the hospital on the 6th day after birth.

In the third participant, the one with unknown GBS carrier status, fetal tachycardia manifested in subsequent CTG recordings 6 hours after PROM, while her inflammatory marker tests remained negative. Due to the above symptoms together with an unfavorable cervix, she gave birth by cesarean section 8 h after PROM. The newborn was in good condition, with Apgar score of 9, cord blood pH at 7.29 and negative inflammatory markers, and did not require any therapy. They were discharged from the hospital on the 3rd day after delivery.

Twenty-two women (15.2%) in the subgroup primarily intended for spontaneous delivery, who eventually delivered by cesarean section, were initially eligible for the watchful waiting procedure and developed spontaneous uterine contractions. The predominant indication for cesarean section in this group was fetal distress (n = 11), in 5 cases cesarean section was performed because of non-progressive labor and in another 6 because of abnormal mechanism of labor in the form of prolonged fetal presentation. All newborns were in good general condition, none of them required antibiotic administration or hospital stay longer than 3 days. Taking into account the condition of newborns at birth, it seems that in this group detailed analysis is necessary, especially in the aspect of subjective and too conservative diagnosis of fetal distress symptoms.

Of the two hundred and four persons included in our study group, fifty-nine women (28.9%) delivered by cesarean section for various indications without attempting vaginal delivery. In eighteen cases (18.5%) the indication was tokophobia. The average time from PROM to delivery in this subgroup was 5 h. Two women delivered later than 10 h (11 and 12 h) due to delayed arrival at the hospital. The mean time from PROM to delivery for women who reported immediately to the maternity ward was 4.2 h. All eighteen participants had clear amniotic fluid and a CRP concentration of less than 10 mg/L. They all delivered neonates in good general condition with an Apgar score of at least 8 in the first min and normal cord blood gas analysis results. In this subgroup, the only antibiotic administration was standard preoperative prophylaxis. Most of the participants left the hospital with their newborns at the latest on the 3rd postpartum day, while one woman remained in the

hospital until the 6th postpartum day due to her newborn's hyperbilirubinemia.

Another cluster included ten women (16.9%) who delivered by cesarean section for breech presentation of the fetus. All had unstained amniotic fluid. The mean time from PROM to delivery was 6.2 h. Two women delayed their arrival at the hospital to 10 and 12 h. In one of them, who delivered after 12 h from the onset of fluid leakage, the plasma CRP concentration exceeded 10 mg/L and was 10.7 mg/L. Among those who arrived at the delivery room without delays, the average PROM-delivery time was 4.4 h. Except for preoperative prophylaxis, there was no need for antibiotic administration in this subgroup. All neonates were in good condition with Apgar scores of 9 or 10 and normal cord blood gas results. None of them required antibacterial therapy. Each participant in the above subgroup left the hospital with her newborn no later than 3 days postpartum.

Outcomes were similar in women who had cesarean delivery for ophthalmic (n = 6), orthopedic (n = 6), neurologic (n = 2) indications, and in those who refused to consent to vaginal delivery because of a previous cesarean delivery (n = 6), qualified because of two previous cesarean sections (n = 4) or suspected post-cesarean scar rupture (n = 1), one woman after enucleation of uterine fibroids prior to pregnancy, one with an abnormal pelvic bone, one with suspected fetal macrosomia, and three in twin pregnancies.

DISCUSSION

Premature rupture of membranes after 37 weeks of gestation affects 8–10% of all pregnancies [2, 3, 4]. In contrast to pPROM, the biochemical condition associated with ascending infection does not seem to be the main etiologic factor [4]. This peculiar clinical situation creates a risk of subsequent ascending intrauterine infection that increases with the duration of amniotic fluid leakage, threatening both the pregnant woman and the fetus [2, 4, 5]. Therefore, shortening the time from PROM to delivery appears to be favorable. According to American College of Obstetricians and Gynecologists (ACOG), in the absence of indications for cesarean delivery and in the absence of symptoms of spontaneous labor, induction of labor is recommended in tPROM, taking into account a short waiting period [4]. The authors point out that 80% of women spontaneously develop uterine activity within 12 h after tPROM, and even 95% of them within 24 h, which was confirmed by our observations. The researchers emphasize that optional postponement of induction of labor for 12–24 h is reasonable, unless there are problems with the fetal condition and provided that the patient understands and accepts the risk of the procedure.

Similarly, Hannah et al. report spontaneous onset of labor in more than 60% of pregnant women within 24 h and in more than 95% within 72 h [2]. They emphasize how controversial the issue of waiting time is and share their observations that the timing of labor induction often depends not only on the time since tPROM but also on logistical conditions. This was also evident in our analysis, with a significantly lower percentage of labor pre-induction and induction performed at night and during the shift, which is consistent with our patients' preferences. What distinguishes their study is that Hannah et al. did not find an increase in the prevalence of neonatal infection between the conservative and active induction groups, but they did find a lower risk of chorioamnionitis with induction compared to waiting [2].

Sibiude presented similar conclusions, stating that immediate labor induction does not reduce the prevalence of neonatal infection, even in GBS-positive women [8].

According to Seaward et al, the risk of neonatal infection within 24 h of PROM does not exceed 1%, but increases to 3–5% in the presence of clinical signs of chorioamnionitis [3]. According to Sibiude, labor induction with the use of oxytocin reduces the risk of puerperal infection, which was not found in the option of prostaglandins [8]. Hannah et al. also show an association between the use of labor induction and a decrease in the prevalence of puerperal infection [2]. The analysis of Dare et al. proved that an active approach such as labor induction in comparison with waiting reduces the risk of infection in women and newborns without increasing the number of cesarean deliveries and shortens their hospital stay [10]. Hannah et al. and Sibiude show that an active approach does not increase the likelihood of cesarean delivery [2, 8]. The authors agree that women with meconium-stained amniotic fluid or with symptoms of infection such as fever or maternal and/or fetal tachycardia with elevated biochemical markers of inflammation are at high risk of neonatal infection and puerperal endometritis, and suggest striving for immediate delivery [3, 4, 5]. The presence of meconium in the outflowing amniotic fluid increases the risk of intrauterine infection, which can be reduced by intrapartum antibiotic administration, and the risk of postpartum hemorrhage [11, 12, 13].

In our study group, the number of participants with meconium-stained amniotic fluid was too small to make a credible conclusion about the procedures and outcomes.

As mentioned above, labor induction is one of the most common procedures in obstetrics, used in at least one in four pregnancies [7, 14, 15, 16]. There is no doubt that it should be recommended when the risk of waiting for spontaneous onset of labor outweighs the benefits of induction, and should be performed with the patient's signed informed consent [7, 14]. Marconi suggests that such a document should include information about the statistical chance of success of labor induction in a particular medical center [7].

Among the various risk factors for procedural failure, i.e. gestational age, maternal age and BMI, parity or expected fetal weight, unfavorable cervix is also included [7, 14]. One of the methods of cervical assessment is the Bishop scale. If the Bishop score is at least 6, labor induction increases the chance of vaginal delivery [7, 14].

In our hospital, pharmacological means of labor induction are available, i.e. i.v. oxytocin, oral and vaginal misoprostol, vaginal dinoprostone, as well as mechanical means such as Foley catheter. Each can be used alone or in combination. The analysis by Mozurkewich et al. showed that in women with

PROM, i.v. oxytocin was more effective in reducing the time to delivery than waiting, but less effective than vaginal PGE2, and also increased the rate of cesarean section [15].

As mentioned above, Hannah et al. and Sibiude found no such effect of oxytocin on the prevalence of cesarean delivery [2, 8]. After analyzing the research of Mozurkewich et al, they also stated that mechanical methods have a lower risk of uterine hyperstimulation than vaginal prostaglandins, but increase the risk of puerperal and neonatal infection [15]. Amorosa et al. found no benefit of combined Foley catheter and i.v. oxytocin in nulliparous women compared to i.v. oxytocin alone [17]. Like Mozurkewich et al, the authors emphasize the risk of infection when using a Foley catheter [15, 17]. Mckeen et al, who compared Foley catheter with vaginal misoprostol in PROM at 36 weeks' gestation, found that mechanical induction of labor shortened the time to delivery and did not increase the percentage of cesarean sections or the prevalence of chorioamnionitis [16]. Sarreau et al. state that it is a safe and effective method to be used in women after previous cesarean section [18]. However, in both studies the study groups were rather small, as Mackeen had 122 and Sarreau et al. 151 participants. Our material was also too small for credible conclusions, but the procedure seems to be relatively safe, especially in women after previous cesarean section, and inexpensive and acceptable to patients. Nevertheless, the only neonate in our study group who required treatment for infection came from a Foley catheter induction of labor.

Wallstrom et al. show that induction of labor using oral prostaglandins is as safe as the mechanical method in women with a previous cesarean delivery, and both are safer than vaginal dinoprostone [19].

According to Seaward et al, the risk of neonatal infection within 24 h of PROM is less than 1%, rising to 3–5% in the presence of clinical signs of chorioamnionitis [3]. Therefore, the need for antibiotic administration in pregnant women with tPROM who present with clinical symptoms or elevated biochemical markers of inflammation is unquestionable [4]. The risk of maternal and fetal infection is also higher in women who are GBS carriers, which means that this group, as well as those with unknown GBS status, are in need of prophylactic administration of antibiotics [4, 20, 21]. According to some researchers, other important risk factors are the duration of the period from the onset of amniotic fluid leakage to delivery and the number of vaginal obstetric examinations, especially more than 7 [3, 6, 20, 22]. Limiting the number of examinations to the necessary minimum should be considered in such circumstances, especially in GBS-positive women [3]. Antibiotic therapy in every case of tPROM does not seem justified [6, 22]. With the exception of GBS carriers, antibiotics should be considered in women with prolonged amniotic fluid leakage. As Saccone et al. showed in their analysis, antibacterial treatment reduces the prevalence of chorioamnionitis and puerperal endometritis in the group with a tPROM duration of more than 12 h [6]. Their postulate of antibiotic use in every woman with tPROM whose duration to delivery is predicted to exceed 12 h has been confirmed by other analyses [6, 10, 20, 22].

In our study group, all GBS carriers and women with unknown GBS status received antibiotics immediately after hospital admission. Those who qualified for the waiting period and had no clinical symptoms or biochemical markers of inflammation were started on antibiotics at least 12 h after tPROM. In our analysis, we did not find an increased rate of chorioamnionitis, puerperal endometritis, or neonatal infection, which may be due to the small size of the cluster. What caught our attention was the different approaches of individual physicians, especially during the waiting period.

CONCLUSIONS

In our study group of women with tPROM, no one required treatment for infection despite the chosen approach. Infection was confirmed in only one newborn.

The use of a Foley catheter should be limited to women with contraindications to prostaglandins, such as previous cesarean section or those who refuse to consent to pharmacologic induction of labor.

There are differences in the approach taken by different health professionals within the team, particularly in terms of waiting time.

It seems that in order to standardize the procedure it is necessary to develop detailed principles, including allowable waiting time according to the initial clinical situation, maternal and fetal monitoring, use of biochemical markers of inflammation, antibiotic therapy as well as methods of labor preinduction, based on experience, available recommendations and literature. Such a standard should be presented and discussed with patients with tPROM.

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