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Original Article

The clinical management and outcome of term premature rupture of membrane in East China: results from a retrospective multicenter study

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Abstract: In this study, we investigated the management of term premature rupture of membranes (PROM) and maternal-fetal outcomes in East China. Between January and December 2012, the term delivery data for 111390 pregnant women was retrospectively analyzed. The subjects were divided into two groups: those women who had term PROM (PROM Group, n=13927) and those who did not (Control Group, n=94341). The general patient characteristics, the mode of delivery, and the maternal and fetal complications were recorded. Statistical analysis was completed using the Student's t-test and χ^2-test. The incidence of term PROM in East China is approximately 12.5%. The maternal demographic and obstetric characteristics were similar between the two groups. Patients in the PROM group had a higher incidence of bacterial vaginitis (BV), chlamydia trachomatis (CT) infection, postpartum hemorrhage, and cesarean section deliveries. Infants in the PROM group experienced higher rates of infection, asphyxia, and jaundice. There was a high cesarean section rate, and further efforts are needed to increase the vaginal delivery rate for women with term PROM.

Keywords: Premature rupture of membranes (PROM), cesarean section, asphyxia neonatorum, term birth

Introduction

Premature rupture of membranes (PROM), most commonly defined as the rupture of membranes before the onset of labor, with a reported incidence of approximately 2.7%-7% in China and 5-15% in America [6]. PROM has a major impact on fetal and maternal outcomes. For term pregnancies with PROM, the risk of infection-associated morbidity to the mother and fetus is increased with prolonged rupture of membranes.

There is general consensus that term pregnant patients with PROM should be delivered to avoid infection to both the mother and the infant, as the dangers of infection increase with a prolonged latent period. In 2013, the American College of Obstetricians and Gynecologists (ACOG) published an updated practice guideline for PROM based on the 2007 guideline, recommending the induction of labor immediately after a term PROM diagnosis to reduce maternal and neonatal infection rates. However, early interference may increase the incidence of cesarean section (CS). Recent studies show that expectant management is safe and more often leads to vaginal delivery. However, there is currently no practice guideline for this clinical situation in China, and the management of term PROM remains controversial. To our knowledge, most obstetricians in China agree that the induction of labor should be initiated in term PROM women if spontaneous labor does not occur within 12-24 hours [12]. We selectively collected the delivery data for women, all of whom underwent induction of labor within 24 hours in 16 large cities in East China, and retrospectively analyzed the impact of term PROM on maternal and fetal outcomes.

Methods

The study is an observational retrospective study of 111390 pregnant women who under-

Table 1. Maternal demographic characteristics

Characteristics	PROM group (n=13927)	Control group (n=94341)	*P* value
Maternal age, year	27.8±4.7	28.3±5.0	0.79
Gestational age at delivery, week	38.1±2.1	38.9±1.9	0.10
Body mass index, kg/m^2	28.4±2.1	27.9±3.7	0.43
Miscarriage, No. (%)	5599 (40.2%)	35358 (37.5%)	0.00
Parity	0.71±0.68	0.69±0.70	0.62

went delivery at hospitals in 16 East China cities, including Shanghai, Hangzhou, Chengdu, Xi'an, Nanjing, Jinan etc, between January and December 2011. The women were divided into two groups; the PROM group included 13927 pregnant women with term PROM (at ≥37 weeks of gestation), while the control group included 94341 pregnant women who gave birth without PROM during the same period. For the women with PROM, all the physicians allowed for spontaneous labor to occur within a maximum of 24 hours before initiating the induction of labor.

A vaginal cultures routinely obtained in all pregnant patients at the second stage of pregnancy and repeated at the onset of PROM. The ultrasounds were performed on all patients at presentation for delivery. The diagnosis of PROM was based on the patient's history, including either unexpected and abundant or scanty and steady vaginal amniotic fluid leakage. The diagnosis was confirmed with a sterile vaginal examination that was performed to assess the Bishop score and to rule out umbilical cord prolapse. A sterile speculum examination was performed to visualize the amniotic fluid leakage through the cervical canal or pooling of amniotic fluid in the posterior vaginal fornix. The vaginal fluid pH was also assessed to confirm the diagnosis. Simultaneously, vaginal swabs were taken to assess for bacterial vaginitis (BV) and for the culture and identification of microorganisms (Chlamydia trachomatis, N. gonorrhea, etc.). The patients were immediately admitted to the hospital following the PROM diagnosis. After a comprehensive evaluation of possible obstetric and medical complications and the exclusion of any contraindications to vaginal delivery, the women underwent expectant management. If spontaneous labor did not occur within a maximum of 24 hours (6-24 hours at different hospitals), induction of labor by oxytocin was initiated. Prophylactic antibiotics with either cephalosporins (if woman was not allergic to cephalosporins) or erythromycin (if was allergic to cephalosporins) were administered since 12 hours after the onset of PROM.

The maternal demographic characteristics considered in the analysis as possible risk factors were maternal age, gestational age at delivery, body mass index (BMI, calculated as weight (kg)/[height (m)]^2), miscarriage, and parity. Antenatal risk factors, such as gestational diabetes, hypertension, anemia, intrahepatic cholestasis, and vaginal infections were also analyzed for both groups. The maternal and obstetric outcomes were compared between the two groups, including the amniotic fluid index (AFI), the CS rate, and the incidence of postpartum hemorrhage. The neonatal outcomes included birth weight, fetal length, sex, and complications, such as neonatal asphyxia, jaundice and infection. We divided the CS patients into two groups either medical indication or none-medical indications.

Statistical analysis

The data were collected using Microsoft Office 2007 (Window XP; Microsoft Corp., Redmond, WA, USA) and analyzed using PASW 17.0 software package (PASW Inc., Chicago, IL, USA). Data were expressed as the mean ± standard deviation (m ± s) or rate (%) and were tested for significance using the Student's t-test and the χ^2-test or Fisher's exact test. A *P*-value <0.05 was considered statistically significant.

Results

From the original data set of 111390 deliveries, we identified 17049 (15.3%) women with PROM, and of these, 13927 (12.5%) with term PROM. The maternal demographic and obstetric characteristics were similar between the two groups, with no significant differences in maternal age (27.8±4.7 vs. 28.3±5.0, *P*>0.05), gestational age at delivery (38.1±2.1 vs. 38.9±1.9, *P*>0.05), body mass index (28.4±2.1 vs. 27.9±3.7, *P*>0.05), or parity (0.71±0.68 vs. 0.69±0.70, *P*>0.05). The incidence of a miscarriage history in the PROM group was significantly higher than in the control group (40.2% vs. 37.5%, *P*<0.05) (**Table 1**).

Table 2. Antenatal risk factors in two groups

Antenatal risk factors	PROM group (n=13927)	Control group (n=94341)	*P* value
None, No. (%)	11740 (84.3%)	80379 (85.2%)	0.89
Gestational diabetes, No. (%)	822 (5.9%)	4057 (4.3%)	0.16
Gestational hypertension, No. (%)	100 (0.72%)	2547 (2.7%)	0.00
Intrauterine growth restriction, No. (%)	65 (0.47%)	358 (0.38%)	0.99
Chronic hypertension, No. (%)	18 (0.13%)	387 (0.41%)	0.63
Anemia, No. (%)	468 (3.36%)	2295 (2.43%)	0.38
Intrahepatic cholestasis, No. (%)	18 (0.13%)	673 (0.71%)	0.00
Thyroid dysfunction, No. (%)	121 (0.87%)	443 (0.47%)	0.43
Uterine myoma, No. (%)	344 (2.47%)	2367 (2.51%)	0.56
Bacterial Vaginitis (BV), No. (%)	345 (2.48%)	642 (0.68%)	0.00
Chlamydia trachomatis (CT), No. (%)	962 (6.91%)	689 (0.73%)	0.00

Table 3. Maternal and obstetric outcomes

Outcome	PROM group (n=13927)	Control group (n=94341)	*P* value
Mode of delivery			
Aginal delivery, No. (%)	6253 (44.9%)	54287 (57.5%)	0.00
Spontaneous, No. (%)	6053(96.8%)	52713 (97.1%)	0.17
Forceps, No. (%)	200 (3.2%)	1574 (2.9%)	0.15
Cesarean delivery, No. (%)	7674 (55.1%)	40054 (42.5%)	0.00
AFI, cm	9.4±4.7	10.9±3.9	0.00
Postpartum hemorrhage, No. (%)	710 (5.1%)	3491 (3.7%)	0.00

Abbreviation: AFI: Amniotic fluid index in the Ultrasound; CRP: C-Reactive action protein (g/L).

The incidence of some antenatal risk factors, such as gestational diabetes (5.9% vs. 4.3%, *P*>0.05), intrauterine growth restriction (0.47% vs. 0.48, *P*>0.05), chronic hypertension (0.13% vs. 0.41%, *P*>0.05), anemia (3.36% vs. 2.43%, *P*>0.05), thyroid dysfunction (0.87% vs. 0.47%, *P*>0.05), and uterine leiomyoma (2.47% vs. 2.51%, *P*>0.05), was similar between the two groups. The proportion of patients with gestational hypertension (0.72% vs. 2.7%, P<0.05) and intrahepatic cholestasis (0.13% vs. 0.71%, P<0.05) in the PROM group was significantly lower than the proportion in the control group. However, the proportion of patients with BV (2.48% vs. 0.68%, P<0.05) and CT (6.91% vs. 0.73%, P<0.05) in the PROM group was significantly higher than the proportion in the control group (**Table 2**).

Regarding the maternal and obstetric outcomes, the patients in the PROM group had lower AFI values (9.4±4.7 vs. 10.9±3.9, P<0.05) compared with the control group. The incidence of postpartum hemorrhage was significantly higher in the PROM group than in the control group (55.1% vs. 42.5%, *P*<0.05). As compared with none medical indications for CS, there was no statistic difference in two groups (data not shown). None medical reasons for a maternal request for CS, including choice of a specific birth date, fear of pain, the wish to keep fit, and desire to obtain better health for the child and herself. The PROM group had a higher rate of CS delivery (55.1% vs. 42.5%, P<0.05). No significant difference in obstetric outcomes with respect to forceps delivery (3.2% vs. 2.9%, P>0.05) was found between the groups (**Table 3**).

Table 4 displays the neonatal outcomes for both groups. Neonatal birth weight (3.23±0.81 vs. 3.27±0.56, P>0.05), neonatal length (49.5±2.7 vs. 49.7±2.9, P>0.05), neonatal sex, Apgar score at 1 min (8.2±0.6 vs. 8.6±0.9, P>0.05), and Apgar score at 5 min (9.2±0.4 vs. 9.2±0.4, P>0.05) did not differ significantly between the groups. Infants in the PROM group presented with a significantly higher rate of neonatal asphyxia (3.2% vs. 2.2%, *P*<0.05) and neonatal jaundice (0.21% vs. 0.08%, *P*<0.05). The overall neonatal infection rate was significantly higher in the PROM group compared with the control group (0.27% vs. 0.06%, *P*<0.05).

Discussion

We collected data for pregnant women in East China and demonstrated that 15.3% of a total of 111390 pregnant women suffered from PROM, of which 12.5% had term PROM.

PROM is the result of the interaction of many factors. Pathogenic microorganisms ascending

Table 4. Neonatal outcomes

Outcome	PROM group (n=13927)	Control group (n=94341)	*P* value
Birth weight, kg	3.23±0.81	3.27±0.56	0.23
Neonatal length, cm	49.5±2.7	49.7±2.9	0.15
Neonatal sex			
Male, No. (%)	7284 (52.3%)	53491 (56.7%)	0.54
Female, No. (%)	6643 (47.7%)	40850 (43.3%)	0.34
Apgar score at 1 min	8.2±0.6	8.6±0.9	0.12
Apgar score at 5 min	9.2±0.4	9.1±0.5	0.17
Neonatal asphyxia, No. (%)	446 (3.2%)	2111 (2.2%)	0.00
Neonatal jaundice, No. (%)	29 (0.21%)	75 (0.08%)	0.01
Neonatal infection, No. (%)	38 (0.27%)	61 (0.06%)	0.00

the genital tract and causing infection is one of the main risk factors of preterm PROM. The exactly causes of term PROM are still unknown. We indentified that the women in the PROM group had a higher prevalence of vaginal infection with BV and CT than the women in the control group. These fingdings suggested that infection may also a risk factor of term PROM. Other risk factors for term PROM include uterine distension (i.e., polyhydramnios, multiple pregnancies), abnormal fetal position and cephalopelvic disproportion. Makhlouf demonstrated that two or more spontaneous or induced abortions were associated with an increased risk for preterm PROM (OR, 2.9; 95% CI, 1.6-5.3) [14]. Our results indicated that a history of abortion was significantly more common among women in the term PROM group than among women in the control group, suggesting that abortion is also a risk factor for term PROM. Additionally, we found no difference between the two groups with respect to some antenatal risk factors, including gestational diabetes, intrauterine growth restriction, chronic hypertension, anemia, thyroid dysfunction, or the presence of uterine leiomyomas. However, women in the PROM group had a higher incidence of gestational hypertension and intrahepatic cholestasis. A possible reason for this finding could be that the majority of women suffering from these diseases underwent pregnancy termination prior to rupture of membranes.

The most serious complication of term PROM is maternal and neonatal infection, with an increasing risk of complications observed with prolonged PROM [8]. The morbidity of neonatal infection following PROM was 2%-3%, ten-fold higher than the incidence following delivery without PROM and increased two-fold when complicated with chorioamnionitis [13]. In our study, the incidence of neonatal infection in the PROM group was 0.27%, significantly higher than the 0.06% found in the control group. The incidence of neonatal infection in the PROM group in our study was much lower than reports from the literature. There are two possible explanations for this apparent discrepancy; first, prophylactic antibiotics were administered every 12 hours following the onset of PROM, and second, following the onset of PROM, the induction of labor was initiated after only 24 hours of waiting for spontaneous labor to occur. Infants in the PROM group also had significantly higher incidences of other neonatal complications, such as neonatal asphyxia (3.2% vs. 2.2%) and neonatal jaundice (0.21% vs. 0.08%) when compared to the control group.

The optimal approach to the clinical assessment and treatment of women with term PROM remains controversial. The 2013 ACOG guideline stated that “For women with PROM at 37 0/7 weeks of gestation or more, if spontaneous labor does not occur near the time of presentation in those who do not have contraindications to labor, labor should be induced.” While guidance is given with regards to expectant management or labor induction, the appropriate waiting period from PROM to labor induction is not specified in terms of hours. Early intervention may result in an increased risk of labor induction failure and lead to a higher CS rate [7]. In contrast, a delayed induction may result in higher maternal and fetal infection rates. The appropriate waiting time from PROM to spontaneous onset of labor, as reported by different authors, includes 96 h [10], 72 h, 48 h, 24 h, 18 h, or 12 h [9, 5, 11, 15-17]. Currently no uniform guidelines exist for the management of term PROM in China, and most physicians wait 12-24 hours before inducing labor.

Rising cesarean delivery rates in North America and Europe as well as in China continue to be a major concern for medical professionals [18]. In the setting of term PROM, large clinical trials

and meta-analyses have demonstrated that the induction of labor does not increase the risk of CS delivery [3, 4]. In our study, we found that women with term PROM had a higher CS rate compared with women who did not have PROM (55.1% vs. 42.5%). This difference might be explained by the insufficient waiting period (no more than 24 hours) before the induction of labor in the patients in our study, as the expectant management approach for term PROM allows more time for cervical ripening to take place, thus increasing the chance of a vaginal delivery. As previously reported, a lower cervical dilatation score is an independent antenatal risk factor for failed induction of labor in nulliparous women [7].

Conclusion

In summary, for women with term PROM in East China, the CS delivery rate in this population is higher in East China, and further efforts are needed to increase the vaginal delivery rate in term PROM women. Methods include the appropriate extension of the waiting period until spontaneous labor, the active prevention of infection, the use of aseptic techniques, reduction in the frequency of vaginal examinations, and the judicious use of prophylactic antibiotics.

Disclosure of conflict of interest

None.

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