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Original Article

# Premature rupture of the membranes in twin pregnancies: Maternal and fetal outcomes

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ABSTRACT

*Aim:* To analyse outcomes of twin pregnancies complicated by membranes rupture between 24 and 37 weeks of gestation.
*Methods:* Retrospective matched cohort study on twin pregnancies with premature membranes rupture, through review of clinical records at the Policlinico S. Orsola di Bologna, a tertiary hospital, between 2010 and 2020.
*Results:* 171 twin pregnancies were admitted, over 10 years, with a diagnosis of premature rupture of membranes PPROM (fluid pooling on speculum and/or Insulin Growth Factor Binding Protein1 positive on vaginal secretions and oligohydramnios at ultrasound). The maternal and fetal outcomes of these pregnancies were compared to those of uneventful 178 twin pregnancies. There was no difference on risk factors. The mean gestational age at PROM was 33.9 weeks. PPROM newborns showed a lower birth weight (2072 ± 515 g vs. 2384 ± 454, $p < 0.001$), a higher rate of admission to neonatal intensive care unit (45.6 % vs 22.2 %, $p < 0.001$), and a higher rate of adverse outcomes, even if it did not achieve statistical significance (crude OR: 3.05, 95 % CI: 2.04–4.56; adjusted OR: 1.45, 95 % CI: 0.87–2.41). No cases of sepsis were found.
*Conclusion:* In our cohort of twin pregnancies no significative risk factors for premature rupture of membranes were found. Although PROM is known to increase infectious morbidity, not all patients will develop these complications. PROM in twin pregnancies does not appear to be an independent risk factor for adverse maternal or neonatal outcomes when the effect of prematurity is accounted for. Strategies to prolong pregnancy, when feasible, may mitigate adverse neonatal outcomes associated with PPROM in twin pregnancies.

## Introduction

Incidence of twin births has significantly increased over the past decade, largely due to the widespread use of assisted reproductive technologies (ART) and a general trend toward delayed childbearing. Both the transfer of multiple embryos during ART and advanced maternal age—which is associated with increased rates of multiple ovulation—have contributed to this escalation [1].

Twin pregnancies are associated with a higher risk of maternal and fetal complications compared to singleton pregnancies [2]. One of the most significant factors to perinatal morbidity and mortality in twin gestations is preterm birth, which occurs in approximately 41 % of twin pregnancies before 37 weeks, 13 % before 34 weeks, and 7 % before 32 weeks of gestation [3].

Among the causes of preterm birth, preterm premature rupture of membranes (PPROM)—defined as rupture of the chorioamniotic membranes before the onset of labor and before 37 weeks of gestation—plays a key role [4]. PPROM is more frequent in multiple gestations and can lead to serious complications, including cord prolapse, chorioamnionitis, placental abruption, and neonatal prematurity [5]. These outcomes contribute to both maternal and neonatal morbidity. The duration of membrane rupture is particularly important, as prolonged rupture increases the risk of maternal infection and puerperal sepsis [6].

Several risk factors for PPROM have been identified, including a history of PPROM or preterm birth, extreme maternal age (<18 or >40 years), Black or Caribbean ethnicity and genitourinary infections [7]. In

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addition, specific conditions such as twin-to-twin transfusion syndrome (TTTS) or twin reversed arterial perfusion (TRAP)—often treated with fetal surgery in monochorionic twins—may further increase the risk of membrane rupture [8]. Some evidence also suggests that pregnancies conceived through ART are more susceptible to PPROM than spontaneously conceived pregnancies [9].

This retrospective cohort study aimed to evaluate maternal and neonatal outcomes in twin pregnancies complicated by PPROM and to identify potential risk factors associated with its occurrence.

We hypothesized that PPROM in twin pregnancies is associated with increased neonatal morbidity.

## Matherial and methods

This is a retrospective cohort study carried out at the Department of Obstetrics and Prenatal Medicine, University Hospital IRCCS Sant'Orsola Malpighi, Bologna, Italy. The study protocol was approved by the institutional review board (IRB) of IRCCS Azienda Ospedaliero-Universitaria di Bologna (CE-AVEC Area Vasta Emilia Romagna Centro, protocol number 8/2020/Oss/AOUBo), and was lead in accordance with the principles of the Declaration of Helsinki.

We identified all twin pregnancies complicated by PPROM admitted between January 2010 and July 2020 and compared them with a sample of twin pregnancies without PPROM admitted during the same period. PPROM was diagnosed based on at least two of the following criteria:

Visible leakage of amniotic fluid from the internal cervical os observed during sterile speculum examination;

Positive biochemical testing of vaginal fluid using the AMNIOQUICK® rapid test, which detects Insulin-Like Growth Factor Binding Protein-1 (IGFBP-1) — a marker found in high concentrations in amniotic fluid;

Ultrasound evidence of anhydramnios or a maximum vertical pocket of amniotic fluid <2 cm.

Control pregnancies were randomly selected from the hospital database using ICD-9 diagnostic codes to ensure group homogeneity. We included all twin pregnancies, either monochorionic or dichorionic but excluding trichorionic ones, regardless the mode of delivery or method of conception. We did not exclude twin pregnancies reduced spontaneously or through selective feticide either those hesitated in abortion or stillbirth.

Data regarding maternal or obstetric pathologies, pregnancy management and following outcomes, were collected through our records. Neonatal data were collected through inpatient records and discharge letters. All patients with diagnosis of PPROM were managed following the existing guidelines [7].

In our Institute, we routinely hospitalize patients diagnosed with PPROM. According to our internal protocol, computerized cardiotocographic (CTG) monitoring is performed three times daily starting at 30 weeks of gestation. Daily ultrasound assessments and maternal vital signs are recorded three times per day. Blood tests, including C-reactive protein (CRP), are carried out every two days. In all cases, a vaginal swab is performed to detect bacteria and yeasts, and patients receive antenatal corticosteroids and a combined antimicrobial therapy during the first week of hospitalization [8–10].

## Statistical analysis

Numerical variables were summarized as mean ± standard deviation [interquartile range (IQR)]; categorical variables were summarized as frequencies and percentages. Crude comparisons of maternal baseline characteristics and maternal/fetal complications between PROM and non-PROM patients were conducted with the *t*-test, chi-squared test and Fisher's exact test, where appropriate. To control for potential correlation owing to twins born to the same mother, logistic regression analysis with cluster-robust estimators was used for testing the differences in neonatal characteristics, complications and mortality between PROM and non-PROM newborns.The selection of variables for inclusion in the multivariable model was based on:-clinical relevance based on prior literature and biological plausibility (e.g., maternal age, chorionicity, ART conception, smoking, infections);-statistical significance in univariate analysis ($p < 0.10$ threshold); -availability and completeness of data in the medical records. Variables included in the final model were: maternal age, parity, mode of conception (ART vs. spontaneous), chorionicity (monochorionic vs. dichorionic), previous history of PPROM or preterm birth, presence of genitourinary infection and pregnancy-related complications (e.g., gestational diabetes, hypertensive disorders). Adjusted odds ratios (aOR) with 95 % confidence intervals (CI) were reported. A p-value < 0.05 was considered statistically significant. Results of regression analysis were presented as odds ratios (ORs) and 95 % confidence intervals (CIs). To account for potential confounding related to chorionicity, we performed a sensitivity analysis restricted to dichorionic twin pregnancies. Monochorionic and dichorionic twin pregnancies have different baseline risks, with monochorionic pregnancies being associated with higher rates of complications such as twin-to-twin transfusion syndrome, selective intrauterine growth restriction and placental abnormalities. Including both types in the main analysis could introduce bias, as adverse outcomes may be due to chorionicity rather than to the exposure of interest (PPROM). Therefore, focusing the sensitivity analysis on dichorionic pregnancies allowed us to assess the robustness of our findings in a more homogeneous population and determine whether the associations observed between PPROM and perinatal outcomes persisted independently of chorionicity.

All analyses were carried out by using Stata software, version 15 (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LP). All tests were 2-tailed, and the significance level was set at 5 %.

## Results

### *Maternal data*

The maternal baseline characteristics of the study sample ($n = 349$), overall and by exposure to PROM, are presented in Table 1. In the PROM group, 28 monochorionic pregnancies (16.4 %) and 143 dichorionic pregnancies (83.6 %) were observed. In the non-PROM group, 45 monochorionic pregnancies (25.3 %) and 133 dichorionic pregnancies (74.6 %) were observed, with a borderline statistical significance in the difference in chorionicity status ($p = 0.041$). In general, 75.6 % of mothers were at first pregnancy, with no statistically significant difference between PROMs and non-PROMs ($p = 0.056$). There were no differences in exposure to potential risk factors, such as invasive procedures (CVS, amniocentesis, laser for TTTS, selective feticide and intrauterine blood transfusion). In the PROM group, the most frequent indication to deliver was the inevitable onset of labor, so delivery was "unavoidable" (61.4 % vs. 9.1 %, $p < 0.001$). 93.0 % of PROM patients received antibiotic therapy. On average, PROM occurred at 33.9 ± 2.9 weeks [IQR: 32.7–35.9]. The latency between the PROM event and the delivery was 2.4 ± 8.2 days [IQR: 0–2]. In this group, eight vaginal deliveries were recorded.

In the non-PROM group, all patients (178 out of 178) delivered by cesarean section, while in the PROM group a slightly lower percentage was observed, with 163 out of 171 patients (95.3 %) ($p < 0.001$). As shown in Table 2, the overall rate of antenatal pregnancy complications (Vaginal blood loss, preeclampsia, eclampsia, gestational diabetes etc.) was higher in the non-PROM group (75.3 % vs. 58.5 %, $p = 0.001$). Postnatal maternal complications, including anemia, fever, blood transfusion, and postpartum hemorrhage, were similar in the two compared groups ($p = 0.228$).

### *Neonatal data*

After excluding 17 records with extensive missing data (3 PROMs

**Table 1**
Maternal baseline characteristics, overall and stratified by premature rupture of membranes (PROM) status. Summary measures are counts (percentages) or mean ± standard deviation [interquartile range].

| Characteristic | All ($n$ = 349) | PROM ($n$ = 171) | Non-PROM ($n$ = 178) | $P$-value |
|---|---|---|---|---|
| Age, y | 35.6 ± 5.3 [32–39] | 35.7 ± 5.0 [33–39] | 35.4 ± 5.6 [32–39] | 0.615 |
| Multipara | 85 (24.4) | 34 (19.9) | 51 (28.7) | 0.056 |
| Chorionicity | | | | 0.041* |
| Monochorionic | 73 (20.9) | 28 (16.4) | 45 (25.3) | |
| Dichorionic | 276 (79.1) | 143 (83.6) | 133 (74.6) | |
| Assisted reproduction | | | | 0.269 |
| No | 159 (45.6) | 76 (44.4) | 83 (46.6) | |
| Yes | 174 (49.9) | 90 (52.6) | 84 (47.2) | |
| Unspecified | 16 (4.6) | 5 (2.9) | 11 (6.2) | |
| One or more invasive procedures | 104 (29.8) | 50 (29.2) | 54 (30.3) | 0.823 |
| CVS | 62 (17.8) | 26 (15.2) | 36 (20.2) | 0.220 |
| Amniocentesis | 44 (12.6) | 26 (15.2) | 18 (10.1) | 0.152 |
| Laser for TTTS | 4 (1.1) | 3 (1.8) | 1 (0.6) | 0.363 |
| Selective feticide | 2 (0.6) | 1 (0.6) | 1 (0.6) | 1.000 |
| Intrauterine blood transfusion | 1 (0.3) | 1 (0.6) | 0 (0.0) | 0.490 |
| Delivery indications | (2 missing) | (0 missing) | (2 missing) | |
| Inevitable delivery | 121 (34.9) | 105 (61.4) | 16 (9.1) | <0.001** |
| Elective c-section | 118 (34.0) | 0 (0.0) | 118 (67.0) | <0.001** |
| Previous c-section | 19 (5.5) | 7 (4.1) | 12 (6.8) | 0.265 |
| Pathologic cardiotocography | 12 (3.5) | 5 (2.9) | 7 (4.0) | 0.591 |
| Breech presentation | 11 (3.2) | 9 (5.3) | 2 (1.1) | 0.028* |
| Abruptio placentae | 3 (0.9) | 3 (1.8) | 0 (0.0) | 0.119 |
| Increase in CRP levels | 1 (0.3) | 1 (0.6) | 0 (0.0) | 0.493 |
| Cesarean section | 341 (97.7) | 163 (95.3) | 178 (100.0) | · |
| White blood cells, $10^9$/L | 10.86 ± 3.66 [8.41–12.37] | 11.67 ± 4.00 [8.97–13.20] | 10.1 ± 3.15 [8.06–11.72] | <0.001** |
| Induction of fetal lung maturation | 151 (43.3) | 100 (58.5) | 51 (28.7) | <0.001** |
| Use of tocolytics | 49 (14.0) | 38 (22.2) | 11 (6.2) | <0.001** |

* Significant at the 5 % level.
** Significant at the 1 % level.
Abbreviations: CVS, chorionic villus sampling; TTTS, twin-to-twin transfusion syndrome; CRP = *C*-reactive protein.

**Table 2**
Fetal and maternal complications, overall and stratified by premature rupture of membranes (PROM) status. Summary measures are counts (percentages).

| Complication | All ($n$ = 349) | PROM ($n$ = 171) | Non-PROM ($n$ = 178) | $P$-value |
|---|---|---|---|---|
| *Fetal complications* | *146 (41.8)* | *63 (36.8)* | *83 (46.6)* | *0.064* |
| IUGR | 28 (8.0) | 13 (7.6) | 15 (8.4) | 0.777 |
| Single Umbilical Artery | 9 (2.6) | 3 (1.8) | 6 (3.4) | 0.503 |
| Congenital Heart Disease | 6 (1.7) | 1 (0.6) | 5 (2.8) | 0.215 |
| Fetal abnormalities (es club feet) | 5 (1.4) | 2 (1.2) | 3 (1.7) | 1.000 |
| *Antenatal maternal complications* | *234 (67.1)* | *100 (58.5)* | *134 (75.3)* | *0.001*** |
| Gestational Diabetes | 24 (6.9) | 7 (4.1) | 17 (9.6) | 0.044* |
| Vaginal blood loss | 18 (5.2) | 3 (1.8) | 15 (8.4) | 0.005** |
| Cholestasis | 18 (5.2) | 10 (5.8) | 8 (4.5) | 0.568 |
| Eclampsia | 14 (4.0) | 0 (0.0) | 14 (7.9) | <0.001** |
| Preeclampsia (proteinuria) | 8 (2.3) | 0 (0.0) | 8 (4.5) | 0.005** |
| *Postpartum maternal complications* | *160 (45.85)* | *84 (49.1)* | *76 (42.7)* | *0.228* |
| Anemia | 133 (38.1) | 70 (40.9) | 63 (35.4) | 0.287 |
| Hypertension | 9 (2.6) | 3 (1.8) | 6 (3.4) | 0.503 |
| Hyperpyrexia | 7 (2.0) | 5 (2.9) | 2 (1.1) | 0.275 |
| Post partum hemorrhage | 4 (1.1) | 3 (1.8) | 1 (0.6) | 0.363 |
| Blood transfusion | 5 (1.4) | 3 (1.8) | 2 (1.1) | 0.680 |

* Significant at the 5 % level.
** Significant at the 1 % level.
Notes: Composite indicators include any fetal, maternal, and postpartum complications gathered in the study. For the sake of simplicity, not all individual complications are reported in the table. The following complications, although recorded, were not individually summarized: hypothyroidism, need for uterotonics in postpartum.

and 14 non-PROMs), we analyzed 681 newborns, 338 (49.6 %) PROMs and 343 (50.4 %) non-PROMs. The characteristics, complications and neonatal mortality of livebirths, overall and by PROM status, are shown in Table 3. There was a statistically significant difference ($p < 0.001$) in the gestational age at labor between pregnancies complicated by PROM (34,3 ± 2,5, IQR: 33.0–36.1) and those not complicated by PROM (36.2 ± 1.9, IQR: 35.3–37.4). PROM newborns showed a lower birth weight (2072 ± 515 g vs. 2384 ± 454, $p < 0.001$), a higher rate of admission to neonatal intensive care units (45.6 % vs 22.2 %, $p < 0.001$), but no significant differences in the mortality rate. Newborns born to mother experiencing PROM during pregnancy showed significantly higher rates of adverse outcomes such as respiratory distress syndrome, significant feeding difficulties, jaundice, necessity of surfactant, and patent foramen ovale. However, after adjusting for relevant clinical covariates (especially duration of pregnancy, which was significantly different between PROMs and non-PROMs), the strength of the association between PROM and any neonatal complications decreased and failed to achieve statistical significance (crude OR: 3.05, 95 % CI: 2.04–4.56; adjusted OR: 1.45, 95 % CI: 0.87–2.41).

### *Sensitive analysis on dichorionic pregnancies*

Maternal baseline characteristics in dichorionic twin pregnancies, overall and stratified by premature rupture of membranes (PPROM) status, are showed in table S1. In the PPROM group were observed 143 dichorionic pregnancies (83.6 %), in the non-PPROM group, 133 dichorionic pregnancies (74.6 %). The two groups were homogeneous in term of maternal age and type of conception (p 0.75 and p 0.61, respectively).

As in the mixed group, there were no differences in exposure to potential risk factors, such as invasive procedures (CVS, amniocentesis, selective feticide and intrauterine blood transfusion). Even in the

**Table 3**
Neonatal characteristics, mortality and complications, overall and stratified by premature rupture of membranes (PROM) status; records with extensive missing data ($n$ = 17) are excluded. Summary measures are counts (percentages) or mean ± standard deviation [interquartile range].

| Characteristics, mortality and complications | All | PROM | Non-PROM | P-value |
|---|---|---|---|---|
| | ($n$ = 681) | ($n$ = 338) | ($n$ = 343) | |
| Female sex | 342 (50.2) | 167 (49.4) | 175 (51.0) | 0.674 |
| Gestational age at delivery, wk | 35.2 ± 2.4 [34.0–37.1] | 34.3 ± 2.5 [33.0–36.1] | 36.2 ± 1.9 [35.3–37.4] | <0.001** |
| Duration of pregnancy | | | | <0.001** |
| Very preterm (<33 wk) | 100 (14.7) | 80 (23.7) | 20 (5.8) | |
| Preterm (33–36 wk) | 372 (54.6) | 204 (60.4) | 168 (49.0) | |
| Early-to-full term (≥37 wk) | 209 (30.7) | 54 (16.0) | 155 (45.2) | |
| Birth weight, g | 2229 ± 509 [1935–2550] | 2072 ± 515 [1730–2390] | 2384 ± 454 [2140–2670] | <0.001** |
| Apgar score after 5 min | | | | 0.062* |
| <7 | 12 (1.8) | 9 (2.7) | 3 (0.9) | |
| ≥7 | 667 (97.9) | 329 (97.3) | 338 (98.5) | |
| Intensive care | 230 (33.8) | 154 (45.6) | 76 (22.2) | <0.001** |
| Length of hospital stay, d | 11 ± 20 [2–12] | 14 ± 21 [3–18] | 8 ± 18 [2–6] | <0.001** |
| Neonatal mortality | 4 (0.6) | 2 (0.6) | 2 (0.6) | 1.000 |
| *Complications* | *412 (60.5)* | *247 (73.1)* | *165 (48.1)* | *<0.001*** |
| Respiratory distress syndrome | 165 (24.2) | 114 (33.7) | 51 (14.9) | <0.001** |
| Significant feeding difficulties | 90 (13.2) | 62 (18.3) | 28 (8.2) | 0.001** |
| Hypoglycemia | 77 (11.3) | 44 (13.0) | 33 (9.6) | 0.126 |
| Small for gestational age | 55 (8.1) | 22 (6.5) | 33 (9.6) | 0.095 |
| Tachypnea | 43 (6.3) | 17 (5.0) | 26 (7.6) | 0.120 |
| Anemia | 37 (5.4) | 23 (6.8) | 14 (4.1) | 0.086 |
| Jaundice | 37 (5.4) | 35 (10.4) | 2 (0.6) | <0.001** |
| Surfactant | 31 (4.6) | 27 (8.0) | 4 (1.2) | 0.001** |
| Atrial septal defect/Patent foramen ovale | 30 (4.4) | 25 (7.4) | 6 (1.7) | 0.001** |
| Patent ductus arteriosus | | | | 0.254 |
| No | 672 (95.6) | 330 (94.0) | 342 (97.2) | |
| Spontaneous closure | 14 (2.1) | 9 (2.7) | 5 (1.5) | |
| Closure with ibuprofen | 1212 (1.7) | 9 (2.6) | 3 (0.9) | |
| Surgical closure | 3 (0.4) | 1 (0.3) | 2 (0.6) | |
| Hyaline membrane disease | 5 (0.7) | 5 (1.4) | 0 (0.0) | 0.444 |
| Bronchopulmonary dysplasia | 7 (1.0) | 5 (1.4) | 2 (0.6) | 0.295 |
| Necrotizing enterocolitis | | | | 0.415 |
| No | 695 (98.9) | 345 (98.3) | 350 (99.4) | |
| Yes | 6 (0.9) | 4 (1.1) | 2 (0.6) | |
| Intraventricular hemorrhage | 6 (0.9) | 6 (1.7) | 0 (0.0) | 0.544 |
| Periventricular leukomalacia | 1 (0.3) | 1 (0.3) | 0 (0.0) | 1.000 |
| Retinopathy of prematurity | 3 (0.4) | 3 (0.9) | 0 (0.0) | 0.122 |

[*] Significant at the 5 % level.
[**] Significant at the 1 % level.
Notes: The composite indicator includes any neonatal complications gathered in the study. For the sake of simplicity, not all individual complications are reported in the table. The following complications, although recorded, were not individually summarized: hypocalcemia. In only two cases in NON PPROM group, Apgar Score was missing.

subanalysis on dichorionic twins, for the PPROM group, the most frequent indication to deliver was the inevitable onset of labor, so delivery was "unavoidable" (60.8 % vs. 9.8 %, $p < 0.001$). Indeed, the only statistically significant difference between the two groups is in the induction of fetal lung maturation (58.7 vs 25.6 $p < 0.001$) and use of tocolytics (21 vs 6.8 $p < 0.001$). 97 % of dichorionic twin pregnancies delivered throughout a c-section. In 68 % of non PPROM dichorionic pregnancies, the c- section was elective, while in 27 % of PPROM patients it was made as an emergency intervention ($p < 0.001$). The most common indication to an emergency c section in PPROM dichorionic pregnancies was the onset of labor. The only cases of abruptio placentae were recorded in the PPROM group, even if they do not reach a statistically significant difference (3 cases VS 0, p 0.248).

In Non-PROM (103/133; 77.4 %) than in PPROM group (89/143; 62.2 %), there was a statistically significant difference ($P = 0.006$) in antenatal maternal complications (gestational diabetes, preeclampsia and vaginal blood loss). There were no statistically significant differences in fetal abnormal findings, such as fetal growth restriction or congenital abnormalities, between the two groups (p 0.675 and p 0.853, respectively). No differences in the PPROM dichorionic mothers were recorded in term of postpartum complications, such as anemia, hyperpyrexia, postpartum hemorrhage and need for blood transfusions (p 0.324). Table S 2

After excluding records with extensive missing data (13), we collected outcomes of 541 newborns, 283 in PPROM group and 258 in non PROM group.

The characteristics, complications and neonatal mortality of livebirths, overall and by PPROM status, are shown in Table S3. Newborns from dichorionic pregnancies complicated by PPROM had a lower gestational age at birth, with the most born between 33 and 36 weeks, a lower birth weight ($p < 0.001$), a lower APGAR score <7 at 5 min and higher admission to intensive neonatal care unit (44.5 % vs 16.7, $p < 0.001$).

Dichorionic twins from PPROM group experienced an higher risk of respiratory distress (33 % vs 11 %, $p < 0.001$), need for surfactant (8 % vs0.1 %, $p < 0.001$), patent foramen ovale (20 % vs 4 %, $p < 0.001$), intraventricular hemorrhage (2 % vs 0, $p < 0.001$). The only two cases of neonatal death were recorded in the PROM group, even if it didn't reach statistical significance. However, after adjusting for relevant clinical covariates, the strength of the association between PPROM and any neonatal complications decreased and failed to achieve statistical significance (crude OR: 3.56, 95 % CI: 2.29–5.53; adjusted OR: 1.35, 95 % CI: 0.77–2.38). (table s3)

## Discussion

This study investigated the impact of prelabor rupture of membranes (PPROM) on maternal and neonatal outcomes in a cohort of twin pregnancies, with a sensitivity analysis on dichorionic pregnancies. We weren't able to define the incidence of this event in the population of pregnant women who deliver in our Hospital, as it is a center where complicated pregnancies are referred from smaller neighboring hospitals. Maternal baseline characteristics indicate difference in chorionicity distribution between PROM and non-PROM groups, with a higher proportion of monochorionic pregnancies in the non-PROM group (25.3 %) compared to the PROM group (16.4 %). This difference reached statistical significance ($p = 0.041$), but close to the threshold. Having a dichorionic pregnancy was, indeed, an independent risk factor for the investigated event; probably, the low compliance of the uterus to a greater distension determined by multiple pregnancy and double placentas, in association to higher pressure in uterine cavity, cause a high stress upon membranes near the internal os of the cervix, resulting in premature rupture of membranes. Furthermore, the increase in uterine pressure is responsible for compression on the pelvic vascular compartment causing hypoxia which leads to uterine contractions and, consequently, premature rupture of membranes [11]. Most mothers of the cohort were experiencing their first pregnancy, and no significant differences in exposure to invasive procedures or risk factors such as medical assisted reproduction, were identified, suggesting comparable baseline maternal profiles between the two groups. Despite our hypothesis, these findings appear to be in contrast with what reported in literature, probably the small sample and low incidence of invasive procedures in our cohort, may explain the difference [12].

Our analysis confirmed that PPROM typically occurred at around 34 weeks of gestation, in line with already published data [12]-about 40 % of twins will have spontaneous labor or PPROM before 37 weeks' gestation- with a median latency of few days before delivery [13]. Most PROM cases led to inevitable onset of labor, reflected in the high rate of cesarean deliveries—almost all in the non-PROM group and a slightly lower but still high rate in the PROM group ($p < 0.001$). Indeed, although vaginal delivery is generally preferred in twin pregnancies when the first twin is in cephalic presentation after approximately 32 weeks of gestation [7]-provided that experienced staff is available—the mode of delivery for preterm premature rupture of membranes (PPROM) in twin pregnancies remains non-standardized. Due to the high risk of complications associated with twin PPROM, such as cord prolapse,or emergency cesarean section after the delivery of the first twin, our institution typically opts for cesarean delivery, especially before 34 weeks of gestation. Nevertheless, in the PROM group, 8 vaginal deliveries were recorded; all occurred before 30 weeks of gestation, and in each case, labor was so fast that performing a cesarean section would have been of greater risk than vaginal delivery.

As expected, in the non-p-PROM group there was an higher incidence of antenatal pregnancy complications such as vaginal blood loss, preeclampsia, eclampsia since those are complications that usually present later in pregnancy compared to the mean gestational age of delivery of the p-PROM group [13]. Postnatal maternal complications, including puerperal fever, were comparable among groups, showing similar postpartum risks regardless of PROM status. Clinical chorioamnionitis was defined in presence of persistent maternal fever >37.5C or a single pick >38 °C, maternal leucocitosis >20.000/mL or foul-smelling amniotic fluid. 93.4 % of PROM patients received antibiotic therapy, following international guidelines [14,15]; despite that, there is a significant increase in white blood cells levels in PROM group (8.97–13.20) compared with non PROM one (8.06–11.72), $p < 0.001^{**}$, with the same result for dichorionic group alone in the sensitivity analysis. No cases of sepsis were recorded in our study.

Newborns from PPROM pregnancies were delivered earlier (around 34 weeks) and had significantly lower birth weights, higher rates of admission to neonatal intensive care units and increased complications, such as respiratory distress syndrome, jaundice and atrial septal defects. However, after adjusting for gestational age and other relevant covariates, the strength of the association between PROM and neonatal complications weakened, and most outcomes no longer reached statistical significance. This suggests that prematurity primarily mediates the observed adverse neonatal outcomes rather than PPROM itself [16]. Despite our multivariable analysis suggests that the observed neonatal complications are largely mediated by earlier gestational age at delivery, we acknowledge that a direct contribution of PPROM to adverse neonatal outcomes cannot be excluded. Indeed, we recognize that PPROM may have direct effects on neonatal health, potentially through mechanisms such as intrauterine infection or fetal inflammatory response [17]. This is consistent with prior literature suggesting that the fetal inflammatory response associated with PPROM may contribute to complications such as respiratory distress or intraventricular hemorrhage IVH, independently of gestational age. However, our data did not confirm a statistically significant independent effect [18].

Subgroup analysis of dichorionic pregnancies showed similar trends. PROM was associated with earlier deliveries, higher rates of emergency cesarean sections, and increased neonatal complications, including respiratory issues and IVH.

Older gestational age at PPROM may be protective against severe perinatal complications (mortality, sepsis, bronchopulmonary dysplasia, necrotising enterocolitis) [18].

Due to the observational nature of this study and the close interdependence between PPROM and preterm birth, residual confounding cannot be ruled out. Therefore, causality should be interpreted with caution and further studies with larger cohorts should be encouraged to investigate these aspects.

The high number of cases enrolled, the multitude of outcomes explored and the assessment of the impact of potential confounders on maternal and perinatal outcomes are the main strengths of this study. The retrospective design, the lack of standardized treatments over such a long-time lapse, the lack of data regarding smoking status and maternal BMI, known as potential risk factors [11], represents the main weakness of this analysis.

In conclusion, PROM in twin pregnancies does not appear to be an independent risk factor for adverse maternal or neonatal outcomes when the effect of prematurity is accounted for. This information may help obstetricians in counseling and managing twin pregnancies complicated by PROM. Where clinically feasible, strategies aimed at prolonging pregnancy may help mitigate some of the neonatal risks associated with PPROM in twin gestations.

## Declaration of competing interest

All authors disclose no financial and personal relationships with other people or organizations that could inappropriately influence this work.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jogoh.2025.103074.

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