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Review article

Outcomes of twin pregnancies complicated by prelabor rupture of membranes before 26 weeks of gestation: systematic review and *meta*-analysis

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ABSTRACT

Objective: To investigate the rate of obstetric and perinatal outcomes of premature rupture of membranes (PROM) occurring before 26 weeks in twin pregnancies.
Data source: Medline, Embase, Cinahl and Web of Science databases were searched electronically up to January 2024.
Study eligibility criteria: The selection criteria included both prospective and retrospective studies of twin pregnancies with PROM before 26 weeks of gestation. Case reports, case series with fewer than 5 cases, review articles, letters to the editor and editorials were excluded. Studies including both singletons and twin pregnancies were also excluded.
Study appraisal and synthesis method: We used *meta*-analyses of proportions to combine data and assess the pooled proportions. We used a random-effect model to perform the pooled data analyses. The study was registered with the PROSPERO database (CRD 42022368057). Quality assessment of the included studies was performed using the Newcastle-Ottawa Scale for cohort studies.
Results: Eight studies including 227 twin pregnancies were included in the analysis. The pooled proportion of termination of pregnancy (TOP) was 4.6 % (95 % CI 1.5–13.4), while the rate of selective TOP (sTOP) was 24.5 % (95 % CI 7.1–57.7). After the exclusion of cases of TOP, the overall rate of spontaneous miscarriage or fetal demise was 20.9 % (95 % CI 11.1–35.8), whereas the live birth rate of at least one twin was 71.6 % (95 % CI 61.2–80.1) of the ongoing pregnancies. The mean gestational age at delivery was 26.5 (95 % CI 25.1–28.0) weeks and the mean latency between PROM and delivery was 5.4 weeks (95 % CI 4.8–5.9) in all cases including those with fetal deaths.
Neonatal outcomes showed that the overall neonatal mortality was 26.4 % (95 % CI 16.7–39.2). When focusing only on pregnancies undergoing sTOP, the observed livebirth rate was 87.7 %. The gestational age at rupture of membranes in these cases was 16.8 (95 % CI 14.9–18.6) weeks and the latency between PROM and delivery was significantly longer (19.9 (95 % CI 18.0–21.7) weeks) than that observed in unterminated pregnancies, with a mean gestational age at delivery nearly in the range of term (36.9 weeks).
Conclusions: PROM in twins before 26 weeks is associated with overall high rates of adverse obstetric and neonatal outcomes, and it represents a clinical challenge for both counseling and management. Larger prospective studies unified objective protocols in terms of antenatal surveillance and management are needed.

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Introduction

Prelabor rupture of membranes (PROM) before viability or in periviable gestational age occurs in up to 0.5 % of pregnancies and is associated with a high burden of morbidity and mortality [1].

The main cause of spontaneous rupture of membranes, is likely to be due to inflammatory factors, but also to other etiologies, such as invasive procedures (i.e. amniocentesis or chorionic villous sampling) [2].

In the case of PROM before viability or in the periviable gestational age, neonatal complications are mainly related to extreme prematurity, but might also be caused by different conditions such as cord prolapse, intraamniotic infection and oligohydramnios [3,4].

In twin pregnancies, PROM typically occurs in the presenting twin sac, and dichorionicity has been shown to be associated with a lower risk co-infection in the other gestational sac. However, PROM can also occur in the non-presenting twin sac, in particular when caused by invasive procedures.

Regardless of which sac is involved, the management of PROM before viability or in the periviable gestational age in twin pregnancies is extremely challenging and the options may include either termination of the entire pregnancy (TOP), selective TOP of the twin with ruptured membranes (sTOP), or expectant management with antibiotic prophylaxis and close monitoring of wellbeing of both the mother and the fetus [5]. To date, no experimental interventions such as amnio-patch or amnioinfusion have been evaluated in twin pregnancies.

In the setting of counselling of twin pregnancies complicated by PROM before viability or in the periviable gestational age, maternal fetal specialists should therefore provide the most accurate data on the prognosis of the expectant management to reach an evidence-based, shared decision-making.

In singleton pregnancies, a recent *meta*-analysis provided a comprehensive outline of the high burden of either obstetric, maternal, and neonatal adverse outcomes in case of PROM before or at the limit of viability [6]. However, the evidence is scarce in twin pregnancies, thus limiting the robustness of the information provided to the parents.

This systematic review and *meta*-analysis aimed to define the risk of obstetric and perinatal outcomes in twin pregnancies complicated by PROM before 26 weeks of gestation, managed either with expectant management or sTOP.

Materials and methods

Protocol, information sources and literature search

This study was conducted according to the designed protocol recommended for systematic reviews and *meta*-analysis [7–9]. Medline, Embase, Cinahl and Web of Science databases were searched electronically up to January 2024, utilizing combinations of relevant medical subject heading terms, keywords and word variants for 'twins', 'twin pregnancy' 'periviable premature rupture of membranes', 'periviable', 'midtrimester', 'early', 'before viability', 'maternal outcomes', 'perinatal outcomes', 'obstetric outcomes', 'neonatal outcomes'.

The search and selection criteria were restricted to the English language. Reference lists of relevant articles and reviews were searched manually for additional reports. PRISMA guidelines were followed [10–12]. The study was registered with the PROSPERO database (registration number CRD42022368057).

Outcomes measures, study selection and data collection

The outcomes of this systematic review and *meta*-analysis included obstetric and perinatal outcomes.

Obstetric outcomes included:

- TOP
- sTOP
- spontaneous miscarriage or fetal demise
- live birth
- mean gestational age at delivery
- mean latency time between PROM and delivery
- cesarean delivery (considering the total group of cases, including fetal demise)
- placental abruption
- chorioamnionitis
- composite maternal morbidity (including intensive care unit admission, sepsis, acute renal injury, severe post-partum hemorrhage, blood transfusion, endometritis, hysterectomy, deep vein thrombosis, pulmonary embolism, and readmission)

Neonatal outcomes included:

- neonatal mortality
- respiratory distress syndrome (RDS) or pulmonary hypoplasia
- intraventricular hemorrhage (IVH)
- necrotizing enterocolitis (NEC)
- retinopathy of the preterm (ROP)
- composite neonatal morbidity (including grade III or IV intraventricular hemorrhage, bronchopulmonary dysplasia, pulmonary hypoplasia, necrotizing enterocolitis requiring surgical intervention, retinopathy of prematurity grade 3 or 4, sepsis or neonatal death)
- birthweight

Moreover, outcomes of pregnancies managed with sTOP were reported separately (mean gestational age at rupture of membranes, mean gestational age at delivery, mean latency time between PROM and delivery, fetal demise, live births, birthweight, cesarean deliveries).

Outcomes were included in the analysis only if reported by at least two studies.

The selection criteria included both prospective and retrospective studies of twin pregnancies with PROM before 26 weeks of gestation.

Case reports, case series with fewer than 5 cases, review articles, letters to the editor and editorials were excluded. Studies including both singletons and twin pregnancies were also excluded. When outcomes about the "first" or "second" twin were reported, we assumed that the first twin was the presenting twin.

Two authors (SS, FZ) reviewed all abstracts independently. Agreement regarding potential relevance was reached by consensus. Full-text copies of papers were obtained, and the same two reviewers independently extracted relevant data regarding study characteristics and outcomes. Inconsistencies were resolved through discussion between the two reviewers until consensus was reached or by consulting a third author (DDM).

Quality assessment, risk of bias and statistical analysis

Quality assessment of the included studies was performed using the Newcastle–Ottawa scale (NOS) for cohort studies [13]. According to the NOS, each study is judged on three broad perspectives: selection of study groups, comparability of groups and ascertainment of the outcome of interest. Assessment of the selection category includes evaluation of the representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and demonstration that the outcome of interest was not present at the start of the study. Assessment of the comparability category includes evaluation of the comparability of cohorts based on design or analysis. Finally, ascertainment of the outcome of interest includes evaluation of the type of assessment of the outcome of interest and length and adequacy of follow-up. According to the NOS, a study can be awarded a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars can be given for comparability [13].

Data extraction and statistical analysis

We used *meta*-analyses of proportions to combine data and reported pooled proportions. Tests for funnel plot asymmetry were not used because of the small total number of publications included (<10). In this case, the power of the tests is too low to distinguish chance from real asymmetry.

Between-study heterogeneity was explored using the I^2 statistic, which represents the percentage of between-study variation that is due to heterogeneity rather than chance. A value of 0 % indicates no observed heterogeneity, whereas I^2 values > 50 % indicate a substantial level of heterogeneity. Given the heterogeneity among the included studies, a random-effect model was used to compute the pooled data analyses. All proportion *meta*-analyses were carried out by using Comprehensive Meta-analysis V4 (Biostat; Englewood, NJ, USA).

When the median values were available, the mean and standard deviation estimates were obtained through the equation proposed by Hozo et al.; according to their recommendations, when the sample size was greater than 25, the sample's median was considered the best estimate of its mean and the standard deviation was calculated by range/4 [14]. When the outcome was reported by less than three studies, the heterogeneity (I2) was not reported.

Results

Study selection and characteristics

A total of 677 articles were identified, 24 were assessed with respect to their eligibility for inclusion and eight were included in this systematic review [15–22] (Table 1, Fig. 1).

These eight studies included 227 twin pregnancies, both monochorionic diamniotic and dichorionic diamniotic. Two studies [21,22] reported data from two higher-order multiple pregnancies, but these two cases were excluded from the analysis. Seven studies [15,16,18–22] were retrospective and one study was a secondary analysis of a prospective cohort study [17].

Three studies included cases of PROM after an invasive procedure (i.e., amniocentesis) [15,16,22]; four studies only reported cases of spontaneous preterm PROM (pPROM) [17–20]. In the remaining study [21], the potential cause for PROM was not reported. Four studies [15,16,18,22] showed the outcomes of pregnancies managed with sTOP separately from the other cases; this cohort only included dichorionic diamniotic twin pregnancies.

The characteristics of the study groups are outlined in Table 2. The lower gestational age limit of the included studies was 13 weeks of gestation, while the upper limit was 26 weeks. The clinical management for each study group in terms of antibiotic prophylaxis, tocolysis, antenatal corticosteroid therapy to reduce the incidence and severity of RDS and intrapartum magnesium sulphate for neuroprotection was reported (Table 3).

The results of the quality assessment of the included studies using the NOS scale are presented in Table 4. Most of the included studies showed an overall good score regarding the selection and comparability of study groups, and for ascertainment of the outcome of interest. The main weaknesses of these studies were their retrospective design, small sample size and heterogeneity of the outcomes observed.

Synthesis of the results

The results were synthetized as obstetric and perinatal outcomes and were presented in detail in Tables 5 and 6 and summarized in Figs. 2 and 3.

In the population of twin pregnancies complicated by PROM before 26 weeks, the pooled proportion of TOP was 4.6 %, although only a few studies reported this outcome, while the rate of sTOP was 24.5 %. The technique used for the termination was intracardiac injection of potassium chloride, as reported by the authors.

After the exclusion of cases of both TOP and sTOP, the overall rate of spontaneous miscarriage or fetal demise was 20.9 %, whereas the live birth rate of at least one twin was 71.6 % of the ongoing pregnancies.

The mean gestational age at delivery was 26.5 weeks; the mean latency between PROM and delivery was 5.4 weeks in all cases including those with fetal death.

The pooled proportion of cesarean delivery was 53.5 %, including cases with fetal demise.

When focusing on maternal complications, chorioamnionitis occurred in 33 % of pregnancies, while composite maternal morbidity was observed in 28.6 % of cases. Placental abruption was reported in 3.5 % of cases.

Neonatal outcomes showed that the overall neonatal mortality was 26.4 %, while the composite neonatal morbidity was 54.4 %. RDS or pulmonary hypoplasia complicated 18.4 % of cases, while IVH occurred in 16.3 % of newborns. Other neonatal complications including NEC and ROP were reported only by one study (20.6 % and 17.6 %, respectively).

The mean birthweight at delivery in this study group was not suitable for analysis in the included papers.

The outcomes of pregnancies undergoing sTOP are reported in Table 7. In this subset of pregnancies, the observed livebirth rate was 87.7 %, with almost half of cases of fetal demise compared to ongoing twin pregnancies. The gestational age at rupture in these cases was 16.8 weeks and the latency between PROM and delivery was significantly longer (19.9 weeks) than that observed in ongoing pregnancies. The mean gestational age at delivery was nearly in the range of term (36.9 weeks) and the mean birthweight was reported to be 2809.8 g. The rate of cesarean delivery in this group was 32.4 %.

We did not perform a subgroup analysis comparing sTOP with expectant management due to the small number of cases of each group.

Comment

Main findings

The findings from this *meta*-analysis demonstrated that PROM before 26 weeks in twin pregnancies is associated with an overall rate of spontaneous miscarriage or fetal demise of 20.9 % and a live birth rate of at least one twin was 71.6 % in pregnancies not undergoing TOP, with a

Table 1
Characteristics of the included studies.

	Study	Study period	Study location	Study design	Sample size	Type of twin pregnancy
1	Ponce 2023[15]	2015–2022	Spain	Retrospective	38	DCDA and MCDA
2	Zajicek 2020[16]	2001–2016	Israel	Retrospective	20	DCDA
3	Lorthe 2018[17]	2011	France	Secondary analysis of prospective cohort	48	Unspecified
4	Lim 2018[18]	2004–2016	Canada	Retrospective	27	DCDA
5	Wagner 2017[19]	2005–2015	Germany	Retrospective	29	DCDA
6	Myrick 2016[20]	2000–2015	USA	Retrospective	30	DCDA and MCDA
7	Wong 2015[21]	2002–2013	USA	Retrospective	23	DCDA and TCQA
8	De Catte 1998[22]	1991–1996	Belgium	Retrospective	12	DCDA and TCTA

DCDA: dichorionic diamniotic; MCDA: monochorionic diamniotic; TCQA: trichorionic quadriamniotic; TCTA: trichorionic triamniotic.

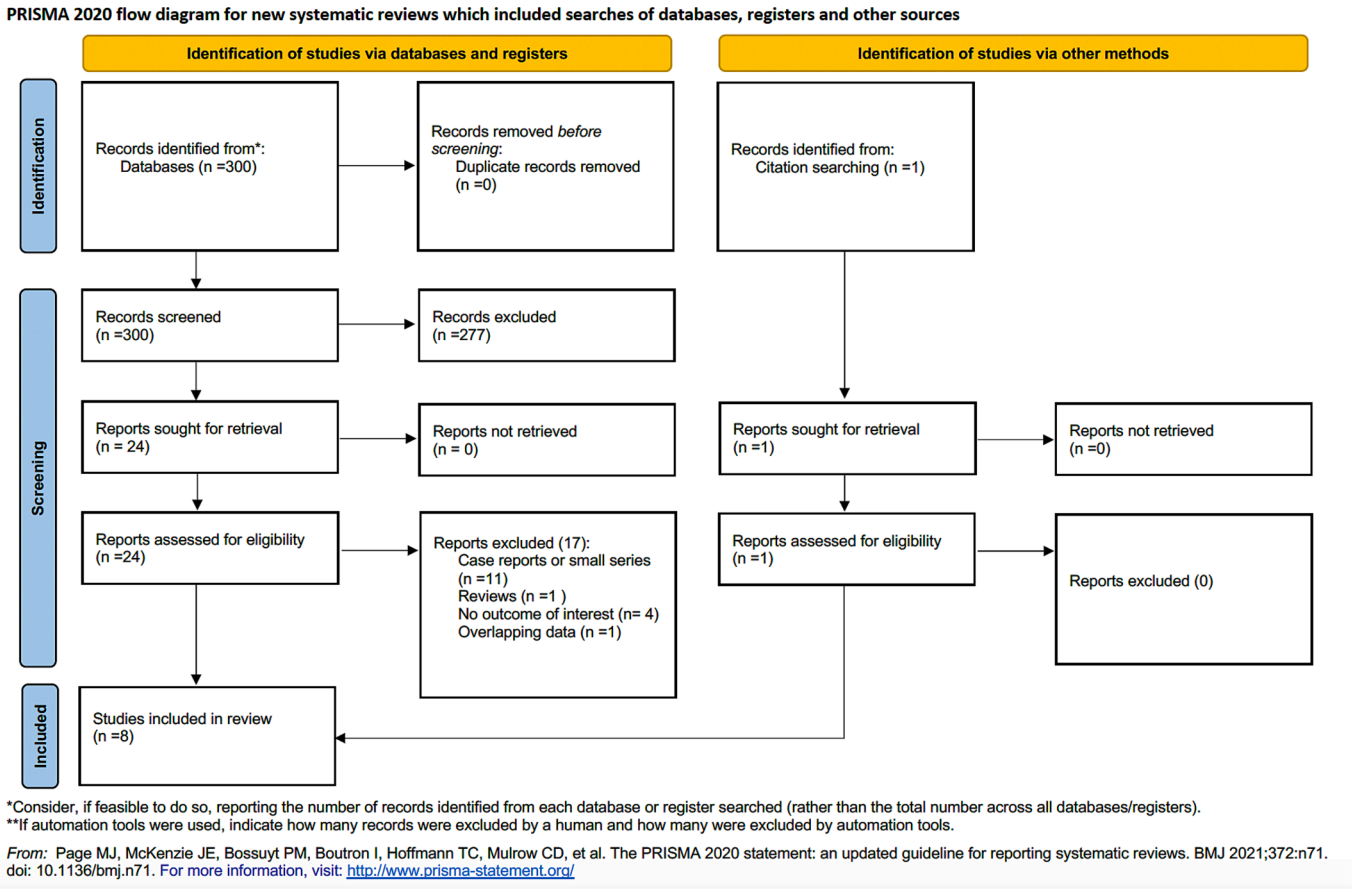

Fig. 1. PRISMA flow diagram.

Table 2
Characteristics of the study cohorts.

	Study	Maternal age	Nulliparous	BMI	Spontaneous conception	GA at PROM	PROM after invasive procedures	PROM of the presenting twin
1	Ponce 2023[15]	32.4 (30.1–37.2)	25/38 (65.8 %)	24.7 (20.3–29.7)	25/38 (65.8 %)	18.6 (16.0–22.0)	7/38 (18.4 %)	32/38 (84.2 %)
2	Zajicek 2020[16]	NA	10/20 (50 %)	NA	8/20 (40 %)	13–20	7/20 (35 %)	7/20 (35 %)
3	Lorthe 2018[17]	29 (26–32)	30/48 (62.5 %)	NA	NA	24 (23–25)	Excluded	24/48 (50 %)
4	Lim 2018[18]	NA	NA	NA	NA	20.5 (mean)	NA	NA
5	Wagner 2017[19]	33.6 (29.3–36.9)	NA	NA	16/29 (55.2 %)	20.4 (17.9–22.4)	NA	NA
6	Myrick 2016[20]	NA	11/30 (36.7 %)	NA	NA	$14–22^{+6}$	NA	29/30 (96.7 %)
7	Wong 2015[21]	32.5 ± 6.9	13/23 (56.5 %)	NA	NA	22.9 (20.7–24.1)	NA	NA
8	De Catte 1998[22]	NA	NA	NA	NA	(13–20)	1/9 (11.1 %)	2/12 (16.7 %)

Values are expressed as mean ± standard deviation or median (range); BMI: body mass index; GA: gestational age; PPROM: premature rupture of membranes; NA: not available.

mean latency between PROM and delivery was 5.4 weeks and a mean gestational age at delivery of 26.5 weeks. The rate of sTOP due to PROM was about 25 %, with this subset of pregnancies associated with a significantly lower rate of fetal demise and a significantly longer latency between PROM and delivery, although this subgroup analysis was limited by the very small number of included studies.

Strengths and limitations

The main strength of this study is that this is the only *meta*-analysis reporting obstetric and perinatal outcomes in twin pregnancies complicated by PROM before 26 weeks. The extensive literature search and the consistent number of outcomes reported represent additional strengths of this study.

We must acknowledge that this *meta*-analysis also has some limitations, mainly including the very small sample size of the study cohorts, their retrospective nature, and the different gestational ages at occurrence of PROM in each study.

There is also a significant heterogeneity between the studies, which is mainly due to the lack of standardized criteria for antenatal care and

Table 3
Management of twin pregnancies complicated by PPROM prior to 26 weeks of gestation in the included studies.

	Study	Antibiotic therapy	Tocolysis	RDS prophylaxis	Magnesium sulphate
1	Ponce 2023[15]	All patients received antibiotics (intravenous ampicillin 1 g/6h and gentamicin 80 mg/8h and a single dose of azithromycin 1 g, until 2019, and intravenous ampicillin 2 g/6h and ceftriaxone 1 g/12 h and oral clarithromycin 500 mg/12 h, from 2020 onwards) at hospital admission for five days.	Administered in cases of preterm labor and no contraindication to prolong pregnancy. 16/36 (44.4 %)	Betamethasone 12 mg/24 h (two doses) administered for lung maturation after 24 + 0 weeks if delivery was expected in the subsequent 7 days.	Administered when delivery was expected between 23 + 0 and 32 + 0 weeks.
2	Zajicek 2020[16]	Administered according to protocols of the centers	NA	Administered according to protocols of the centers	NA
3	Lorthe 2018[17]	Administered according to national guidelines (National College of French Gynecologists and Obstetricians) [34] 46/48 (95.8 %)	Administered if necessary, according to national guidelines (National College of French Gynecologists and Obstetricians) [34] 36/48 (75 %)	Administered from viability to 34 weeks of gestation 32/48 (66.7 %)	Not routinely administered
4	Lim 2018[18]	23/27 (85.2 %) Different antibiotic regiments	2/27 (7.4 %)	NA	NA
5	Wagner 2017[19]	Prophylactic administration of antibiotics for 5–7 days	NA	Two injections of 12 mg Betamethasone 24 h apart administered intramuscularly after 24 weeks. Repeated in 2–3 weeks if undelivered or if the clinical status changed.	NA
6	Myrick 2016[20]	Antibiotic prophylaxis was offered to 17 cases (57 %): ampicillin 2 gm intravenous (IV) every 6 h and erythromycin 250 mg IV every 6 h for 48 h, followed by amoxicillin 250 mg orally every 8 h and erythromycin 333 mg orally every 8 h for 5 days.	NA	10/30 (33 %) received at least one course of corticosteroids	NA
7	Wong 2015[21]	16/17 (94.1 %) received latency antibiotics.	NA	15/17 (88.2 %) received antenatal corticosteroids	One woman received magnesium sulfate for fetal neuroprophylaxis.
8	De Catte 1998[22]	No antibiotic treatment was installed routinely	No tocolytic treatment was installed routinely	Two administration of 12 mg of dexamethasone (12 h apart), after 24 weeks	NA

RDS, respiratory distress syndrome; NA, not assessed; PPROM, preterm premature rupture of membranes; IV, intravenous.

Table 4
Quality assessment of the included studies according to Newcastle – Ottawa Scale for cohort studies.

Study	Selection	Comparability	Outcome
Ponce 2023[15]	***	*	**
Zajicek 2020[16]	***	*	***
Lorthe 2018[17]	**	*	**
Lim 2018[18]	***	*	**
Wagner 2017[19]	***	*	**
Myrick 2016[20]	***	*	**
Wong 2015[21]	***	*	***
De Catte 1998[22]	***	*	**

the use of different protocols for antibiotic prophylaxis, antenatal corticosteroid therapy for RDS prophylaxis, tocolysis and magnesium sulphate for neuroprotection.

Moreover, it should be recognized that PROM before 26 weeks may have different etiologies, and some studies included cases following invasive procedures, some others excluded these cases, while others did not mention whether they were included or not. The different underlying pathology might indeed have an impact on the outcomes of these pregnancies. Furthermore, the different types of twin pregnancies included might be a confounding factor (dichorionic vs monochorionic pregnancies), as well as the unspecified twin (presenting vs non-presenting) that had rupture of membranes.

Finally, different healthcare settings might have different policies regarding neonatal resuscitation and intensive care, and this may influence the rate of neonatal death and other adverse outcomes among the included studies.

Table 5
Pooled proportions and cumulative means of obstetric outcomes.

Outcome	Studies	Raw proportion	Pooled proportion or cumulative mean (95 % CI)	I^2
Termination of pregnancy	2	3/77 (4 %)	4.6 (1.5–13.4)	NE
Selective termination of pregnancy	4	23/96 (23.9 %)	24.5 (7.1–57.7)	85 %
Spontaneous miscarriage or fetal demise	7	71/337 (21.1 %)	20.9 (11.1–35.8)	83 %
Live birth	7	239/337 (70.9 %)	71.6 (61.2–80.1)	67 %
GA at delivery* (weeks)	3	–	26.5 (25.1–28.0)	96 %
Latency between PPROM and delivery* (weeks)	2	–	5.4 (4.8–5.9)	NE
Cesarean delivery*	3	32/60 (53.3 %)	53.5 (36.9–69.3)	30 %
Placental abruption	2	2/59 (3.4 %)	3.5 (0.9–12.9)	NE
Chorioamnionitis	4	31/96 (32.3 %)	33.0 (23.2–44.6)	18 %
Maternal morbidity**	2	19/66 (28.8 %)	28.6 (9.7–59.8)	NE

*including cases of fetal demise. ** including intensive care unit admission, sepsis, acute renal injury, severe post-partum hemorrhage, blood transfusion, endometritis, hysterectomy, deep vein thrombosis, pulmonary embolism, and readmission; CI, confidence interval; GA: gestational age; PPROM: preterm premature rupture of membranes; NE, not estimable.

Table 6
Pooled proportions of neonatal outcomes.

Outcome	Studies	Raw proportion	Pooled proportion (95 % CI)	I^2
Neonatal mortality	7	61/235 (25.9 %)	26.4 (16.7–39.2)	68 %
Composite neonatal morbidity	3	55/92 (59.8 %)	54.4 (25.6–80.5)	83 %
Pulmonary hypoplasia	4	26/130 (20 %)	18.4 (8.1–36.5)	73 %
Intraventricular hemorrhage	2	15/73 (20.5 %)	16.3 (2.5–59.8)	NE
Necrotizing enterocolitis	1	7/34 (20.6 %)	–	–
Retinopathy of the prematurity	1	6/34 (17.6 %)	–	–

RDS, Respiratory distress syndrome; CI, confidence interval; NE, not estimable. *includes grade III or IV intraventricular hemorrhage, bronchopulmonary dysplasia, pulmonary hypoplasia, necrotizing enterocolitis requiring surgical intervention, retinopathy of prematurity grade 3 or 4, sepsis or neonatal death;

Comparison with existing literature

Twin pregnancies are at increased risk of perinatal mortality and morbidity compared with singletons mainly due to preterm birth (PTB) and growth disorders, as well as to monochorionicity-related complications, such as twin-twin transfusion syndrome (TTTS) [23–29].

PROM occurring in twin pregnancies at an early gestational age is often burdened by low overall survival rate and high risk of maternal as well as perinatal morbidity. Indeed, extreme prematurity has been described as one of the main determinants of both short- and long-term adverse outcomes, with the rate of both immediate survival and survival at 2 years of age with neurodevelopmental and functional outcome gradually improving from 22 to 28 weeks of gestations [30]. In this scenario, compared with very preterm singletons, twins have been associated with even higher mortality and slightly lower score at cognitive assessment at 5 years. [31].

In this *meta*-analysis, the live birth rate of at least one twin was 71.6 % after excluding pregnancies undergoing TOP, and this might be putatively attributed to the mean gestational age at delivery of 26.5 weeks, with the upper bound of confidence interval not exceeding 28 weeks of gestation, thus indicating that potentially all twin pregnancies complicated by PROM before 26 weeks of gestation and managed expectantly delivered in the gestational period labelled as "extreme prematurity".

Conversely, when focusing on pregnancies undergoing sTOP, the livebirth rate was 87.7 %, with almost half of cases of fetal demise compared to those undergoing expectant management and a latency between PROM and delivery significantly longer (19.9 weeks vs 5.4 weeks), resulting in a mean gestational age at delivery of 36.9 weeks. However, this finding may not appear surprising, as there is increased evidence that reduction from twin to singleton pregnancy is associated with higher gestational age at delivery, lower rates of preterm birth and pregnancy complications [32]. Therefore, we could speculate that in the case of PPROM before 26 weeks sTOP might improve pregnancy outcomes, possibly by decreasing the risk of spreading the infection to the other gestational sac. Moreover, the gestational age at sTOP may have an impact on perinatal outcomes, as earlier procedures are associated with higher survival rates and lower risk of preterm birth, and therefore this option could be considered when counseling patients with very early rupture of membranes (<18 weeks) [33].

In this scenario, counseling using evidence-based data on the burden of complications associated with expectant management or sTOP in twin pregnancies complicated by PPROM before 26 weeks is essential to enable parents to reach an informed shared decision about the management of the pregnancy.

Conclusions and implications

PROM prior to 26 weeks' gestation in twin pregnancies is associated with an overall high burden of adverse obstetric and perinatal outcomes, thus representing a clinical conundrum for both counseling and management. Counseling should balance between a possible higher survival and a lower rate of severe prematurity associated with sTOP and the possibility of a double survival but a higher chance of morbidity when opting for expectant management. This *meta*-analysis might help maternal-fetal specialists in their daily clinical practice to offer the best state-of-the-art knowledge to the patients until further prospective studies, sharing objective protocols in terms of antenatal surveillance and management will better elucidate the natural history of this complication.

Fig. 2. Graphical representation of obstetric outcomes.

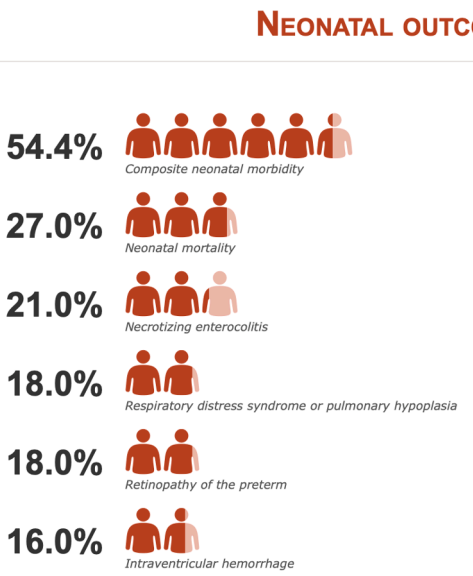

Fig. 3. Graphical representation of neonatal outcomes.

Table 7
Pooled proportions and cumulative means of obstetric and neonatal outcomes in twin pregnancies complicated by preterm premature rupture of membranes (PPROM) undergoing selective termination.

Outcome	Studies	Raw proportion	Pooled proportion or cumulative mean (95 % CI)	I^2
Spontaneous miscarriage or fetal demise	3	1/21 (4.8 %)	12.3 (2.9–39.9)	1 %
Live birth	3	20/21 (95.2 %)	87.7 (60.1–97.1)	1 %
GA at PPROM (weeks)	3	–	16.8 (14.9–18.6)	61 %
GA at delivery (weeks) of liveborns	3	–	36.9 (35.5–38.4)	3 %
Latency between PPROM and delivery (weeks)	2	–	19.9 (18.0–21.7)	NE
Cesarean delivery*	3	6/21 (28.6 %)	32.4 (5.4–79.9)	65 %
Birthweight (grams)	3	–	2809.8 (2550.8–3068.8)	0 %

CI, confidence interval; GA: gestational age; NE, not estimable.
*including cases of fetal demise.

Disclosure

Authors report no conflict of interest.

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CRediT authorship contribution statement

Sara Sorrenti: Writing – original draft, Methodology, Data curation. **Asma Khalil:** Validation, Supervision. **Antonella Giancotti:** Supervision. **Fabrizio Zullo:** Formal analysis. **Elena D'alberti:** Methodology. **Antonio Sasanelli:** Methodology. **Valentina D'ambrosio:** Data curation. **Ilenia Mappa:** Methodology. **Francesco D'antonio:** Supervision. **Giuseppe Rizzo:** Supervision. **Daniele Di Mascio:** Writing – original draft, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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