

OBSTETRICS

Maternal morbidity after preterm premature rupture of membranes at <24 weeks' gestation



Ariel Sklar, MD, MS; Jeanelle Sheeder, MSPH, PhD; Anne R. Davis, MD, MPH; Carrie Wilson, MD, MPH; Stephanie B. Teal, MD, MPH

BACKGROUND: After preterm premature rupture of membranes at <24 weeks' gestation, pregnant women may choose continuation (expectant management) or termination of pregnancy, via either dilation and evacuation or labor induction. Neonatal outcomes after expectant management are well described. In contrast, limited research addresses maternal outcomes associated with expectant management compared to termination of pregnancy.

OBJECTIVE: This study aimed to compare maternal morbidity after preterm premature rupture of membranes at <24 weeks' gestation in women who choose either expectant management or termination of pregnancy.

STUDY DESIGN: This retrospective cohort study included women with preterm premature rupture of membranes between 14 0/7 and 23 6/7 weeks' gestation with singleton or twin pregnancies at 3 institutions from 2011 to 2018. We excluded pregnancies complicated by fetal anomalies, rupture of membranes immediately after obstetrical procedures (chorionic villus sampling, amniocentesis, cerclage placement, fetal reduction), spontaneous delivery <24 hours after membrane rupture, and contraindications to expectant management. Our primary outcome was the difference in composite maternal morbidity between women choosing expectant management and women choosing termination of pregnancy. We defined composite maternal morbidity as at least 1 of the following: chorioamnionitis, endometritis, sepsis, unplanned operative procedure after delivery (dilation and curettage, laparoscopy, or laparotomy), injury requiring repair, unplanned hysterectomy, unplanned hysterotomy (excluding cesarean delivery), uterine rupture, hemorrhage of >1000 mL, transfusion, admission to the maternal intensive care unit, acute renal insufficiency, venous thromboembolism, pulmonary embolism, and readmission to the hospital within 6 weeks. We compared the demographic and antenatal characteristics of women choosing expectant management with that of women choosing termination of pregnancy and used logistic regression to quantify the association between initial management decision and composite maternal morbidity.

RESULTS: We identified 350 women with pregnancies complicated by preterm premature rupture of membranes at <24 weeks' gestation, and 208 women were eligible for the study. Of the 208 women, 108 (51.9%) chose expectant management as initial management, and 100 (48.1%) chose termination of pregnancy as initial management. Among women selecting termination of pregnancy, 67.0% underwent labor induction, and 33.0% underwent dilation and evacuation. Compared to women who chose termination of pregnancy, women who chose expectant management had 4.1 times the odds of developing chorioamnionitis (38.0% vs 13.0%; 95% confidence interval, 2.03–8.26) and 2.44 times the odds of postpartum hemorrhage (23.1% vs 11.0%; 95% confidence interval, 1.13–5.26). Admissions to the intensive care unit and unplanned hysterectomy only occurred after expectant management (2.8% vs 0.0% and 0.9% vs 0.0%). Of women who chose expectant management, 36.2% delivered via cesarean delivery with 56.4% non—low transverse uterine incisions. Composite maternal morbidity rates were 60.2% in the expectant management group and 33.0% in the termination of pregnancy group. After adjusting for gestational age at rupture, site, race and ethnicity, gestational age at entry to prenatal care, preterm premature rupture of membranes in a previous pregnancy, twin pregnancy, smoking, cerclage, and cervical examination at the time of presentation, expectant management was associated with 3.47 times the odds of composite maternal morbidity (95% confidence interval, 1.52–7.93), corresponding to an adjusted relative risk of 1.91 (95% confidence interval, 1.35–2.73). Among women who chose expectant management, 15.7% avoided morbidity and had a neonate who survived to discharge.

CONCLUSION: Expectant management for preterm premature rupture of membranes at <24 weeks' gestation was associated with a significantly increased risk of maternal morbidity when compared to termination of pregnancy.

Keywords: maternal morbidity, periviability, previability, PPRM, second trimester of pregnancy complication, termination of pregnancy

Introduction

Preterm premature rupture of membranes (PPROM) at <24 weeks' gesta-

tion occurs in 0.3% to 0.4% of pregnancies.¹ The American College of Obstetricians and Gynecologists states that “immediate delivery and expectant management should be offered”² and that patients should receive the most accurate information on how management decisions affect their health and the health of their fetus. Counseling in this clinical scenario relies on neonatal outcomes research^{3–8} that estimates gestational age (GA)-dependent neonatal survival (0%–56%)^{4,8–12} and severe

neonatal morbidity (40%–100%).^{4,8–12} PPRM at <24 weeks' gestation can also cause substantial maternal morbidity. Approximately 40% to 50% of women who choose expectant management experience maternal morbidity: infection, retained placenta, and/or hemorrhage.^{1,9,13} Women delivering near the lower limits of viability are nearly 6-fold more likely to have poor outcomes, including chorioamnionitis, blood transfusion, hysterectomy, and/or admission to the maternal intensive

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AJOG at a Glance

Why was this study conducted?

This study aimed to help women experiencing preterm premature rupture of membranes (PPROM) at <24 weeks' gestation make more informed decisions about expectant management vs termination of pregnancy (TOP) by examining maternal outcomes.

Key findings

The risk of maternal morbidity differed by initial management decision: 60.2% with expectant management vs 33.0% with TOP. Expectant management was associated with 3.47 times the odds of maternal morbidity (adjusted relative risk, 1.91; 95% confidence interval, 1.35–2.73). Admissions in the intensive care unit (2.8%) and unplanned hysterectomy (0.9%) only occurred after expectant management. Among women choosing expectant management, 15.7% avoided maternal morbidity and had a neonate survive to discharge.

What does this add to what is known?

This study added information about the risk of maternal morbidity among pregnant women terminating a pregnancy because of PPRM at <24 weeks' gestation. By including information on maternal morbidity based on the initial management choice, this study provided critical data to inform shared decision-making.

care unit (ICU), than those at term.¹⁴ However, expectant management preserves the possibility of neonatal survival.

Termination of pregnancy (TOP), via either dilation and evacuation (D&E) or labor induction, precludes that possibility. The reasons for choosing TOP include avoiding futile neonatal medical services, severe neonatal morbidity, and maternal morbidity. However, limited data exist regarding whether or to what extent terminating a pregnancy complicated by PPRM at <24 weeks' gestation mitigates the risk of maternal morbidity. Safety data for TOP for other indications may underestimate the excess risk associated with PPRM, such as infection² or antepartum bleeding.¹ This study compared maternal morbidity in women who chose expectant management with that of women who chose pregnancy termination for initial management after PPRM at <24 weeks' gestation.

Materials and Methods

We conducted a retrospective cohort study of women with pregnancies complicated by PPRM at <24 weeks' gestation at 3 tertiary care hospitals

between 2011 and 2018. We searched the electronic medical records (EMRs) of University of Colorado Hospital (UCH; Aurora, CO), NewYork-Presbyterian Hospital (NYP; New York, NY), and Denver Health Medical Center (DHMC; Denver, CO). All 3 hospitals are university affiliated; are staffed by obstetricians, maternal-fetal medicine specialists, skilled D&E providers, and obstetrics residents; and have level IV neonatal ICUs (NICUs) and adult ICUs. Women with PPRM were identified by International Classification of Diseases, Ninth Revision and Tenth Revision, codes (ICD-9 and ICD-10) for PPRM (ICD-9: 658.1, 658.10, 658.11, 658.13, 658.2, 658.20, 658.21, 658.23; ICD-10: O42.10, O42.111, O42.112, O42.113, O42.119, O42.91, O42.911, O42.912, O42.913, O42.919). Trained researchers with access to the EMRs reviewed all potential cases and managed data with Research Electronic Data Capture tools hosted at the University of Colorado and Columbia University. The institutional review boards of the University of Colorado and Columbia University approved this study. We screened for GA at PPRM to identify women from 14 0/7 to 23 6/7 weeks' gestation using the

best available gestational dating. We ascertained membrane rupture by EMR documentation of history and a physical examination with transcervical amniotic fluid or pooling in the posterior fornix with nitrazine or ferning or both positive, low amniotic fluid by ultrasonography, and/or confirmatory results after injection of intra-amniotic indigo carmine. We excluded pregnancies complicated by chromosomal abnormalities or fetal anomalies, including renal anomalies associated with oligo- and anhydramnios, iatrogenic rupture within 48 hours of an obstetrical procedure (amniocentesis, cerclage placement, or fetal reduction), spontaneous delivery within 24 hours of PPRM, uncertain date of PPRM, missing delivery data, and contraindications to expectant management (eg, chorioamnionitis or active heavy bleeding). We defined the initial management decision as the decision to choose either expectant management or TOP within 48 hours of membrane rupture. For example, a woman initially choosing expectant management who 5 days later decided to undergo TOP would be analyzed in the expectant management group.

We created a composite primary outcome of maternal morbidities that can occur after TOP or expectant management, including at least 1 of the following: clinical chorioamnionitis, endometritis, sepsis, unplanned operative procedure after fetal delivery (dilation and curettage, laparoscopy, or laparotomy), injury requiring repair, unplanned hysterectomy, unplanned hysterotomy excluding cesarean delivery, uterine rupture, hemorrhage of >1000 mL, transfusion, acute renal insufficiency, venous thromboembolism, pulmonary embolism, admission to the maternal ICU, and readmission to the hospital within 6 weeks of delivery or TOP.

We created a second composite morbidity variable identical to that used by Rossi and DeFranco¹⁴ to directly compare our outcomes with their outcomes. Their composite morbidity results consisted of any one of the following: chorioamnionitis, unplanned

operative procedure, unplanned hysterectomy, blood product transfusion, and admission to the ICU. We created a third composite variable for severe maternal morbidity composed of sepsis, admission to the ICU, acute renal insufficiency (creatinine level of >1.2), unplanned hysterectomy, pulmonary embolism, and blood transfusion of ≥ 2 units of red blood cells (2 U RBC). Furthermore, we examined cesarean delivery and neonatal survival separately. In the case of twins, for consistency,¹³ survival data were only collected for the twin with PPRM.

During the study period, the definitions for chorioamnionitis and suspected intra-amniotic infection changed, and maternal tachycardia and fundal tenderness were de-emphasized.¹⁵ To capture the entire study period from 2011 to 2018, we defined clinical chorioamnionitis as chorioamnionitis documented by a physician and prompting treatment with intravenous antibiotics. We defined maternal sepsis as clinical sepsis documented by a physician and evidence of infection (ie, fever or positive blood cultures) with end-organ dysfunction (ie, hypotension, oliguria, elevated creatinine, disseminated intravascular coagulation, decreased consciousness, or respiratory compromise). At all institutions, prophylactic antibiotics were given for D&E but not for labor induction. Similarly, patients received prophylactic antibiotics for cesarean delivery but not vaginal delivery.

Previous retrospective studies of PPRM at <24 weeks' gestation found composite maternal morbidity of approximately 40% in the expectant management group.^{1,9,13} Previous retrospective cohort studies of second-trimester pregnancy terminations by both D&E and labor induction (for any indication) found that maternal morbidity occurred in approximately 20% of cases.^{16–19} Thus, we chose to test the hypothesis that composite maternal morbidity in the termination group would be at least 20 percentage points lower than composite maternal morbidity in the expectant management group. With a limited sample from the UCH, we found one-third of women

with PPRM at <24 weeks' gestation chose termination of pregnancy and two-thirds of women with PPRM at <24 weeks' gestation chose elected expectant management. Using this assumption of unequal group allocation, we calculated that we would need ≥ 208 cases to detect the difference of interest with 80% power and 2-sided alpha of 0.05. We screened all eligible records from the UCH and DHMC. Given the larger delivery volume at the NYP, we selected a random sample of 40% of available cases, stratified by year to ensure representation throughout the study period, and reviewed the cases in random order until we met the planned sample size.

We analyzed demographic and antenatal characteristics using the χ^2 test, Fisher exact test, Student *t* test, or Mann-Whitney *U* test. We used multiple logistic regression to adjust for potential confounders and evaluate independent predictors of our composite outcomes. Variables that were statistically significant in the bivariate analysis with $P < .1$ were included in the model. In addition, risk ratios were adjusted for GA at PPRM, site, race and ethnicity, GA at entry to prenatal care, PPRM in a previous pregnancy, twin pregnancy, smoking, cerclage, and cervical examination at time of presentation using a log-binomial regression model to estimate the adjusted relative risk for the maternal composite variable.²⁰ Statistical analyses were performed using the SPSS statistical software (version 26.0; SPSS IBM, Verona, WI).

Results

Our search strategy identified 6747 potential cases. After screening each of the 6747 medical records, we confirmed 350 pregnancies complicated by PPRM at <24 weeks' gestation (Figure 1). Of these cases, we excluded 142 (40.6%), most commonly because of chorioamnionitis on initial presentation, delivery at <24 hours, fetal structural or chromosomal abnormalities, or iatrogenic PPRM. Moreover, 9 excluded cases were lost to follow-up after their initial PPRM diagnosis: 6 elected expectant

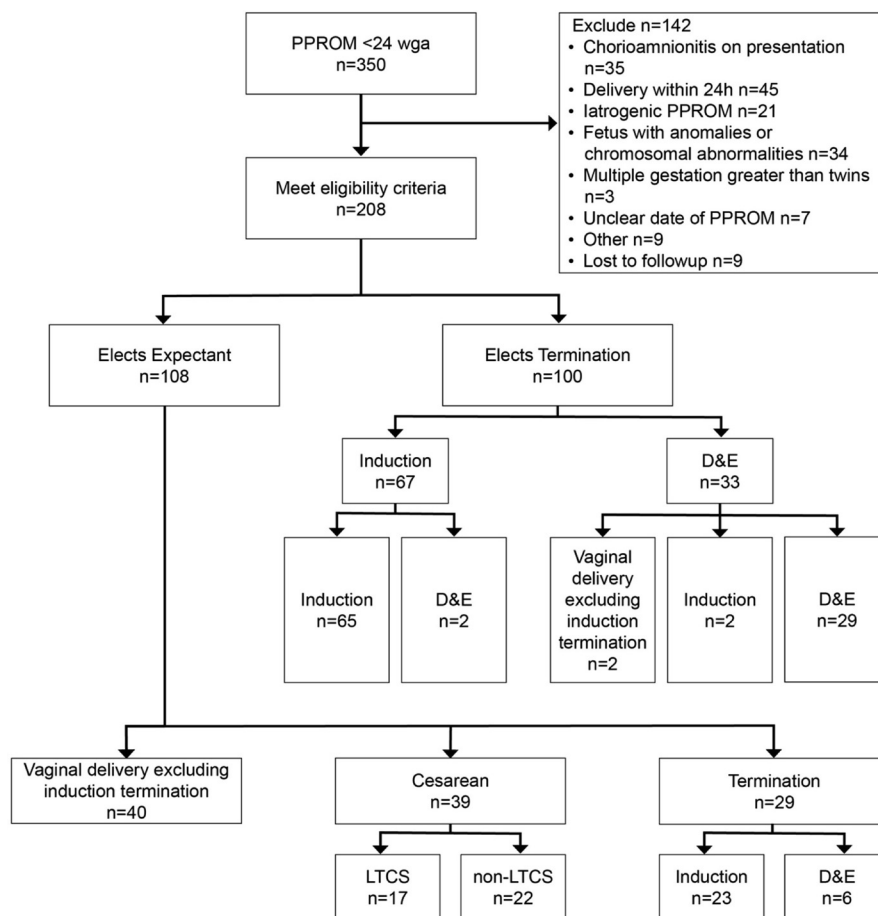
management and 3 elected TOP. We included 208 pregnancies (59.4%) complicated by PPRM at <24 weeks' gestation. In addition, 2 women had 2 pregnancies complicated by PPRM during the study period that met the inclusion criteria; we analyzed these pregnancies separately. Among the 208 pregnancies, 108 (51.9%) were managed with expectant management, and 100 (48.1%) were managed with TOP.

Of 108 women who chose expectant management, 29 (26.9%) ultimately underwent TOP, usually because of a maternal indication, such as chorioamnionitis or placental abruption, 40 (37.0%) had vaginal deliveries, and 39 (36.1%) underwent cesarean delivery, of which 22 (56.4%) were non—longitudinal transverse uterine incisions.

Among 100 women who elected TOP, 67 chose termination of labor induction, and 33 chose D&E. Of the 33 women who chose D&E, 4 did not ultimately undergo D&E. Of the 4 women, 2 labored and had vaginal deliveries prior to their scheduled procedures. One received laminaria but failed to dilate adequately and subsequently underwent induction. One developed a fever prior to laminaria placement and underwent induction instead. Of the 67 women who chose termination of labor induction, 2 underwent D&E because of placental abruption with hemorrhage during their inductions.

Table 1 presents demographic and antenatal characteristics. Women who chose expectant management experienced PPRM later in pregnancy (median GA, 21 6/7 vs 18 6/7 weeks' gestation; $P < .001$). There were significant differences noted by race and ethnicity: women who identified as White non-Hispanic or Black non-Hispanic were twice as likely to select expectant management than TOP. Women who identified as "other" or declined to give race and ethnicity information were twice as likely to select TOP than expectant management ($P = .021$). Women who chose expectant management were more likely to be smokers (16.7% vs 6.0%; $P = .018$). Although the median cervical dilation at admission to the hospital for women

FIGURE 1
Study population flow diagram



D&E, dilation and evacuation; LTCS, low transverse cesarean section; PPROM, preterm premature rupture of membranes.

Sklar. Maternal morbidity after PPROM <24 weeks' gestation. *Am J Obstet Gynecol* 2022.

who pursued TOP was 1 cm vs 0 cm ($P=.003$), there was no difference in the proportion with cervical dilation of ≥ 3 cm between the groups (10.7% for the TOP group vs 9.5% for the expectant management group; $P=.81$). Women in Colorado were more likely to choose expectant management than women in New York. At all sites, termination of labor induction was twice as common as D&E.

The women who chose expectant management vs those who chose TOP were similar in insurance status, gravidity, parity, GA at entry to prenatal care, PPROM in a previous pregnancy, twin pregnancy, history of medical comorbidities (chronic hypertension, pregestational diabetes mellitus, or asthma), infection in pregnancy before

PPROM (urinary tract infection, bacterial vaginosis, chlamydia, gonorrhea, or trichomonas), cerclage presence, and bleeding in pregnancy before PPROM.

Table 2 presents maternal morbidities experienced in each group. Morbidities by type of TOP are available in Appendix 1. Compared with those who chose TOP, women who chose expectant management had 4.1 times the odds of developing chorioamnionitis (38.0% vs 13.0%; 95% confidence interval [CI], 2.03–8.26) and 2.44 times the odds of having a postpartum hemorrhage (23.1% vs 11.0%; 95% CI, 1.13–5.26). The rate of composite maternal morbidity was higher in the expectant management group at 60.2% than in the TOP group at 33.0%, with women choosing expectant management having

3.07 times the odds of experiencing composite maternal morbidity (95% CI, 1.74–5.41). Using the less exhaustive composite measure of maternal morbidity devised by Rossi and DeFranco for periviable delivery, expectant management was again associated with a significantly increased risk of maternal morbidity compared with TOP (47.2% vs 28.0%, respectively; odds ratio [OR], 2.30; 95% CI, 1.30–4.10).

In logistic regression, after adjusting for GA at PPROM, site, race and ethnicity, GA at entry to prenatal care, PPROM in a previous pregnancy, twin pregnancy, smoking, cerclage, and cervical examination at the time of presentation, the only independent predictor of the composite maternal morbidity was attempting expectant management. After adjustment, expectant management was associated with 3.47 times the odds of composite maternal morbidity (adjusted OR, 3.47; 95% CI, 1.52–7.93), which corresponded to an adjusted relative risk of 1.91 (95% CI, 1.35–2.73).

In addition, we separately assessed severe morbidities, which included sepsis, admission to the ICU, unplanned hysterectomy, pulmonary embolism, acute renal insufficiency, and blood transfusion of ≥ 2 U RBC (Appendix 2). Of note, 13 pregnancies (12.4%) in the expectant management group and 5 pregnancies (5.0%) in the TOP group were complicated by a severe morbidity ($P=.08$). All admissions to the ICU, 5 of 6 cases of sepsis, and 1 unplanned hysterectomy occurred in the expectant management group. Furthermore, 4 women in the expectant management group experienced >1 severe morbidity. Notably, 1 woman who initially pursued expectant management after PPROM at 20 weeks' gestation developed chorioamnionitis at 21 weeks' gestation. The patient underwent a successful labor induction but developed sepsis necessitating admission to the ICU and intubation; the patient ultimately required a hysterectomy for infectious source control.

Cases of severe morbidity in the group that initially chose TOP included 1 of sepsis that responded to intravenous antibiotics after a labor induction.

TABLE 1

Characteristics of women with preterm premature rupture of membranes at <24 weeks' gestation

Characteristic	Expectant management n=108 (51.9)	Termination of pregnancy n=100 (48.1)	P value
GA at PPRM (wk)	21 6/7(15 0/7 to 23 6/7)	18 6/7(14 0/7 to 23 6/7)	<.001 ^a
Age (y)	31 (18–49)	31 (18–42)	.962
Site			<.001 ^a
UCH	72 (66.7)	36 (36.0)	
DHMC	10 (9.3)	10 (10.0)	
NYP	26 (24.1)	54 (54.0)	
Race and ethnicity			.021 ^a
White non-Hispanic	28 (25.9)	14 (14.0)	
White Hispanic	10 (9.3)	13 (13.0)	
Black non-Hispanic	18 (16.7)	6 (6.0)	
Black Hispanic	0 (0)	3 (3.0)	
Other non-Hispanic	1 (0.9)	1 (1.0)	
Other Hispanic	23 (21.3)	22 (22.0)	
Asian non-Hispanic	5 (4.6)	0 (0)	
Asian Hispanic	0 (0)	0 (0)	
Other, not reported	20 (21.9)	41 (41.0)	
Insurance			.424
Medicaid	53 (49.1)	53 (53.0)	
Private	46 (42.6)	42 (42.0)	
Uninsured	9 (8.3)	4 (4.0)	
Not reported	0 (0)	1 (1.0)	
Gravidity	3.0 (1.0–11.0)	3.5 (1.0–23.0)	.108
Primigravid	20 (18.5)	17 (17.0)	.857
Parity	1.0 (0.0–9.0)	0.0 (0.0–8.0)	.472
GA at entry to prenatal care (wk)	8.2 (5.0–21.0)	10.6 (4.9–23.4)	.052
PPROM in a previous pregnancy	16 (14.8)	26 (26.0)	.057
Preterm labor in a previous pregnancy	23 (21.5)	30 (30.0)	.202
History of uterine surgery	28 (26.2)	25 (25.0)	.875
Pregnancy result of in vitro fertilization	10 (9.3)	4 (4.0)	.169
Twin pregnancy	15 (13.9)	6 (6.0)	.068
History of chronic hypertension	15 (13.9)	8 (8.0)	.192
History of pregestational diabetes mellitus	2 (1.9)	4 (4.0)	.431
History of asthma	11 (10.2)	12 (12.0)	.825
Smoker	18 (16.7)	6 (6.0)	.018 ^a
Infection in pregnancy before PPRM ^b	22 (20.4)	22 (22.0)	.865

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. Am J Obstet Gynecol 2022.

(continued)

Another occurred in a woman who developed chorioamnionitis during labor induction, had a retained placenta requiring dilation and curettage, and

received a blood transfusion of ≥ 2 U RBC. Among women that elected D&E, 2 were readmitted to the hospital with pulmonary embolisms; both had known

thrombophilic conditions and were on anticoagulation before their readmissions to the hospital. The final instance of severe morbidity after TOP

TABLE 1

Characteristics of women with preterm premature rupture of membranes at <24 weeks' gestation (continued)

Characteristic	Expectant management n=108 (51.9)	Termination of pregnancy n=100 (48.1)	P value
Cerclage in place	10 (9.3)	18 (18.0)	.069
Bleeding in pregnancy before PPRM	41 (38.0)	33 (33.0)	.472
Cervical examination at time of presentation (cm)	0 (0–5)	1 (0–6)	.003 ^a
Cervical dilation of ≥ 3 cm	10 (9.3)	10 (10)	1.00

Data are presented as number (percentage) or median (range), unless otherwise indicated.

DHMC, Denver Health Medical Center; GA, gestational age; NYP, NewYork-Presbyterian Hospital; PPRM, preterm premature rupture of membranes; UCH, University of Colorado Hospital.

^a $P < .05$ are statistically significant; ^b Infections included urinary tract infection, bacterial vaginosis, chlamydia, gonorrhea, and trichomonas.

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. Am J Obstet Gynecol 2022.

TABLE 2

Maternal morbidities by initial management of pregnancies complicated by preterm premature rupture of membranes at <24 weeks' gestation

Morbidity	Expectant management n=108(51.9)	TOP n=100(48.1)	Expectant management vs TOP P value	Expectant management vs TOP OR (95% CI)
Chorioamnionitis	41 (38.0)	13 (13.0)	<.001 ^a	4.10 (2.03–8.26)
Sepsis	5 (4.6)	1 (1.0)	.214	4.81 (0.55–41.67)
Endometritis	6 (5.6)	3 (3.0)	.501	1.90 (0.46–7.81)
Dilation and curettage	13 (12.0)	13 (13.0)	1.00	0.92 (0.40–2.08)
Laparotomy excluding cesarean delivery	1 (0.9)	0 (0)	1.00	
Injury to the uterus or cervix requiring repair	1 (0.9)	1 (1.0)	1.00	0.93 (0.06–14.93)
Unplanned hysterectomy	1 (0.9)	0 (0)	1.00	
Postpartum hemorrhage ^b	25 (23.1)	11 (11.0)	.027 ^a	2.44 (1.13–5.26)
Transfusion	11 (10.2)	5 (5.0)	.198	2.16 (0.72–6.45)
Admission to the ICU	3 (2.8)	0 (0)	.247	
Acute renal insufficiency ^c	2 (1.9)	0 (0)	.498	
Pulmonary embolism	1 (0.9)	2 (2.0)	.609	0.46 (0.04–5.13)
Readmission to the hospital within 6 wk of delivery or TOP	4 (3.7)	3 (3.0)	1.00	1.24 (0.27–5.71)
Composite maternal morbidity	65 (60.2)	33 (33.0)	<.001 ^a	3.07 (1.74–5.41)
Rossi and DeFranco composite maternal morbidity ^d	51 (47.2)	28 (28.0)	.006 ^a	2.30 (1.30–4.10)
Severe maternal morbidity ^e	13 (12.0)	5 (5.0)	.08 ^a	2.60 (0.89–7.56)
Cesarean delivery	39 (36.1)	0 (0)	<.001 ^a	
Non-LTCS	22 (20.4)	0 (0)	<.001 ^a	

Data are presented as number (percentage), unless otherwise indicated. The incidence of laparoscopy, hysterotomy not as part of cesarean delivery, uterine rupture, venous thromboembolism, and maternal death were zero in all groups.

CI, confidence interval; ICU, intensive care unit; LTCS, low transverse cesarean section; OR, odds ratio; TOP, termination of pregnancy.

^a $P < .05$ are statistically significant; ^b Postpartum hemorrhage was defined as estimated blood loss of >1000 mL; ^c Acute renal insufficiency was defined as a creatinine level of >1.2 mg/dL;

^d Composite morbidity by Rossi and DeFranco consists of any one of the following: chorioamnionitis, unplanned operative procedure, unplanned hysterectomy, blood product transfusion, and admission to the ICU; ^e Severe maternal morbidity consists of any one of the following: sepsis, admission to the ICU, acute renal insufficiency, unplanned hysterectomy, pulmonary embolism, blood transfusion of ≥ 2 U RBC.

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. Am J Obstet Gynecol 2022.

was a transfusion of ≥ 2 U RBC, which occurred because of atony after D&E at 20 weeks' gestation.

As a separate outcome, we assessed neonatal survival among the 108 women who initially chose expectant management (Table 3). Ultimately, 26.9% of women had TOP because of pregnancy complications (usually chorioamnionitis), 11.1% had an intrauterine fetal demise before labor, 9.3% experienced a demise during labor, 13.8% experienced a demise in the NICU, and 38.8% had a neonate who survived to discharge. The most common outcome among women who chose expectant management was to experience both maternal medical morbidity and a fetal or neonatal loss (37.0%) (Table 4).

Comment

Principal findings

Among women experiencing PPRM at <24 weeks' gestation, those choosing expectant management experienced significantly more maternal morbidity than those choosing pregnancy termination (60.2% vs 33.0%; $P < .001$). Furthermore, the rate of severe maternal morbidity was twice as high in the expectant management group (12.0% vs 5.0%; $P = .08$). Among women experiencing severe morbidity, only women in the expectant management group experienced admissions to the ICU, hysterectomy, or >1 severe morbidity.

Results in the context of what is known

To the best of our knowledge, only 1 previous study attempted to compare maternal outcomes of pregnant women who chose between expectant management and TOP. Dotters-Katz et al²¹ conducted a case-control study of 175 women with PPRM at <23 weeks' gestation and did not detect a difference in composite maternal morbidity between the expectant management and TOP groups. However, this study had only 20% power to detect a 30% difference in morbidity. Furthermore, it excluded chorioamnionitis, one of the most common morbidities after PPRM. In addition, it is unclear whether women who chose expectant

TABLE 3

Neonatal outcomes among women who initially chose expectant management after preterm premature rupture of membranes at <24 weeks' gestation

Outcome	n=108
Termination of pregnancy due to pregnancy complications	29 (26.9)
Antenatal intrauterine fetal demise	12 (11.1)
Demise during labor or in the delivery room	10 (9.3)
Death in the neonatal intensive care unit	15 (13.8)
Survival to discharge	42 (38.8)

Data are presented as number (percentage).

Sklar et al. *Maternal morbidity after preterm premature rupture of membranes*. *Am J Obstet Gynecol* 2022.

management and ultimately underwent TOP were analyzed as part of the expectant management or TOP group, making the study less useful for counseling purposes.

Our findings of individual morbidity incidence after expectant management were consistent with previous literature. In their study of women who had expectant management for PPRM from 20 0/7 to 23 6/7 weeks' gestation, Kibel et al⁹ noted a 42.0% rate of chorioamnionitis and 4.8% rate of sepsis, similar to our findings of 38.0% and 4.6%, respectively.¹⁰ Their rate of cesarean delivery was 35.6%, similar to our finding of 36.2%. In our cohort, more than half of the cesarean deliveries were via non-low transverse incisions, increasing future morbidity risk.

In their population-based cohort of live births in Ohio, Rossi and DeFranco¹⁴ found a composite maternal morbidity of 17.2% among deliveries from 20 to 25 weeks' gestation for multiple complications, including PPRM. We tested their composite outcome measure on our

cohort of pregnant patients with PPRM and found the outcome difference by management approach persisted (47.2% vs 28.0%). Our higher composite maternal morbidity at similar GA suggested that PPRM may lead to particularly poor outcomes.

In our study, the most commonly experienced morbidities were chorioamnionitis and hemorrhage; women who chose expectant management had 4.1 times the odds of developing chorioamnionitis and 2.44 times the odds of having a postpartum hemorrhage compared to women who chose TOP. The increased risk of chorioamnionitis and hemorrhage among women choosing expectant management was not restricted to second-trimester PPRM. A study focusing on expectant management vs labor induction after 34 weeks' gestation found the risk of infection and hemorrhage was twice as high in the expectant management group,²² suggesting that a longer duration without the barrier of fetal membranes predisposes to ascending

TABLE 4

Maternal morbidity and neonatal survival to discharge among women who initially chose expectant management after preterm premature rupture of membranes at <24 weeks' gestation

Variable	No maternal morbidity	Maternal morbidity
Neonatal survival to discharge	15.7%	23.2%
No neonatal survival to discharge	24.1%	37.0%

The data consist of 108 women who initially chose expectant management.

Sklar et al. *Maternal morbidity after preterm premature rupture of membranes*. *Am J Obstet Gynecol* 2022.

FIGURE 2**Counseling points for women with pregnancies complicated by preterm premature rupture of membranes at <24 weeks' gestation**

- The risk of maternal morbidity is 60% when a woman initially chooses expectant management
- The risk of maternal morbidity is 33% when a woman initially chooses termination of pregnancy
- Serious morbidities including sepsis, blood transfusion, and intensive care unit admission are more common (OR 2.60) among women who choose expectant management
- Among women who initially choose expectant management the most common outcome is to experience medical morbidity and not have a surviving neonate
 - 15.7% did not experience morbidity and had a neonate who survived to discharge
 - 23.2% experienced morbidity and had a neonate who survived to discharge
 - 24.1% did not experience morbidity and did not have neonate that survived to discharge
 - 37.0% experienced morbidity and did not have neonate who survived to discharge

OR, odds ratio.

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. *Am J Obstet Gynecol* 2022.

infection. Chorioamnionitis may lead to decreased myometrial contractility, which, in turn, increases the risk of hemorrhage because of atony.²³

Clinical implications

Most literature on PPRM at <24 weeks' gestation excluded women who chose TOP.^{5,6,9,13} Among studies that included TOP, it was not an option for all patients. The largest cohort study of PPRM at periviable GAs did not offer TOP in the absence of oligohydramnios or chorioamnionitis.⁴ Conversely, PPRM is often an exclusion criterion in studies of TOP.^{19,24} No previously published study of complications of TOP included >45 women with PPRM, and at most, they made up 14% of the sample of women undergoing TOP for all pregnancy complications.^{16,18} Our composite morbidity of 33% among women who terminate pregnancies complicated by PPRM at <24 weeks' gestation was higher than the approximately 20% complication rate noted in the aforementioned studies.^{16–18} One plausible explanation is that because of the increased risk associated with infection,^{15,23} PPRM itself exposes women to more morbidity than TOP for other pregnancy complications.

Our study provided data on the intersection of maternal and neonatal outcomes among women who chose

expectant management. The overall rate of neonatal survival to hospital discharge was 38.8% in the expectant management group. Fewer than 1 in 6 women (15.7%) avoided morbidity and had a neonate survive to discharge. In contrast, 37.0% of women did suffer morbidity and did not take home a living child. This least optimal outcome was heterogeneous and included a woman who experienced sepsis and admission to the ICU after fetal demise and a woman who developed chorioamnionitis and had an infant that survived for several days in the NICU. Regardless, including the intersection of maternal and neonatal outcomes in counseling will allow for more fully informed decision-making (Figure 2).

We were not powered to compare composite severe morbidities; however, our results showed that severe morbidities occurred twice as frequently in the expectant management group (12.0% vs 5.0%; $P=.08$). Most importantly, pregnancy complications that affect future fertility or prolong hospitalization, such as hysterectomy, admission to the ICU, and experiencing multiple severe morbidities, only occurred with expectant management.

Research implications

Our study compared maternal morbidity among women who initially

chose expectant management with that of women who initially chose TOP at institutions where both expectant management and TOP were available. Here, we combined termination via labor induction and D&E into a single group. Future research comparing morbidity after induction and D&E would provide more complete information to women facing decision-making after PPRM <24 weeks' gestation. This would require the involvement of a national registry or a much broader group of institutions.

Strengths and limitations

The study strengths included data from multiple sites with robust maternal-fetal medicine and complex family planning subspecialists. The patient population was diverse, increasing generalizability. We analyzed patient outcomes by initial decision, increasing the study's usefulness for patient counseling. Furthermore, this study was the largest cohort looking at morbidity among women who chose TOP for pregnancies complicated by PPRM at <24 weeks' gestation, providing critical data for this patient subset.

The study limitations were its retrospective nature and reliance on ICD codes. Data abstraction from clinical records was subject to unmeasured confounding if data were missing in a nonrandom fashion. Unmeasured baseline differences in women choosing TOP or expectant management may be differentially associated with morbidity. In addition, women at earlier GA preferentially chose TOP, likely because of the low chance of neonatal survival.^{6,13} Compared with women in New York, more women in Colorado chose expectant management. Counseling,²⁵ practice patterns,²⁶ and patient preference may underlie this difference but were unlikely to significantly affect the outcome differences observed.

Another limitation was that this study did not provide a robust comparison between termination via labor induction and D&E. In general, the complication rates were reported as higher for termination via labor induction (7%–28%) than for D&E (1%–15%), primarily

because of a retained placenta, although these studies included few patients with PPROM.^{16,19,24} By combining these groups, our results may be weighted more toward the morbidity inherent in termination via labor induction (selected by 69% of women undergoing TOP), which should be considered when counseling patients.

Conclusion

After PPROM at <24 weeks' gestation, women who chose TOP were significantly less likely to experience clinical morbidity than those who chose expectant management. Among those who attempted to preserve the pregnancy, only 15.7% avoided clinical morbidity and had a neonate who survived to discharge. These data will help clinicians and potential parents in shared decision-making. ■

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Author and article information

From the Department of Obstetrics and Gynecology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO (Drs Sklar, Sheeder, Wilson, and Teal); Department of Obstetrics and Gynecology, Kaiser Permanente Northern California, San Leandro, CA (Dr Sklar); Department of Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, NY (Dr Davis); and Department of Obstetrics and Gynecology, Case Western Reserve University School of Medicine, University Hospitals Cleveland Medical Center, Cleveland, OH (Dr Teal).

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Corresponding author: Ariel Sklar, MD, MS. ariel.x1.sklar@kp.org

Appendix 1

SUPPLEMENTAL TABLE 1

Maternal morbidities by type of termination among women who initially selected termination of pregnancy after preterm premature rupture of membranes at <24 weeks' gestation

Morbidity	Labor induction (n=67)	Dilation and evacuation (n=33)	Any termination (n=100)
Chorioamnionitis	8 (11.9)	5 (15.2)	13 (13.0)
Sepsis	1 (1.5)	0 (0)	1 (1.0)
Endometritis	3 (4.5)	0 (0)	3 (3.0)
Dilation and curettage	11 (16.4)	2 (6.1)	13 (13.0)
Laparotomy excluding cesarean delivery	0 (0)	0 (0)	0 (0)
Injury to the uterus or cervix requiring repair	0 (0)	1 (3.0)	1 (1.0)
Unplanned hysterectomy	0 (0)	0 (0)	0 (0)
Postpartum hemorrhage ^a	7 (10.4)	4 (12.1)	11 (11.0)
Transfusion	2 (3.0)	3 (9.1)	5 (5.0)
Admission to the ICU	0 (0)	0 (0)	0 (0)
Acute renal insufficiency ^b	0 (0)	0 (0)	0 (0)
Pulmonary embolism	0 (0)	2 (6.1)	2 (2.0)
Readmission to the hospital within 6 weeks of delivery or TOP	1 (1.5)	2 (6.1)	3 (3.0)
Composite maternal morbidity	22 (32.8)	11(33.3)	33 (33.0)
Rossi and DeFranco composite maternal morbidity ^c	18 (26.9)	10 (30.3)	28 (28.0)
Severe maternal morbidity ^d	2 (3.0)	3 (9.1)	5 (5.0)

Data are presented as number (percentage). The incidence of laparoscopy, hysterotomy not as part of cesarean delivery, uterine rupture, venous thromboembolism, and maternal death were zero in all groups.

ICU, intensive care unit; TOP, termination of pregnancy.

^a Postpartum hemorrhage was defined as an estimated blood loss of >1000 mL; ^b Acute renal insufficiency was defined as a creatinine level of >1.2 mg/dL; ^c Composite morbidity by Rossi and DeFranco consists of any 1 of the following: chorioamnionitis, unplanned operative procedure, unplanned hysterectomy, blood product transfusion, and admission to the ICU; ^d Severe maternal morbidity consists of any one of the following: sepsis, admission to the ICU, acute renal insufficiency, unplanned hysterectomy, pulmonary embolism, blood transfusion of ≥ 2 U RBC.

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. *Am J Obstet Gynecol* 2022.

Appendix 2

SUPPLEMENTAL TABLE 2

Severe morbidities by patient's initial management

Variable	Sepsis	Admission to the ICU	Acute renal insufficiency	Unplanned hysterectomy	Transfusion of ≥ 2 U RBC	Pulmonary embolism	Total number of severe morbidities
Expectant 1	X	X	X	X	X		5
Expectant 2	X	X			X		3
Expectant 3	X	X			X		3
Expectant 4	X				X		2
Expectant 5					X		1
Expectant 6					X		1
Expectant 7	X						1
Expectant 8					X		1
Expectant 9			X				1
Expectant 10					X		1
Expectant 11						X	1
Expectant 12					X		1
Expectant 13					X		1
Termination 1 (induction)	X						1
Termination 2 (induction)					X		1
Termination 3 (D&E)					X		1
Termination 4 (D&E)						X	1
Termination 5 (D&E)						X	1

X indicates the presence of a severe morbidity.

D&E, dilation and evacuation; ICU, intensive care unit.

Sklar et al. Maternal morbidity after preterm premature rupture of membranes. *Am J Obstet Gynecol* 2022.