

# Predictors of Caesarean Delivery in Preterm Premature Rupture of Membranes

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## Abstract

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**BACKGROUND:** Preterm premature rupture of membranes (P-PROM) exerts a tremendous influence on pregnancy prognosis. Additionally, it is a major public health concern, as the cause of up to 40% of all preterm births.

**AIM:** The objective of this study was to identify predictors of Caesarean Delivery in singleton pregnancies complicated by P-PROM.

**MATERIALS AND METHODS:** This is a retrospective observational study of all consecutive singleton P-PROM deliveries (24-37 weeks) over an 18 months at a tertiary referral centre. Pertinent data was collected comprising demographics, obstetric history, pregnancy-associated pathology and delivery from electronic patient records. Univariate statistical analysis comprised Odds Ratio, 95% Confidence interval and Chi-square test with subsequent *p*-value with statistical significance set at *p* < 0.05.

**RESULTS:** A total of 240 women delivered singletons following P-PROM over an 18-month period. Maternal age ranged between 12-41 years with an average age of 28 ± 6.27 years. Vaginal delivery (VD) was the predominant mode of delivery, accounting for 52.9% (n = 127) of deliveries. The following parameters were identified as predictors of Caesarean Section (CS) in P-PROM: vaginal infection (*p* = 0.04), previous CS (*p* < 0.0001), primiparity (*p* = 0.004), gravidity > 5 (*p* = 0.009), university education (*p* = 0.0006) and prenatal care (*p* < 0.0001).

**CONCLUSION:** The advantage of CS over vaginal delivery is expedited delivery of the distressed fetus, while that of vaginal delivery entails avoiding postoperative morbidity. However, large multicentric randomised-controlled studies are needed to elucidate this dilemma definitively.

## Introduction

Preterm premature rupture of membranes (P-PROM) exerts a tremendous influence on pregnancy prognosis. This pregnancy complication not only jeopardises maternal and neonatal outcomes, but is a major public health concern due to its association with preterm birth [1], [2], [3], [4]. Although P-PROM only complicates between 2-3% of pregnancies, it is the single most common identifiable cause of preterm birth, responsible for up to 40% of all preterm births [5], [6].

P-PROM is defined as membrane rupture

between 24 and 37 + 6 weeks of gestation. The WHO classification of P-PROM encompasses membrane rupture during the pre-viable period (< 24 weeks), the extreme (24-28 weeks), the very early (28-31 weeks), the moderate (32-34 weeks) and the late (35-37 weeks) preterm period. The clinical presentation, severity and management differ according to gestational age [7].

The aetiology of P-PROM is multifactorial, influenced by maternal physiology, environmental factors and genetics. The most prominent risk factors associated with P-PROM comprise a previous history of P-PROM, previous preterm birth, genital infection, cigarette smoking, multiple pregnancy, polyhydramnios, cervical incontinence, antepartum

hemorrhage, invasive prenatal procedures and connective tissue disease [8], [9], [10], [11], [12], [13], [14], [15], [16], [17].

The most intrepid debate regarding the therapeutic conduit of P-PPROM continues to spark opposing views concerning the optimum time and mode of delivery. Pregnancy prolongation combats prematurity-associated pathology but increases the risk of chorioamnionitis [18]. Conservative management refers to antibioprophyllaxis, tocolysis and fetal pulmonary maturation before 34 weeks [19], [20], [21].

Interventional management refers to amnioinfusion and fibrin glue sealing, both of which are targeted for second-trimester rupture [22], [23]. Induction of labour (IOL) in P-PPROM is indicated once the pregnancy reaches 34 weeks, without the necessity of checking for fetal lung maturity [24].

P-PPROM carries a 20-fold recurrence risk. As such, the importance of preventing P-PPROM should be a common goal for professional Obstetric societies worldwide [25].

The objective of this study was to identify predictors of Caesarean Delivery in singleton pregnancies complicated by P-PPROM.

## Material and Methods

This is a retrospective observational study of all consecutive singleton P-PPROM deliveries (24-37 weeks) over an 18 months at a tertiary referral centre. Electronic patient records were retrieved from the hospital computer system. Pertinent data was collected comprising demographics, obstetric history, pregnancy-associated pathology and delivery.

Statistical analysis encompassed both descriptive and analytical statistics with parametric and non-parametric tests. The descriptive statistical analysis was performed for numerical parameters using Microsoft Excel 2010 functions including mean, median, range (minimum-maximum) and standard deviation. The analytical statistical analysis included univariate tests comprising Chi-square and subsequent *p*-value for parametric variables. Odds Ratio with 95% Confidence Interval was used to evaluate potential risk factors. Statistical significance was set at *p* < 0.05.

This study was carried out according to STROBE guidelines.

No ethical approval was necessary for this study since this analysis consisted of pre-existing computer records, based solely on the routinely collected information, with a cohort represented as a de-identified data set.

## Results

In the 18 months between January 2016 and June 2017, a total of 240 women delivered singletons following P-PPROM. A total of 239 live births were registered, yielding a 99.6% live birth rate. Maternal age ranged between 12-41 years with an average age of  $28 \pm 6.27$  years. Some two-thirds (*n* = 153) of women resided in an urban environment. The most common level of education was high school (*n* = 96, 40%). Sixty-five percent (*n* = 157) of women had prenatal care since the first trimester.

Gravidity ranged between 1-19 with an average of three. Parity ranged between 1-11, with an average of two. Forty-five percent (*n* = 108) of women were primiparous while 51.2% (*n* = 123) were multiparous and 3.8% (*n* = 9) were grand multiparas. Gestational age ranged between 24-37 weeks with an average of  $35.1 \pm 2.76$  weeks. The highest proportion of preterm neonates were delivered during the late preterm period (*n* = 170, 70.8%) as demonstrated in Table 1. The most frequent gestational age at admission was 36 weeks, accounting for 35.4% of the cohort.

**Table 1: Preterm Delivery According to the WHO Classification**

Preterm Delivery Intervals	Number	Percentage (%)
Extremely preterm (24-28 w)	12	5%
Very preterm (29-32 w)	22	9.2%
Moderate preterm (33-35 w)	36	15%
Late preterm (36-37 w)	170	70.8%
Total	240	100%

Presentation to hospital following membrane rupture ranged between 10 minutes and 24 days. The largest proportion of women: 27% (*n* = 64) presented to the hospital between 61-120 minutes of membrane rupture, as shown in Table 2. Two women (0.8%) were pyrexial upon presentation, which was subsequently diagnosed as chorioamnionitis.

**Table 2: Interval Between Membrane Rupture and Hospital Admission**

Rupture to Admission Interval	Number	Percentage (%)
10-30 minutes	25	10.4
31-60 minutes	56	23.3
61-120 minutes	64	26.7
2-4 hours	56	23.3
4-6 hours	12	5
6-10 hours	9	3.8
10-16 hours	6	2.5
16-24 hours	3	1.3
>24 hours	9	3.8
Total	240	100%

Gestational diabetes mellitus (GDM) accounted for the sole pregnancy-associated pathology (PAP) present in this cohort (*n* = 10, 4.2%). Eighteen percent (*n* = 44) of patients presented with significant anaemia upon admission (below the threshold for physiological dilutional anaemia of pregnancy: Hb < 10.5 g/dL). Excessive weight gain in pregnancy (weight gain > 15 kilograms (kg) accounted for 18% (*n* = 45) of the study cohort and ranged between 15-33 kg with an average of  $19.8 \pm 4.09$  kg.

Fifteen percent ( $n = 37$ ) of women were diagnosed with a vaginal infection upon admission. *Candida albicans* was the most common causative microorganism ( $n = 12$ , 32.4%), followed by 11 (29.7%) cases of Group B Streptococcus (*S. agalactiae*). Nine (3.8%) patients had a concurrent urinary tract infection (UTI). *Escherichia coli* (*E. coli*) was the common causative microorganism accounting for two-thirds ( $n = 6$ ) of uropathogens. Amniotic fluid cultures were taken from 107 women (44.5%), 96 (89.7%) of which were monomicrobial. Again, *Candida albicans* was the most frequent microorganism isolated ( $n = 35$ , 32.7%). The most common latency interval was 2-4 hours ( $n = 38$ , 15.8%), with a range of: 60 minutes-26 days.

Vaginal delivery (VD) was the predominant mode of delivery accounting for 52.9% ( $n = 127$ ) of deliveries. Of the 36 women who had a previous Caesarean Section (CS), two (5.5%) opted for a vaginal birth after cesarean (VBAC) (OR: 289, 95% CI: 238.45-2171.66,  $p < 0.0001$ ). Statistically significant differences were obtained between modes of delivery at weeks 31 and 36 of gestation. Caesarean delivery dominated at 31 weeks, whereas the opposite trend was observed at 36 weeks (Table 3).

**Table 3: Gestational Age at Delivery According to Mode of Delivery**

Gestational Age	CS (n = 113)	NVD (n = 127)	Total	Odds Ratio	95% CI	p-value
24	0 (0%)	2 (1.6%)	2 (0.8%)	0.22	0.01 – 4.65	0.33
25	1 (0.9%)	1 (0.8%)	2 (0.8%)	1.12	0.06 – 18.19	0.93
27	2 (1.8%)	3 (2.4%)	5 (2.1%)	0.74	0.12 – 4.53	0.74
28	2 (1.8%)	1 (0.8%)	3 (1.25%)	2.27	0.20 – 25.37	0.50
29	1 (0.9%)	0 (0%)	1 (0.4%)	3.4	0.43 – 84.30	0.45
30	1 (0.9%)	1 (0.8%)	2 (0.8%)	1.12	0.06 – 18.19	0.93
31	8 (7.1%)	0 (0%)	8 (3.3%)	20.54	1.17 – 360.13	0.03
32	5 (4.4%)	5 (3.9%)	10 (4.2%)	1.12	0.31 – 4.00	0.85
33	2 (1.8%)	3 (2.4%)	5 (2.1%)	0.74	0.12 – 4.53	0.74
34	8 (7.1%)	5 (3.9%)	13 (5.4%)	1.85	0.59 – 5.85	0.28
35	12 (10.6%)	5 (3.9%)	17 (7.08%)	2.89	0.98 – 3.50	0.05
36	30 (27.4%)	56 (44.1%)	86 (35.8%)	0.45	0.26 – 0.79	0.005
37	41 (36.3%)	45 (35.4%)	86 (35.8%)	1.03	0.61 – 1.76	0.89
Total	113	127	240	-	-	-

Table 4 illustrates that vaginal infection, gravidity > 5, primiparity, prenatal care and university education are predictors of CS.

**Table 4: Predictors of Delivery by Caesarean Section for P-PROM**

Characteristic (n = 240)	CS (n = 113)	VD (n = 127)	Odds Ratio	95% CI	p-value
Age > 35	24 (55.9%)	19 (44.1%)	1.53	0.78 – 2.97	0.20
Urban residence	77 (68%)	76 (60%)	1.43	0.84 – 2.44	0.18
Gravidity > 5	10 (8.8%)	27 (21.3%)	0.35	0.16 – 0.70	0.009
Primiparity	62 (55%)	46 (36%)	2.14	1.27 – 3.59	0.004
Prenatal care	93 (82%)	64 (50%)	4.57	2.52 – 8.30	< 0.0001
University education	33 (29%)	14 (11%)	3.32	1.67 – 6.62	0.0006
GDM	8 (80%)	2 (20%)	4.76	0.98 – 22.91	0.05
Anaemia	22 (50%)	22 (50%)	1.15	0.59 – 2.21	0.66
Excessive weight gain of pregnancy	24 (21%)	21 (17%)	1.36	0.71 – 2.60	0.35
Vaginal infection	23 (20%)	14 (11%)	2.02	1.00 – 4.23	0.04
UTI	4 (4.4%)	5 (66.6%)	0.89	0.23 – 3.41	0.87
+ amniotic fluid culture	51 (47.7%)	56 (52.3%)	1.04	0.62 – 1.73	0.87
Time to delivery > 120 min	28 (43.7%)	36 (56.3%)	0.82	0.46 – 1.48	0.53
Delivery < 34/40	23 (60.5%)	15 (39.5%)	1.90	0.94 – 3.87	0.07
Chorioamnionitis	2 (100%)	0 (0%)	1.12	0.15 – 8.12	0.90

## Discussion

P-PROM is not only a critical pregnancy complication, but also a public health concern due to its strong association with PTB [26], [27].

There is an ongoing debate regarding the optimum mode and timing of delivery in P-PROM [28], [29], [30], [31], [32], [33]. The optimum time for delivery that guarantees to avoiding both chorioamnionitis and preventing the consequences of prematurity has yet to be identified [30].

The most common indications for an emergency CS include placental abruption, cord prolapse and systemic chorioamnionitis with fetal distress. Although CS is often considered a life-saving procedure for both the mother and the fetus in the setting of chorioamnionitis, an intra-amniotic infection increases the risk of subsequent surgical site infection, endometritis, visceral injury due to tissue friability, thrombotic events and hospital-acquired infections [34].

Our rate of CS: 52.9% ( $n = 113$ ) is significantly higher than that of 28% in Ibishi et al.'s prospective study examining modes of delivery in P-PROM [33]. Kayiga et al., obtained a similar rate of CS compared to Ibisha et al.: 30.5% compared to 28% [28]. Pasquier et al., reported the most comparable rate of CS to the present study, even slightly higher at 58.7% [35].

Kayiga et al., did not find a statistically significant difference in perinatal mortality between the two modes of delivery. However, CS was associated with an increased incidence of maternal postpartum infections, death and admission to the special care baby unit. Kayiga et al., concluded that although there was no statistically significant difference in perinatal-neonatal mortality, vaginal delivery is a safer mode of delivery as it carries lower rates of maternal and perinatal morbidity compared to CS [28].

The following parameters were identified as predictors of CS in P-PROM: vaginal infection ( $p = 0.04$ ), previous CS ( $p < 0.0001$ ), primiparity ( $p = 0.004$ ), gravidity > 5 ( $p = 0.009$ ), university education ( $p = 0.0006$ ) and prenatal care ( $p < 0.0001$ ).

VBAC is not routinely offered to women delivering in Romanian public hospitals since they are not staffed with a dedicated obstetric anaesthetist to attend as a matter of urgency in the event of uterine rupture already at the stage of dehiscence to prevent fetal demise.

The incidence of chorioamnionitis was exceedingly low in the present study: 0.8% compared to 4.8% in Kayiga et al., prospective study [28].

From this cohort, 35% ( $n = 84$ ) of women did not seek prenatal care. The reasons encompassed remote geographical location, low socioeconomic

status, in addition to a low level of education. Only a single patient with university education did not seek prenatal care compared to 82 without university education (OR: 29.01, 95% CI: 3.92 – 214.47,  $p = 0.001$ ).

The reasons behind high gravidity in this cohort comprise a low level of maternal education, low socioeconomic status, a lack of national educational programme regarding family planning, as well as the absence of a national limit of the number of elective pregnancy terminations.

The limitations of this study comprise its retrospective nature, small sample size, uneven distribution among categories of prematurity and the lack of implementation of IOL into this centre's practice.

In conclusion, P-PROM exerts a tremendous influence on pregnancy prognosis. The objective of this study was to identify predictors of Caesarean Delivery in singleton pregnancies complicated by P-PROM.

The following parameters were identified as predictors of CS in P-PROM: vaginal infection ( $p = 0.04$ ), previous CS ( $p < 0.0001$ ), primiparity ( $p = 0.004$ ), gravidity  $> 5$  ( $p = 0.009$ ), university education ( $p = 0.0006$ ) and prenatal care ( $p < 0.0001$ ).

The advantage of CS over vaginal delivery is expedited delivery of the distressed fetus, while that of vaginal delivery is the avoidance of postoperative morbidity. However, large multicentric randomised-controlled studies are needed to definitively elucidate this dilemma.

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