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Materno-Fetal Prognosis and Factors Associated with Neonatal Death after Preterm Premature Rupture of Membranes at More than 28 Weeks Gestation in Yaoundé, Cameroon

William Derrick Zambo Zambo[1], Serge Guifo Foubi[1], Véronique Mboua Batoum[1], Junie Metogo Ntsama[1], Felix Essiben[1], Evelyn Mah Mungyeh[2], Esther Ngo Um Meka[1]

[1]Department of Gynaecology and Obstetrics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon
[2]Department of Paediatrics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon
Email: williamderrickzambo@yahoo.com

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Abstract

Introduction: Premature rupture of membranes (PROM) causes considerable maternal and perinatal morbidity and mortality. Adequate management is therefore essential to reduce the complications associated with it. The main objective of our study was to determine the maternofetal and neonatal outcomes after a pregnancy complicated by PPROM, as well as the factors associated with neonatal death in this context. **Methodology:** We conducted a descriptive and analytical longitudinal study on a population of pregnant women with PPROM who gave their free and informed consent. Newborns were assessed from birth until the 7th day of life. The association between study variables and neonatal death was established using the chi-square test and expressed as odds ratios with a p-value < 0.05 and a 95% CI after logistic regression. **Results:** A total of 115 women met the inclusion criteria, corresponding to an incidence of premature rupture of membranes of 6.18%. Maternal complications were dominated by threatened preterm labor (50.9%), caesarean deliveries (25%), retroplacental haematoma (3.6%) and intrauterine infections (6.3%). Fetal and early neonatal outcomes were most commonly characterised by early neonatal infections (73.14%), prematurity (52.8%), respiratory distress (5.6%), neonatal asphyxia (2.8%) and neonatal death (12.9%). After multivariate analysis by logistic regression, the only factor that remained associated with the occurrence of neonatal death was an Apgar score < 7 at 5 minutes (adjusted OR = 8.77; 95% CI: 1.27 -

60.59; p = 0.028). **Conclusion:** The maternofetal and neonatal prognosis after PPROM remains poor in our setting due to multiple maternal and perinatal factors.

Keywords

Premature Rupture of Membranes, Maternal Complications, Neonatal Mortality

1. Introduction

Preterm premature rupture of membranes (PROM) is a common occurrence in obstetric practice. It complicates 3% to 10% of pregnancies worldwide. It exposes the mother to a risk of infection and her fetus to premature delivery [1]. These complications are all the more serious when the rupture occurs prematurely.

In Cameroon, according to a study conducted by Pisoh *et al.* in 2021, PPROM significantly contributes to maternal and perinatal morbidity and mortality. According to this study, 10.53% of women who had preterm premature rupture of membranes (PPROM) had an unfavorable outcome, as did the newborns from these pregnancies (OR = 14.44; 95% CI: 5.42 - 38.48; p < 0.001) [2]. To our knowledge, very few studies clearly present these adverse maternal and fetal outcomes after PPROM in Cameroon. The objectives of this study were to determine the incidence of PPROM, then to assess maternal, fetal and early neonatal outcomes after PPROM, and finally to identify the factors associated with neonatal death in the context of PPROM.

2. Materials and Methods

2.1. Ethical Considerations

The study was conducted in accordance with the fundamental principles of research as set out in the Declaration of Helsinki. We obtained ethical clearance from the Institutional Ethics and Research Committee (CIER) of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I and the Gynaecology, Obstetrics and Paediatrics Hospital of Yaoundé, as well as research authorisation from the Central Hospital of Yaoundé. All women were included after giving their informed consent or parental consent for minors.

2.2. Methodology

We conducted a cohort study with prospective data collection. It took place from 1 January to 30 April 2022. We included all pregnant women diagnosed or referred for RPM occurring after 28 weeks of gestation at the Central Hospital and the Gynaecology, Obstetrics and Pediatrics Hospital in Yaoundé. The diagnosis of RPM was clinical; examination with a speculum revealed fluid discharge of endo uterine origin. We did not have colorimetric tests available to confirm that the fluid

was amniotic fluid.

Data were collected using a pre-established questionnaire. Maternal variables included maternal sociodemographic characteristics, maternal history, pregnancy history, clinical examination of patients on admission, additional tests performed, treatment and maternal complications observed. Fetal-neonatal variables included the clinical profile of the newborn and fetal and neonatal outcomes. Follow-up was then carried out using medical records until the early neonatal period, and any complications in mothers and their newborns were recorded. The data collected were recorded on a technical data sheet designed for this purpose, then recorded and analyzed.

This data was analyzed using SPSS (*Statistical Package for Social Sciences*) version 23.0. Microsoft Office Excel 2016 was used to create tables and figures. The incidence of RPM, fetal and neonatal outcomes, and maternal complications were interpreted in terms of frequencies and percentages. Bivariate analysis was performed using the chi-square test, followed by multivariate logistic regression to identify independent predictors. The association between variables and neonatal death was statistically significant if the p-value was <0.05 with a 95% CI after logistic regression.

3. Results

3.1. Maternal Results

During our study, 115 patients were diagnosed with RPM, of whom 3 were discharged from hospital against medical advice, leaving 112 patients.

Table 1. Sociodemographic characteristics of the population.

Variables (n = 112)	Number (n)	Percentages (%)
Age (in years)		
<20	8	7.1
[20 - 30[	70	62.5
>30	34	30.4
Occupation		
Housewife	26	23.2
Pupil	15	13.4
Student	24	21.4
Civil servant	11	9.8
Shopkeeper	4	3.6
Other	32	28.6
Marital status		
Single	48	42.9
Married	20	17.9
Cohabiting	44	39.3

We obtained a PPRM incidence rate of 6.18%. The average age was 27.07 ± 5.82 years. A majority of women (62.5%) were between 20 and 30 years old; this population consisted largely (76.8%) of women who had given birth to few children (Table 1).

Table 2. Background of the population.

Variables (n = 112)	Number of individuals (n)	Percentages (%)
Gynaecological and obstetric background		
Parity		
<4	86	**76.8**
>4	26	23.2
History of abortion	38	33.9
RPM ATCD	11	**13.6**
MAP ATCD	7	6.3
ATCD cervical-isthmic gap	4	3.6
History of cerclage	2	1.8
ATCD genital infection	20	17.9
Associated pregnancy-related conditions		
Metrorrhagia	4	3.6
Chorioamnionitis	2	1.8
Other	50	44.6
History of caesarean section	10	8.9

Table 3. Physical examination characteristics.

Variables (n = 112)	Number (n)	Percentages (%)
Mode of labour onset		
Spontaneous	88	**78.6**
Induced	24	21.4
Foetal heart rate (bpm)	111	**99.1**
Valsalva	103	**92**
Amniotic fluid colour		
Clear	80	**71.4**
Tinted	12	**10.7**
Bloody	1	0.9
Meconium	19	**17.0**

The most common gynecological and obstetric past history finding was abortion (33.9%), followed by genital infections (17.9%), PPRM (13.6%), cervical incom-

petence (3.6%) and cerclage (1.8%). Previous caesarean section was the most common surgical history (8.9%) (Table 2). Most of the women in labor went into labor spontaneously (78.6%) and fetal heartbeat was present in almost all women (99.1%). Vaginal fluid discharge (positive Valsalva) was observed in 92% of patients; amniotic fluid was clear in 71.4% of women. Meconium was found in 17% of cases, stained fluid in 10.7% and bloody fluid in 0.9% (see Table 3). The most common biological tests performed were complete blood count and C-reactive protein level (Table 4). No women were tested for Group B streptococcus. The most common abnormality found on ultrasound was oligohydramnios, with a rate of 23.2%.

Table 4. Paraclinical characteristics.

Variables (n = 112)	Number of subjects (n)	Percentages (%)
Infectious assessment		
ECBU	17	15.2
PCV	10	8.9
NFS	85	75.9
CRP	30	26.8
Obstetric ultrasound	79	70.5
Normal	51	45.5
Oligohydramnios	26	23.2
Anamnios	2	1.8

Table 5. Treatment provided.

Variables (n = 112)	Number of individuals (n)	Percentages (%)
Medication received		
Corticosteroid therapy (n = 58)	37	64
Antibiotic therapy	80	71.4
Tocolytics	22	19.6
Outcome of pregnancy		
IMG	2	1.8
Expectant	110	98.2
Mode of delivery		
Vaginal	84	75
Caesarean	28	25

Among the 58 women with premature rupture of membranes, 64% received corticosteroid therapy and 19.6% received tocolytic therapy for 48 hours. The majority of women, 71.4%, received antibiotic therapy during their hospitalization. The outcome of most pregnancies (98.2%) was expectant, meaning that the preg-

nancy was monitored clinically and paraclinically, and the most common mode of delivery was vaginal delivery at a rate of 75% compared to a caesarean section rate of 25% (Table 5).

The maternal complications observed showed a premature delivery rate of 50.9%. Caesarean section was chosen as the mode of delivery in 25% of cases. In addition, complications such as Abruptio placenta (3.6%) and intrauterine infections were noted: chorioamnionitis (1.8%) and endometritis (4.5%) (Figure 1).

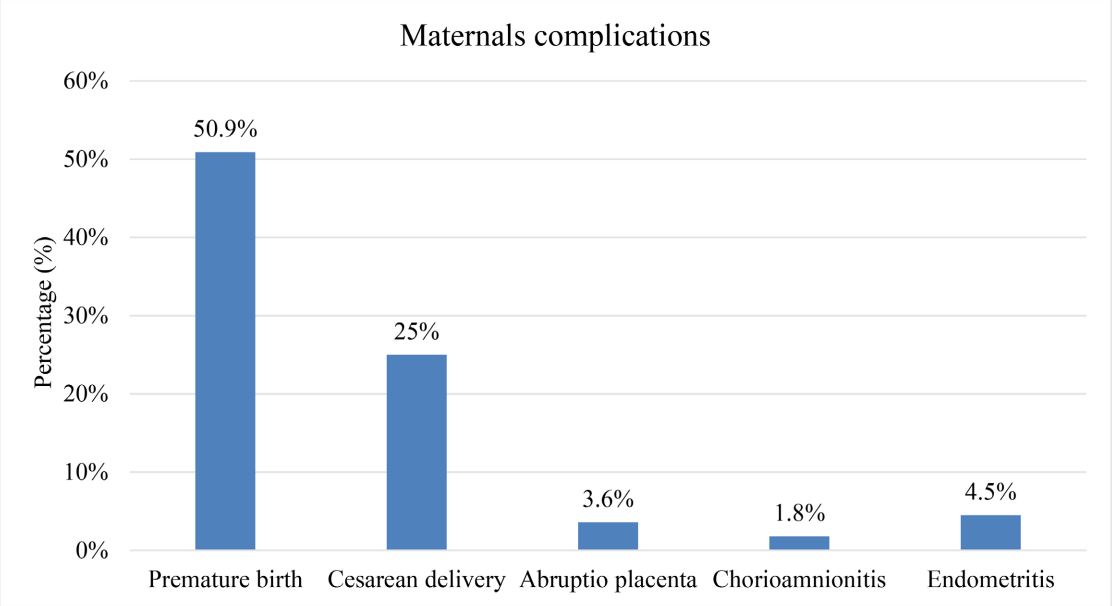

Figure 1. Maternal complications with percentage scale on y-axis.

3.2. Fetal and Neonatal Outcomes

The most common mode of transfer was in utero (94.6%) from another health facility. The majority of newborns were alive at birth (96.4%) with a birth weight > 2500 g (53.6%) and were males (54.5%). Eighty-two per cent of newborns had complications during the perinatal period and 38% of them had received resuscitation at birth. Neonatal death was observed in 12.5% of newborns, admitted to the neonatal unit in context of PROM (Table 6).

The Apgar score at 5 minutes was 8.35 ± 1.94 on average, with a minimum of 0 and a maximum of 10. The average length of hospitalization was 7.55 ± 7.96 days, with a maximum of 42 days (Table 7).

Fetal outcome after RPM was much more marked by premature births (50.9%). In addition, the death rate was 3.6% at birth (stillbirths) and 9.3% during hospitalization.

Perinatal and neonatal complications were dominated by early neonatal infections (73.14%); prematurity (52.8%); respiratory distress (5.6%); neonatal asphyxia (2.8%); and neonatal jaundice (3.7%) (Table 8).

The factors significantly associated with neonatal death were weight < 2500 g (p-value = 0.001), prematurity (p-value = 0.017), vaginal delivery (p-value = 0.035),

an Apgar score at 5 minutes < 7 (p-value = 0.001), and oligohydramnios (p-value = 0.020). After multivariate analysis with logistic regression, only an APGAR score at 5 min < 7 was associated with neonatal death in the context of RPM, with an OR of 8.77 (1.27 - 60.59) and a p-value of 0.028 (Table 9).

Table 6. Clinical profile of newborns.

Variables (n = 112)	Number (n)	Percentages (%)
Mode of transfer		
In utero	106	**94.6**
Postnatal	6	5.4
Status at birth		
Alive	108	**96.4**
Stillborn	4	3.6
Resuscitation at birth	42	**37.5**
Birth weight (g)		
<2500	52	46.4
>2500	60	**53.6**
Gender		
Male	61	**54.5**
Female	51	45.5
Neonatal complications	92	**82.1**
Neonatal mortality	14	**12.5**
Pathologies at 7 days of life	19	17

Table 7. Different characteristics of the APGAR score and length of hospital stay.

APGAR score	Min - Max	Mean ± SD
1stminute	0 - 9	7.49 ± 1.71
5th minute	0 - 10	8.35 ± 1.94
10th minute	0 - 10	9.10 ± 2.11
Length of stay (days)	0 - 42	7.55 ± 7.96

Table 8. Perinatal and neonatal complications.

Complications (n = 108)	Number (n)	Percentages (%)
Early neonatal infections	79	73.1
Prematurity	57	52.8
Respiratory distress	6	5.6
Neonatal jaundice	4	3.7
Neonatal asphyxia	3	2.8

Table 9. Factors associated with neonatal death.

(a) Bivariate analysis				
Variables (n = 112)	Deaths, n (%)		OR (95% CI)	p-value
	Yes	No		
Mode of transfer				
In utero transfer	11 (10.4%)	95 (89.6%)	0.579 (0.06 - 5.41)	0.502
Postnatal transfer	1 (16.7%)	5 (83.3%)		
Time to rupture				
<12 hours	11 (10.4%)	95 (89.6%)	0.579 (0.06 - 5.41)	0.502
>12 hours	1 (16.7%)	5 (83.3%)		
Prematurity	10 (17.5%)	47 (82.5%)	5.638 (1.17 - 27.05)	0.017
Birth weight (g)				
<2500	11 (21.2%)	41 (78.8%)	15.82 (1.96 - 127.40)	0.001
>2500	1 (1.7%)	59 (98.3%)		
Mode of delivery				
Caesarean	0 (0%)	28 (100%)	-	
Vaginal delivery	12 (14.3%)	72 (85.7%)	-	0.035
Apgar score at 5 minutes				
<7	4 (44.4%)	5 (55.6%)	9.50 (2.12 - 42.56)	0.001
>7	8 (7.8%)	95 (92.2%)		
Ultrasound				
Oligohydramnios	6 (23.1%)	20 (76.9%)	4 (1.12 - 13.73)	0.020
Anamnios	(0%)	2 (100%)	-	1
Neonatal complications	12 (13%)	80 (87%)	-	0.120
Length of hospital stay				
<7	9 (13.4%)	58 (86.6%)	2.17 (0.55 - 8.51)	0.256
>7	3 (6.7%)	42 (93.3%)		
Gender				
Male	6 (9.8%)	55 (90.2%)	0.82 (0.247 - 2.712)	0.742
Female	6 (11.8%)	45 (88.2%)		
(b) Multivariate analysis				
Variables (n = 112)	Death, n (%)		Adjusted OR (95% CI)	Adjusted p-value
	Yes	No		
Prematurity	10 (17.5%)	47 (82.5%)	1.12 (0.096 - 12.99)	0.930
Birth weight (g) < 2500	11 (21.2%)	41 (78.8%)	6.87 (0.42 - 112.63)	0.177
Mode of delivery				
Vaginal delivery	12 (14.3%)	72 (85.7%)	-	0.998
Apgar score at 5 min				
<7	4 (44.4%)	5 (55.6%)	8.77 (1.27 - 60.59)	0.028
Ultrasound				
Oligoamnios	6 (23.1%)	20 (76.9%)	2.47 (0.58 - 10.49)	0.220

4. Discussion

PPROM is a common condition during both preterm and full-term pregnancies. According to data from African literature, it has a prevalence of 4.63% in Mali and an incidence of 10% in Algeria [3] [4]. In our series, the incidence of PPROM was 6.18%, which is higher than that found in other national studies on PPROM (1.6%, Kasia *et al.*; 4.91%, Pisoh *et al.*) [2] [5]. This difference could be explained by the fact that we worked in two recruitment and referral sites for obstetric complications. In 2017 in Cameroon, Belinga *et al.* found that premature rupture of membranes was statistically significant in patients referred for obstetric complications in Yaoundé [6]. In addition, our population consisted largely of women who had given birth only a few times (77%), in whom PPROM is more common due to the increased fragility of the amniotic membranes, unlike multiparous women, whose membranes have become thicker and more resistant due to repeated pressure during previous pregnancies.

For maternal prognosis after PPROM, a study conducted in India in 2007 by Menon *et al.* found a prevalence of 40% of premature births in the context of PPROM [7]. This rate was as high as that found in our study, which was 50.9%. Indeed, the literature describes that any woman with premature rupture of membranes will spontaneously go into labor 24 hours after the rupture or even earlier, explaining this high rate of threatened premature delivery in cases of premature rupture of membranes before term. Twenty-five per cent of women had resorted to caesarean section as the mode of delivery. Intrauterine infections were found at rates of 1.8% for chorioamnionitis and 4.5% for endometritis. According to the literature, the genital tract is continuously infected in pregnant women. Thus, certain obstetric situations, such as PPROM, expose these women to ascending infections. In 2002 in Cameroon, Foumane *et al.* found a clear predominance of *Candida albicans* (48.45%), *Gardnerella vaginalis* (22.16%) and Group B β-hemolytic streptococcus (6.70%) during pregnancy [8]. These variations in genital flora during pregnancy may explain the occurrence of intrauterine infections in our series, where patients remained on expectant management for several days without antibiotic coverage (28.6% of women). Furthermore, screening for Group B streptococcus is not systematic in women in our environment.

Neonatal and perinatal outcomes were associated with significant morbidity and mortality. In our study, we recorded complications such as prematurity (52.8%), neonatal infection (73.14%) and neonatal mortality (12.9%). Neonatal infections are justified by our high rate of prematurity, given that we considered RPMs from 28 weeks of gestation (age of extreme prematurity). Premature babies are known to be weak and vulnerable due to their immaturity, which exposes them much more than others to infections and, ultimately, death [9] [10]. Furthermore, this high rate of neonatal infections could also be explained by the fact that, in our context, screening for Group B streptococcus is not systematic during pregnancy, even though this bacterium poses a high risk of neonatal infection given the high frequency of vaginal deliveries (75% in our study). Indeed, Group B streptococcus carriage was

found in some women during a study conducted in Cameroon in 2009 by Foumane *et al.* [8]; the newborn can therefore become infected when passing through the mother's genital tract. This finding highlights the importance of screening for Group B streptococcus during pregnancy or risk-based prophylaxis such as PROM. The mortality rate found in our series was higher than those reported by Coulibaly in Mali (4.8%) and Chibani in Algeria (7.5%) [3] [4]. This difference may be due to the fact that we considered deaths at birth and deaths in neonatal hospitalization. In addition, neonatal infections worsen the prognosis due to their severity and more pronounced immune immaturity. In 2008 in Cameroon, Chelo *et al.* found an association between neonatal infection and mortality [10]. Furthermore, as our study was conducted in Africa with limited technical resources, we expected this high neonatal mortality rate. In 2017 in Mali, Coulibaly *et al.* also reported that limited technical resources were a determining factor in neonatal morbidity after RPM [3].

Approximately 38% of the newborns included in our study required resuscitation at birth due to the high number of cases of neonatal asphyxia (16.7%) and respiratory distress (22.2%). This result could be explained by the pulmonary immaturity of premature newborns and the ineffective pulmonary maturation in many of these newborns; only 64% of women had received corticosteroid therapy, which is due to the fact that these women arrived at the maternity ward already in labor and therefore gave birth quickly. In addition, due to insufficient resources, there was a delay in the availability of medication. In 2008 in Cameroon, Chelo *et al.* reported that neonatal asphyxia was the leading cause of death among newborns [10]. Our results confirm the link between an Apgar score < 7 at 5 minutes and neonatal death (OR: 9.50; 95% CI: 2.12 - 42.56; p = 0.001).

Some limitations observed:

- The relatively small sample size.
- The short neonatal follow-up limited to the early neonatal period.

5. Conclusion

PPROM remains a common occurrence in obstetrics. The maternal prognosis continues to be dominated by significant morbidity. The fetal and perinatal outcome remains unfavorable in our setting, compounded by a considerable rate of neonatal mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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