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Vol: 1 & Iss: 1

Research Article

Risk factors for Premature Rupture of Membranes in Two Regional Hospitals in West Region Cameroon: A Case-Control Study

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Citation: Hortence FJ, Rachel TZO, Jovanny FT, et al. Risk factors for Premature Rupture of Membranes in Two Regional Hospitals in West Region Cameroon: A Case-Control Study. *Arch Wom Health 2025;* 1(1): 40-45.

Received: 05 November, 2025; **Accepted:** 18 November, 2025; **Published:** 20 November, 2025

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A B S T R A C T

Objective: The aim of our study was to research the risk factors for PROM in pregnant women in the gynecology-obstetrics department of the Regional Annex Hospital of Dschang (HRAD) and the Regional Hospital of Bafoussam (HRB).

Methods: We conducted a case control study at the HRAD and HRB over a period of 3 months. All pregnant women who presented with a pregnancy complicated by PROM with a gestational age ≥28 weeks were included as cases and as controls the pregnant women at the same gestational age who did not present with PROM. Sampling was non-probability and non-exhaustive. The data were collected from a technical sheet and analyzed using the Statistical Package for Social Sciences (SPSS) version 20 software.

Results: On 554 deliveries recorded, we identified 61 cases of PROM, a prevalence of 11.01%. The risk factors identified were: residence in a rural area [ORa =16.73; 95% CI (2.68-104.50), p =0.003], malaria in pregnancy [ORa =13.47; 95% CI (2.14-84.95), p =0.009] in pregnancy. The achievement of at least 4 CPN [RCa =0.04; 95% CI (0.002-0.72), p =0.029] was a protective factor for PROM.

Conclusion: The risk factors for PMR identified were residence in a rural area and malaria during pregnancy. Access must be placed on the prevention of these factors in the promotional aspect of prenatal contacts.

Keywords: Amniotic fluid, Fetal membranes, High-risk pregnancy, West Cameroon

1. Introduction

Pregnancy is a special physiological state that proceeds normally in most cases and spontaneously leads to normal delivery. However, unexpected events can disrupt its development and compromise the maternal -fetal prognosis. This is the case of premature rupture of membranes (PROM) which is a spontaneous rupture of the bag of waters (amnion and chorion) occurring before any start of labor[1]. It can occur at term, before term or post-term. Worldwide, the prevalence of PROM varies between 5 and 10% regardless of the term[1]. In France,

the frequency of PROM varies between 3% before 37 weeks of amenorrhea (SA) and less than 1% after 37 weeks; Prematurity and intrauterine infection are the major complications of preterm PROM[2]. According to the American College of Obstetricians and Gynecologists (AGOG), preterm PROM complicates approximately 2-3% of all pregnancies in the United States[3]. In Canada, preterm premature rupture of membranes (PPROM) is a complication noted in approximately 3% of pregnancies[4]. In China and Thailand, the prevalences are 2.7% and 2.93%, respectively[5,6]. The pathogenesis of PROM is multifactorial, it can be due firstly to an increase in intra-amniotic pressure as in polyhydramnios , secondly to a congenital or acquired defect in the fetal membranes as in collagen diseases or smoking, thirdly to weakening of the membranes by enzymatic destruction in inflammatory or infectious processes, fourthly by direct trauma to the fetal membrane in the cervical canal in women with cervical incompetence.

In Africa, PROM is one of the main causes of prematurity and its frequency varies between 3 and 18%, in Congo 1.2%; in Mali 1.62%, in Burkina Faso 0.75%[7-9]. The risk factors are predominated by infections, multiple pregnancies, polyhydramnios, history of PROM and the most frequent complications are endometritis and chorioamnionitis with a poor prognosis for premature newborns[7-9].

In Cameroon, RPM has a prevalence of approximately 6.2% in two university hospitals in the cities of Douala and Yaoundé[10]. PPROM, for its part, has a prevalence of 4.91% at the Bamenda regional hospital[11]. It is the second maternal complication in pregnancy, i.e. 1.6% at the Hospital Center for Research and Application in Endoscopic Surgery and Human Reproduction (CHRACERH)[12]. This is the first obstetric complication associated with obstetric referrals in Yaoundé[13]. Data on PROM in the West region of Cameroon are rare, which justifies our study whose objective was to identify the risk factors for premature rupture of membranes in two regional hospitals in West Cameroon.

2. Material and Methods

2.1. Type of study

We conducted a case-control study with prospective data collection.

2.2 Study sites

The study took place in the gynecology-obstetrics and prenatal consultation departments of the Regional Annex Hospital of Dschang and the Regional Hospital of Bafoussam. These are the third category hospitals of the health pyramid which have an adequate platform to take care of high-risk pregnancies.

2.3 Study period

The study took place from November 13, 2023 to February 13, 2024, i.e. over a period of 5 months.

2.4. Study population

2.4.1. Target population: All pregnant women received in these health facilities during the study period.

2.4.2 Source population: Pregnant women with a gestational age ≥ 28 weeks received in these hospitals during the study period.

2.4.3. Selection of participants:

- Inclusion criteria
  - **For cases:** all pregnant women who presented with PROM with an AG≥28 weeks and who gave birth during the study period were included, whether they came on their own (self-reference) or whether they were evacuated or referred and who consented.
  - **For controls:** all pregnant women of the same gestational age as the cases were included who came to prenatal consultation (especially for preterm pregnancies) or to the delivery room in these hospitals during the study period and did not present of RPM.
- **Exclusion criteria:** Pregnant women who refused to give consent were excluded from the study.

2.5. Sampling

2.5.1. Type of sampling: We used a non-probability and non-exhaustive sample.

2.5.2 Calculation of sample size: To assess the minimum sample size required for this study, we used the STATCALC function of the EPI info version 7 software. We used data from the study conducted by Nkwabong, et al[10]. By taking one case for two controls, after numerical application, we obtained a size of 61 cases for 122 controls.

2.6. Procedures

2.6.1. Administrative Procedure: After validation of the protocol by the directors and co-directors of the thesis, we submitted a request for research authorization to the FMSP of the University of Dschang which was accepted. Subsequently, we obtained authorization to conduct research in our various hospitals and ethical clearance from the Western Regional Ethics Committee for Research in Human Health (CRERSH).

2.6.2. Data collection: After obtaining the authorizations, we contacted the pregnant women. An explanation session on the purpose, procedure, advantages and disadvantages of participating in the study was carried out. Participants could then express any concerns they had. The informed consent form was submitted to them for careful reading, after which each participant was free to sign or not. We carried out the interview and the clinical examination, the information was collected using the pretested questionnaire.

2.7. Study variables

- The dependent variable was Premature Rupture of Membranes (PROM).
- Independent Variables
  - **Sociodemographic variables:** age of the pregnant woman, level of education, profession, place of residence, marital status, religion.
  - Toxicological variables linked to the lifestyle of pregnant women with regard to RPM : the concept of passive or active smoking, the concept of carrying heavy loads.
  - **Variables:** history of PROM, notion of cervico-isthmic gap, probable causes, number of prenatal contacts.

2.8. Statistical analyzes

The data was collected through individual survey sheets from pregnant women. These data were then introduced into an input mask designed from the EPI-Info software, then extracted on Microsoft Excel 2016, then were coded and entered into the EPI info version 7.2 program for cleaning. They were subsequently exported to SPSS version 20 for additional analysis and reporting.

The quantitative variables were expressed as mean, standard deviation and in terms of number and percentage.

Simple frequencies, crosstabs, means and standard deviation were used in descriptive statistical analyzes to summarize participants' sociodemographic data. The association between RPM (dependent variable) and independent factors was investigated using binary logistic regression with 95% CI.

To further improve the analysis and adjust for confounding factors, variables with p values < 0.25 in the bivariate model were included in the multivariate model. P value < 0.05 was considered statistically significant. The fitness of the model will be measured using the Hosnmer and Lemeshow test, good fit measures and the Nagelkerke. The tests were entered using Microsoft Word. Fisher's test was used for comparison between categorical data and Student 's t test for numerical data. The results were presented in the form of tables and graphs.

2.9. Ethical considerations

After writing our study protocol, it was first submitted for validation to the Institutional Evaluation Committee of the Faculty of Medicine and Pharmaceutical Sciences of Dschang for institutional authorization. Research authorizations from the Directors of the HRAD and the HRB as well as ethical clearance from the Regional Ethics Committee for Human Health Research (ethical clearance N°988/25/10/2023/CE/CRERSH-OU/VP) were obtained before starting our study.

Our study was carried out in strict compliance with the principles of medical research. As an advantage, the participants benefited from awareness-raising on RPM. Thanks to this study, prevention strategies for PROM will be based on evidence.

3. Results

3.1. Sociodemographic risk factors

Regarding the distribution according to sociodemographic risk factors of cases and controls, residence in rural areas in Dschang and in urban areas in Bafoussam were statistically significant **(Table 1)**.

3.2. Risk factors linked to the lifestyle of pregnant women

Concerning toxicological risk factors, tobacco consumption was a protective factor for RPM. There was no association between heavy lifting and RPM **(Table 2)**.

3.3. Obstetric risk factors

3.3.1. Factors related to current pregnancy: Regarding the current pregnancy history of cases and controls, having a notion of urinary infection, malaria and vaginal infection during pregnancy was statistically significant and associated with a high probability of PROM **(Table 3)**.

Table 1: distribution of the study population according to socio-demographic characteristics.

Variables	Case N=61 n(%)	Control N=122 n(%)	OR (95% CI)	P
Age (in years)				
<20	5 (50.00)	5 (50.00)	1	-
20 – 29	36 (34.60)	68 (65.4)	0.53 (0.14-2.0)	0.339
30 - 39	19 (28.40)	48 (71.6)	0.40 (0.10-1.50)	0.178
≥40	1 (50.00)	1 (50.00)	1.00 (0.05-20.8)	1,000
Marital status				
Bride monogamous	11 (28.2)	28 (71.8)	1	-
Bachelor	19 (46.3)	22(53.7)	2.20(0.87 – 5.57)	0.165
Bride polygamous	1 (10.0)	9(90.0)	0.28(0.03 – 2.50)	0.152
Cohabitation	30 (32.3)	63(67.7)	1.21(0.53–2.76)	0.430
Level instruction				
Superior	20(33.3)	40 (66.7)	1	-
Secondary	37(32.5)	77 (67.5)	0.96(0.49 – 1.87)	0.907
Primary	4(44.4)	5 (55.6)	1.6 (0.39 – 6.60)	0.517
Occupation				
Official	7 (38.9)	11 (61.1)	1	-
Employee (private)	5 (25.0)	15 (75.0)	0.52 (0.13 – 2.10)	0.361
Self- employment	20 (28.2)	51 (71.8)	0.62 (0.21 – 1.81)	0.379
Student	10 (35.7)	18 (64.3)	0.87 (0.23 – 2.97)	0.828
Pupil	8 (66.7)	4 (33.3)	3.14 (0.68 – 14.50)	0.142
Household	11 (32.4)	23 (67.6)	0.75 (0.22 – 2.47)	0.638
Place of residence				
Dschang urban	15 (16, 7)	75 (83.3)	1	-
Rural Dschang	12 (52.2)	11 (47.8)	5.46 (2.03 – 14.65)	<0.001
rural Bafoussam	3(37.5)	5 (62.5)	3.00 (0.65 – 13.92)	0.523
Bafoussam urban	31 (50.0)	31 (50.0)	5.00 (2.37 – 10.53)	<0.001

Table 2: Distribution of the study population according to the lifestyle of pregnant women.

Variables	Case N=61 n (%)	Control N=122 n (%)	OR (95% CI)	P
Tobacco consumption during pregnancy				
Yes	0, 0 (0,0)	0.0(0, 0)	-	-
No	61(33.0)	122(66.7)	0.23(0.11 - 0.48)	<0.001
Proximity to a close smoker				
Yes	1 (100)	0.0 (0.0)	-	-
No	60.0(33.0)	122(67.0)	-	-
Concept of carrying heavy loads				
No	41.0(29.7)	97.0 (70.3)	1	-
Yes	20.0(44.4)	25.0 (55.6)	1.89(0.95 – 3.78)	0.071

3.3.2. Factors related to gyneco-obstetric history: Concerning gyneco-obstetric history, having a history of abortion and premature rupture of membranes was statistically significant and associated with a high probability of PROM **(Table 4)**.

3.4. Risk factors for PROM after multivariate analysis and logistic regression

According to the multivariate analysis, residence in Dschang in a rural area and malaria during pregnancy were significantly at the RPM. On the other hand, the number of CPN≥4 was statistically significant and associated with a low risk of PROM **(Table 5)**.

Table 3: distribution of the study population according to the history of the current pregnancy.

Variables	Case N=61 n (%)	Control N=122 n (%)	OR (95% CI)	P
Type of pregnancy				
Monafetale	54 (33.8)	106 (66.2)	1	-
Gemellar	7 (30.4)	16 (69.6)	0.86(0.33 - 2.21)	0.753
Metrorrhagia				
No	52 (31.7)	112 (68.3)	-	-
Yes	9 (47.4)	10 (52.6)	1.94 (0.74 –5.06)	0.176
Urinary tract infection				
No	45 (30.0)	105 (70.0)	1	-
Yes	16(48.5)	17(51.5)	2.20(1.02 – 4.73)	0.044
Malaria				
No	45(27.8)	117(72.2)	1	-
Yes	16(76.2)	5(23.8)	8.32(2.88–4.73)	<0.001
Polyhydramnios				
No	58(32.6)	120(67.4)	1	-
Yes	3(60.0)	2 (40.0)	3.106(0.51 – 19.09)	0.222
Malpresentation				
No	58(32.6)	120(67.4)	1	-
Yes	3(60.0)	2 (40.0)	3.106(0.51 – 19.09)	0.222
Vaginal infection				
No	50 (29.8)	118(70.2)	1	-
Yes	11 (73.3)	4 (26.7)	6.49 (1.97 – 21.36)	0.002

Table 4: distribution of the study population according to gyneco-obstetric history.

Variables	Case N=61 n(%)	Witnesses N=122 n(%)	OR (95% CI)	P
Antecedent abortion				
No	49(30.2)	9 (42.9)	1	-
Yes	12 (57.1)	109 (70.8)	3.08 (1.22 - 7.77)	0.018
History of premature delivery				
No	57 (32.6)	118 (67.4)	1	-
Yes	4(50.0)	4(50.0)	2.01(0.50 – 8.58)	0.316
History of PROM				
No	45(29.2)	109 (70.8)	1	-
Yes	16(55.2)	13 (44.8)	2.98(1.33 – 6.70)	0.008
History of cesarean section				
No	56(33.3)	112 (66.7)	1	-
Yes	5 (33.3)	10 (66.7)	1 (0.33 – 3.07)	1,000
History of cervical incompetence				
No	58 (32.2)	122 (57.8)	1	-
Yes	3 (100.0)	0 (0.00)	-	-

4. Discussion

4.1. Sociodemographic risk factors

During our study, profession was not associated with RPM. On the other hand, unemployed pregnant women had twice the risk of presenting PROM in the case control study by Chiegue, et al. conducted in the cities of Douala and Yaoundé in 2019 among 150 cases and 150 controls. This observation could be explained by a difference in the place of study. Indeed, there is a decline in employment in Cameroon and the majority of people residing in the cities of Douala and Yaoundé would be the most affected. On the other hand, in the Western region, particularly in Dschang and Bafoussam, women are self-employed[14].

Table 5: Multivariate analysis and logistic regression.

Variables	RCa (95% CI)	p * adjusted
Place of residence		
Dschang (Urban)	1	
Dschang (Rural)	16.73(2.68−104.5)	0.003
Bafoussam (Urban)	4.04(0.95−17.14)	0.059
Number of ANC* performed		
< 4 (ref)	1	
≥4	0.04(0.002-0.72)	0.029
Malaria in current pregnancy		
No	1	
Yes	13.47(2.14-84.95)	0.006

*P= P value; ANC: antenatal care

During our study, the strong point was to note that pregnant women residing in Dschang in a rural area had 5 times more risk of presenting PROM compared to those who resided in an urban area. This result has not been found in any study. On the other hand, this could be explained in our study by a low socio-economic level of pregnant women which could lead to poor monitoring of pregnancies and therefore to an increase in the risk of presenting PROM. Another explanation could be the fact that the Regional Annex Hospital of Dschang is a reference hospital in a small town very close to several rural areas allowing patients with obstetric complications like the RPM to get there easily.

Pregnant women residing in Bafoussam in an urban area were 5 times more likely to present with PROM compared to those who resided in an urban area. This result has not been found in any study. Furthermore, this could be due to the fact that the city of Bafoussam is a very large city and the HRB located in its heart is a reference hospital much more surrounded by urban areas, making it more accessible to the pregnant women who reside there. Another explanation could be the high cost of services in this hospital and the long distance for pregnant women residing in rural areas who would prefer to go to closer centers, thus reducing their attendance at reference hospitals in the event of an obstetric complication.

4.2. Lifestyle risk factors

Thus, not consuming tobacco during pregnancy was associated with a low risk of having PROM, according to the results of the bivariate analysis. Non-consumption of tobacco during pregnancy was therefore a protective factor for PROM. This result is similar to the findings of Workineh et al. after bivariate analysis in his study conducted in 2018 in southern Ethiopia which revealed that smoking was 17 times associated with RPM[15]. This result is explained by the fact that smoking promotes RPM through oxidative stress, modifying the collagen concentration by altering it. Furthermore, tobacco smoke brings superoxide ions, hydrogen peroxide and nitric oxide which cause damage to the collagen matrix or consumption of antioxidants.

4.3. Obstetric risk factors

Gestation 4-5 and parity 2-3 were significantly associated with a drop in RPM after bivariate analysis. Pregnancy 4-5 and parity 2-3 being protective factors for RPM. These results have not been found in any study, but we can justify them by the fact that the cervix of these pregnant women is more competent

compared to that of large multiparous and maldigested women and therefore would prevent prolapse of the membranes. in the internal orifice of the dehiscent neck, causing focal alterations of the membranes.

Parity 4-5 was not associated with PROM in our study. On the other hand, Nkwabong, et al. in Cameroon in 2021 found an association with a 3 times elevated risk between RPM and parity 4-5[10]. The type of pregnancy had no significant association during our study. This result is contrary to that of the cross-sectional study carried out in 2020 in Cameroon on 387 pregnant women by Pisoh et al. who found that pregnant women with multiple pregnancies were 5 times more likely to have PPROM[11]. Multiple pregnancy contributes to an increase in membrane tension and can lead to PROM. This difference could be explained by a difference in our sample size.

The number of CPN ≥ 4 was also a statistically significant independent factor associated with low risk of PROM after multivariate analysis. Thus, achieving CPN ≥ 4 during pregnancy was a protective factor for PROM. The same result was found in the cross-sectional study by Pisoh et al. conducted in Cameroon in 2020 on 387 pregnant women[11]. Tiruye, et al., after a systematic review and meta-analysis in Ethiopia, found that pregnant women who did not attend any prenatal consultation were 3 times more likely to present with PROM[16]. We explain this by the fact that good prenatal monitoring makes it possible to identify certain risk factors and take care of them quickly in order to prevent the occurrence of a possible PROM.

Pregnant women with a notion of urinary infection during pregnancy had twice the risk of presenting PROM in bivariate analysis. These results are similar to those of Pisoh et al in their cross-sectional study carried out in Cameroon on 387 pregnant women who found in bivariate analysis that pregnant women presenting with a notion of urinary infection during pregnancy had 24 times more risk of presenting PPROM[11]. These results can be explained by the fact that urinary infections are potential reservoirs of bacteria which pass through the vagina and ascend through the cervical canal to the membranes where they cause localized inflammation. Bacteria produce several proteolytic enzymes such as collagenase and gelatinase which can cause local weakening of membranes.

After multivariate analysis, pregnant women with a notion of malaria during pregnancy had 13 times more risk of presenting PROM than those who did not have it. These results have not been found in any study. These results are different from those of Nkwabong et al. in its case control study carried out in Cameroon on 255 pregnant women which did not find an association between malaria in pregnancy and PROM after multivariate analysis[10]. This difference can be explained by the fact that our study was carried out in one of the areas of high malaria endemicity. The poor prevention via the LLIN and the taking of Intermittent Preventive Treatment for the fight against malaria in our different study sites (TPI) would also increase the risk of malaria in pregnancy and therefore of PROM in our context.

Pregnant women with a notion of vaginal infection during pregnancy had a 6 times greater risk of presenting PROM after bivariate analysis. These results are similar to those of Pisoh et al. in Cameroon and Assefa et al. in Ethiopia who had respectively found risks 7 and 5 times more risk after bivariate analysis[11,17]. These results can be explained by the fact that the ascending invasion of pathogens from the internal opening of the cervix uterus to the local membranes of the fetus triggers the production of various hydrolytic enzymes, including endotoxins, proteases and inflammatory mediators. These enzymes act on the extracellular matrix of fetal membranes, initiating the hydrolysis process. Therefore, fetal membrane fragility may occur concurrently with decreased local surface tension and cause PROM.

Having a history of abortion was statistically significant and associated with a 12 times higher probability of having PROM after bivariate analysis. These same findings were made by Assefa et al. And Enjamo et al. in Ethiopia which respectively found a probability 3 and 4 times higher in pregnant women presenting with PROM[13,18]. These results can be explained by the fact that mechanical expansion during abortion procedures can disrupt the elasticity of the cervix which leads to scarring of the uterus as well as cervical insufficiency leading to RPM.

Having a history of PROM was statistically significant and associated with a 12 times higher probability of having PROM after bivariate analysis. These same findings were made by Assefa et al. And Enjamo et al. in Ethiopia; Chiegue et al. in Cameroon had respectively found probabilities 7; 6 and 5 times elevated to present an RPM after bivariate analysis[17,18,14]. This may be due to late treatment of genitourinary infections and a short cervix.

Having a history of preterm delivery was not statistically associated with PROM in our study. These results are contrary to those of Nkwabong, et al. Zhou, et al.; Lin, et al., respectively in Cameroon, China and Thailand, who found a significant association with risks 2; 3 and 3 times elevated between a history of preterm birth and PROM after bivariate analysis[10,5,19]. Indeed, certain cases of premature birth are linked to cervical incompetence. Rapid dilation of the internal os of the cervix can lead to protrusion of the fetal membranes into the cervical canal and can promote premature delivery. This difference could be explained by a difference in our sample size.

5. Conclusion

Residence in a rural area in Dschang and malaria during pregnancy are risk factors for PROM in our context while having 4 or more prenatal consultations was a protective factor for PROM. Strategies to prevent membrane rupture should focus on these identified factors.

6. Authors Contributions

- Fouedjio Jeanne Hortence wrote the manuscript.
- Taguimnang Zambou Ornéla Rachel wrote the protocol and analyzed the data.
- Fouogue Tsuala Jovanny collected the data.
- Fouelifack Ymele Florent and Kenfack Bruno corrected the manuscript.

Authors have no conflict of interest

Fundings statement: this research was funded by the authors

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