



ORIGINAL ARTICLE

## Preterm premature rupture of the fetal membranes: association with sociodemographic factors and maternal genitourinary infections ☆,☆☆

Arnildo A. Hackenhaar<sup>a,\*</sup>, Elaine P. Albernaz<sup>a</sup>, Tânia M. V. da Fonseca<sup>b</sup>

<sup>a</sup> Post-graduation program in Health and Behaviour, Universidade Católica de Pelotas, Pelotas, RS, Brazil

<sup>b</sup> Health Sciences, Universidade Federal do Rio Grande, Rio Grande, RS, Brazil

Received 9 May 2013; accepted 10 June 2013

Available online 29 October 2013

### KEYWORDS

Premature rupture of fetal membranes;  
Premature;  
Social conditions;  
Maternal age;  
Female urogenital disorders

### Abstract

**Objective:** this study aimed to investigate the incidence of premature rupture of fetal membranes in preterm singleton pregnancies and its association with sociodemographic factors and maternal self-reported genitourinary infections.

**Methods:** this was a population-based cross-sectional study, which included all mothers of newborns of singleton deliveries that occurred in 2010, with birth weight  $\geq 500$  grams, who resided in the city of Rio Grande. Women were interviewed in the two maternity hospitals. Cases were women who had lost amniotic fluid before hospitalization and whose gestational age was less than 37 weeks. Statistical analysis was performed by levels to control for confounding factors using Poisson regression.

**Results:** of the 2,244 women eligible for the study, 3.1% had preterm premature rupture of fetal membranes, which was more frequent, after adjustment, in women of lower socioeconomic status, (prevalence ratio [PR] = 1.94), with lower level of schooling (PR = 2.43), age > 29 years (PR = 2.49), and smokers (PR = 2.04). It was also associated with threatened miscarriage (PR = 1.68) and preterm labor, (PR = 3.40). There was no association with maternal urinary tract infection or presence of genital discharge.

**Conclusions:** the outcome was more common in puerperal women with lower level of schooling, lower socioeconomic status, older, and smokers, as well as those with a history of threatened miscarriage and premature labor. These factors should be considered in the prevention, diagnosis, and therapy approach.

© 2013 Sociedade Brasileira de Pediatria. Published by Elsevier Editora Ltda. All rights reserved.

☆ Please cite this article as: Hackenhaar AA, Albernaz EP, Fonseca TM. Preterm premature rupture of the fetal membranes: association with sociodemographic factors and maternal genitourinary infections. J Pediatr (Rio J). 2014;90:197–202.

☆☆ Study conducted at Faculdade de Medicina of the Universidade Federal do Rio Grande

\* Corresponding author.

E-mail: [arnildo@vetorial.net](mailto:arnildo@vetorial.net) (A.A. Hackenhaar).

**PALAVRAS-CHAVE**

Ruptura prematura de membranas fetais;  
Prematuro;  
Condições sociais;  
Idade materna;  
Doenças urogenitais femininas

## Ruptura prematura das membranas fetais pré-termo: associação com fatores sociodemográficos e infecções geniturinárias maternas

**Resumo**

**Objetivo:** o objetivo deste estudo foi verificar a ocorrência da ruptura prematura das membranas fetais pré-termo em gestações únicas e sua associação com fatores sociodemográficos maternos e infecções geniturinárias autorreferidas.

**Métodos:** estudo transversal de base populacional onde foram incluídas todas as mães dos recém-nascidos dos partos únicos ocorridos no ano de 2010, com peso ao nascer igual ou superior a 500 gramas, residentes no município. As puérperas foram entrevistadas nas duas maternidades da cidade. Foram considerados casos as gestantes que perderam líquido amniótico antes da internação hospitalar e cujo tempo de gestação fosse inferior a 37 semanas. Foi realizada análise estatística por níveis, para controle de fatores de confusão por meio da regressão de Poisson.

**Resultados:** das 2.244 mulheres elegíveis para o estudo, 3,1% apresentaram ruptura prematura das membranas fetais pré-termo, a qual foi mais frequente, após ajuste, nas mulheres de menor nível econômico, razão de prevalência (RP) de 1,94, menor escolaridade, RP de 2,43, com idade superior a 29 anos, RP de 2,49 e tabagistas, RP de 2,04. Também esteve relacionada com ameaça de aborto, RP de 1,68, e de trabalho de parto pré-termo, RP de 3,40. Não houve associação com infecção urinária materna ou presença de corrimento genital.

**Conclusões:** o desfecho foi mais frequente nas puérperas com menor escolaridade, mais pobres, mais velhas e tabagistas, assim como naquelas com histórico de ameaça de abortamento e trabalho de parto prematuro. Estes fatores devem ser considerados na sua abordagem preventiva, diagnóstica e terapêutica.

© 2013 Sociedade Brasileira de Pediatria. Publicado por Elsevier Editora Ltda. Todos os direitos reservados.

**Introduction**

Preterm premature rupture of fetal membranes (PPROM) is defined as loss of amniotic fluid before the onset of labor in pregnancies of less than 37 weeks.<sup>1</sup> This condition occurs in approximately 3% of pregnancies.<sup>2</sup>

PPROM is associated with maternal and fetal pathologies, contributing to the birth of premature infants.<sup>3</sup> The longer the time elapsed between rupture and delivery, the greater the chance of infection for both mother and fetus.<sup>4</sup>

The most common cause of PPRM is spontaneous, which has a multifactorial etiology. It may be related to a structural defect in the membranes due to collagen deficiency or malformation, to the weakening of the membranes due to enzymatic destruction in inflammatory or infectious processes, and to sac exposure due to isthmus-cervix incompetence. PPRM risk is increased if the mother has had previous occurrence of PPRM and low body mass index.<sup>5</sup> Its occurrence is also related to mechanical factors, such as twin pregnancies, due to distended uterine volume.<sup>6</sup> There is a hypothesis of the association between PPRM and genitourinary infections, but there is no consensus in this regard.

The available studies on PPRM in developed countries are case-control, and do not consider factors such as level of schooling and maternal age.<sup>7-9</sup> These factors are important when observing the increase in the number of infants born prematurely.<sup>10</sup>

The association between prematurity and PPRM indicates the need to investigate its occurrence in singleton pregnancies and its association with maternal socioeconomic factors and self-reported genitourinary infections, and

thus, to develop hypotheses for its occurrence and direct measures of disease prevention.

**Methods**

This was a population-based cross-sectional study. The sample included all mothers of newborns of singleton deliveries in 2010, with birth weight  $\geq 500$  g, whose mothers resided in Rio Grande, Brazil, and signed an informed consent. Mothers who did not live in Rio Grande, multiparous women, and those who refused to participate in the study were excluded.

Data were collected through a single, pre-coded, semi-open questionnaire by interviewers in the two maternity hospitals of the city during hospitalization in the first 72 hours after birth. The signs and symptoms present prior to hospitalization, such as loss of fluid, blood, or uterine contractions, were retrospectively evaluated. The occurrence of all maternal diseases that occurred during pregnancy and those prior to pregnancy, as well as data on sociodemographic status, were investigated.

PPROM was considered when the women had shown loss of amniotic fluid before hospitalization and had gestational age < 37 weeks. The gestational age variable was assessed based on the last menstrual period. When the date of last menstrual period was not recalled, the gestational age estimated by ultrasonography performed between the fifth and 20th week of pregnancy was used, followed by the method of Capurro<sup>11</sup> performed by the

**Table 1** Sociodemographic factors related to the occurrence of preterm premature rupture of fetal membranes. Rio Grande, Brazil, 2010.

Level 1 variables	n	PPROM (%)	Crude PR (95% CI)	p-value	Adjusted PR <sup>a</sup> (95% CI)	p-value
<i>Socioeconomic classification per score in tertiles</i>				0.001 <sup>b</sup>		0.010 <sup>b</sup>
First (poorest)	504	4.2	1.82 (1.26–2.61)		1.94 (1.27–2.97)	
Second	840	3.2	1.40 (0.99–1.98)		1.49 (1.03–2.17)	
Third (richest)	785	2.3	1.00		1.00	
<i>Mother's age (years)</i>				<0.001 <sup>c</sup>		<0.001 <sup>c</sup>
Less than 20	422	3.6	1.67 (1.15–2.41)		1.43 (0.96–2.14)	
20 to 29	1,172	2.1	1.00		1.00	
30 or older	650	4.6	2.16 (1.59–2.94)		2.49 (1.81–3.44)	
<i>Mother's schooling (years)</i>				0.005 <sup>b</sup>		0.035 <sup>b</sup>
Zero to eight	1,004	3.6	2.73 (1.41–5.50)		2.43 (1.20–4.89)	
Nine to 11	1,007	3.1	2.39 (1.21–4.74)		2.30 (1.11–4.77)	
12 or more	233	1.3	1.00		1.00	
<i>Ethnicity</i>				0.169 <sup>c</sup>		0.171 <sup>c</sup>
White	1,569	3.3	1.24 (0.91–1.69)		1.26 (0.92–1.73)	
Non-white	675	2.7	1.00		1.00	

CI, confidence interval; n, number of women; PR, prevalence ratio.

<sup>a</sup> Level 1 variables were adjusted to each other.

<sup>b</sup> Chi-squared test for linear trend.

<sup>c</sup> Chi-squared test for heterogeneity of proportions.

pediatrician. Socioeconomic classification was performed using the Brazilian economic classification criteria of the Brazilian Association of Research Companies, based on possession of items and the head of the family's level of schooling.<sup>12</sup> Skin color was observed by the interviewer.

Cases of self-reported urinary tract infection were considered in cases of symptomatic infections and asymptomatic bacteriuria, the latter detected during routine prenatal care.<sup>13</sup> Cases of self-reported genital discharge were considered, in which the women had a non-white vaginal discharge, associated with bad odor, itching, or dyspareunia.<sup>14</sup>

The missing values were not analyzed; 4.7% of the data on gestational age were unknown. The variable with the greatest amount of missing information was the socioeconomic level, due to the rate of 5.2% lack of data on the years of schooling of the child's father. The analyses had a significance level of 95%. Gestational age was used as reference to calculate sample size, obtaining a prevalence ratio of 1.6, considering the 10% occurrence rate of premature rupture of membranes in term pregnancies (85% in the study population), and 15% were added to the sample size to control for confounders. Thus, 2,231 interviews were required.

Multivariate analysis was based on the conceptual model for hierarchical levels,<sup>15</sup> and was performed using Poisson regression, controlling for confounding factors. Those variables that maintained a p-value  $\leq 0.20$  in the univariate analysis were included in the multivariable analysis. The study was approved by the Ethics Committee of Universidade Federal do Rio Grande (FURG).

## Results

A total of 2,355 women with singleton pregnancies were interviewed, of whom 18 refused to participate in the study; there were 51 losses by hospital discharge before 72 hours after birth. PPROM rate was 3.1%. This proportion was 23.6% in preterm pregnancies.

It was observed that 18.8% of the mothers were adolescents, 44.7% had eight years or less of schooling, 69.9% were white, and 20.1% were smokers. The occurrence of PPROM was higher in women of lower socioeconomic status, lower educational level, and those older than 29 years (Table 1).

Regarding maternal habits and diseases, after adjustment, the occurrence of PPROM was higher in women who had undergone treatment for threatened miscarriage and preterm labor during pregnancy, and among smokers (Table 2).

## Discussion

Infant mortality, especially when associated with the neonatal component<sup>16</sup> and the impact of prematurity on infant morbimortality, indicates a need for knowledge regarding the mechanisms related to PPROM, a risk factor for preterm birth.

In the studied population, 3.1% had PPROM. This proportion is consistent with that found in the literature.<sup>1,2</sup> This study identified a higher rate of PPROM in women of lower socioeconomic status and lower educational level. In women

**Table 2** Maternal diseases related to the occurrence of preterm premature rupture of fetal membranes. Rio Grande, Brazil, 2010.

Level 1 variables	n	PPROM (%)	Crude PR (95% CI)	p-value	Adjusted PR <sup>a</sup> (95% CI)	p-value
<i>Worked out of home during pregnancy</i>				0.581 <sup>b</sup>		
Yes	972	3.0	1.00			
No	1,272	3.2	1.08 (0.82–1.42)			
<i>Previous premature delivery</i>				0.002 <sup>b</sup>		0.232 <sup>b</sup>
Yes	2,033	2.9	1.00		1.00	
No	211	5.2	1.80 (1.24–2.60)		1.27 (0.86–1.88)	
<i>Previous miscarriage</i>				0.767 <sup>b</sup>		
No	1,939	3.0	1.00			
Yes	305	3.3	1.06 (0.72–1.56)			
<i>Threatened miscarriage</i>				0.004 <sup>b</sup>		0.019 <sup>b</sup>
No	2,100	3.0	1.00		1.00	
Yes	144	5.6	1.88 (1.23–2.88)		1.68 (1.09–2.60)	
<i>Smoked during pregnancy</i>				< 0.001 <sup>b</sup>		< 0.001 <sup>b</sup>
No	1,782	2.5	1.00		1.00	
Yes	447	5.8	2.36 (1.78–3.12)		2.04 (1.49–2.78)	
<i>Urinary infection during pregnancy</i>				0.250 <sup>b</sup>		
No	1,377	2.9	1.00			
Yes	849	3.4	1.18 (0.89–1.55)			
<i>Genital discharge during pregnancy</i>				0.263 <sup>b</sup>		
No	1,272	2.9	1.00			
Yes	972	3.4	1.17 (0.89–1.53)			
<i>Threatened preterm delivery</i>				< 0.001 <sup>b</sup>		< 0.001 <sup>b</sup>
No	2,044	2.5	1.00		1.00	
Yes	189	9.0	3.54 (2.58–4.85)		3.40 (2.44–4.73)	

CI, confidence interval; n, number of women; PR, prevalence ratio.

<sup>a</sup> Adjusted for first-level and second-level variables with  $p \leq 0.20$ .

<sup>b</sup> Chi-squared test for heterogeneity of proportions.

of lower socioeconomic level, the prenatal assistance is of poorer quality, as these women undergo a smaller number of consultations and have fewer laboratory tests,<sup>17</sup> which may contribute to the occurrence of this disease.

The association of PPROM in pregnant women aged > 29 years can be explained by endogenous changes in the fetus and its annexes, as fetal aneuploidy rates are higher with increasing maternal age.<sup>18</sup> Studies retrieved in the literature did not identify age as risk factor for this disease, as they paired PPROM cases with age-matched controls.<sup>7–9</sup>

Threatened miscarriage during pregnancy was associated with PPROM, which has also been observed in other studies.<sup>19,20</sup> There may be poor embryonic development in cases of PPROM. This study also demonstrated an association between maternal smoking and PPROM, similarly to the review study by Castles et al.<sup>21</sup>

The lack of association between PPROM and genitourinary infections during pregnancy in this study may be attributed to the treatment completion for these infections

by most women. Other studies have also identified higher values of mediators of infectious processes or bacteria after PPROM.<sup>22–24</sup>

There is an association between PPROM and previous treatment for threatened preterm labor. The presence of uterine contractions during threatened preterm labor can weaken the amniotic membrane. Another study has also found an association between the presence of early contractions during pregnancy and PPROM.<sup>25</sup>

The main limitation of this study was its cross-sectional design, which detects only an association and does not infer causality. Thus, the intention of the study was to raise new hypotheses about the occurrence of PPROM. The use of a recall questionnaire with self-reported information is the method of choice for cross-sectional studies that seek an association. Other studies on premature rupture of the fetal membranes<sup>26</sup> and urinary and genital tract infections<sup>27</sup> also used self-reported information. Another limitation is the non-detection by the study of cases of asymptomatic genital

infection. However, this type of infection appears to have no association with prematurity or PPRM. For instance, screening for *Streptococcus* group B is recommended after the 35th week of gestation.<sup>28</sup>

Maternal and fetal infection does not appear to be prior to the occurrence of PPRM, but rather its consequence. The risk of PPRM maternal and fetal infection could be increased by a longer time of rupture prior to birth in late preterm gestations (34 to 37 weeks) when compared to term pregnancies.<sup>29</sup>

The associations observed indicate the importance of prenatal care quality, especially for pregnant women of lower socioeconomic status. The fight against maternal smoking, a known risk factor for many health problems in childhood, should be one of the goals in health promotion during pregnancy. It is recommended that studies on PPRM stratify the data by maternal age. The evidence of increased risk of PPRM in pregnant women aged > 29 years demonstrate the importance of identifying risk factors and their inclusion in prenatal care and childbirth protocols.

## Funding

Health Secretariat of the city of Rio Grande - CNPq 2009 Universal Edict.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. Modena AB, Kaihura C, Fieni S. Prelabour rupture of the membranes: recent evidence. *Acta Biomed.* 2004;75:5–10.
2. Waters TP, Mercer B. Preterm PROM: prediction, prevention, principles. *Clin Obstet Gynecol.* 2011;54:307–12.
3. Smith G, Rafuse C, Anand N, Brennan B, Connors G, Crane J, et al. Prevalence, management, and outcomes of preterm prelabour rupture of the membranes of women in Canada. *J Obstet Gynaecol Can.* 2005;27:547–53.
4. Roveran V, Tedesco JJ, Forte WC, Yamano LM, Rodrigues LP, Vazquez ML, et al. Valores séricos de imunoglobulinas e dos componentes do complemento em gestantes com ruptura prematura de membranas. *Rev Bras Ginecol Obstet.* 2007;29:175–80.
5. Caughey AB, Robinson JN, Norwitz ER. Contemporary diagnosis and management of preterm premature rupture of membranes. *Rev Obstet Gynecol.* 2008;1:11–22.
6. Belfort P. Amniorrexe prematura. In: Rezende J, editor. *Obstetrícia.* 10<sup>th</sup> ed. Guanabara Koogan: Rio de Janeiro; 2007. p. 918–28.
7. Harger JH, Hsing AW, Tuomala RE, Gibbs RS, Mead PB, Eschenbach DA, et al. Risk factors for preterm premature rupture of fetal membranes: a multicenter case-control study. *Am J Obstet Gynecol.* 1990;163:130–7.
8. Ekwo EE, Gosselink CA, Woolson R, Moawad A. Risks for premature rupture of amniotic membranes. *Int J Epidemiol.* 1993;22:495–503.
9. Hadley CB, Main DM, Gabbe SG. Risk factors for preterm premature rupture of the fetal membranes. *Am J Perinatol.* 1990;7:374–9.
10. Barros FC, Victora CG, Matijasevich A, Santos IS, Horta BL, Silveira MF, et al. Preterm births, low birth weight, and intrauterine growth restriction in three birth cohorts in Southern Brazil: 1982, 1993 and 2004. *Cad Saude Publica.* 2008;24:390–8.
11. Capurro H, Konichezky S, Fonseca D, Caldeyro-Barcia R. A simplified method for diagnosis of gestational age in the newborn infant. *J Pediatr.* 1978;93:120–2.
12. Associação Brasileira de Empresas de Pesquisa (ABEP). Critério de Classificação Econômica Brasil. 2008. [cited 25 Oct 2009]. Available from: <http://www.abep.org/novo/Content.aspx?ContentID=301>
13. Brasil, Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. Área Técnica de Saúde da Mulher. Pré-natal e puerpério: atenção qualificada e humanizada – manual técnico. Brasília: Ministério da Saúde; 2005 (Série A. Normas e Manuais Técnicos).
14. Cesar JA, Mendoza-Sassi RA, González-Chica DA, Menezes EH, Brink G, Pohlmann M, et al. Prevalência e fatores associados à percepção de ocorrência de corrimento vaginal patológico entre gestantes. *Cad Saude Pública.* 2009;25:2705–14.
15. Victora CG, Huttly SR, Fuchs SC, Olinto MT. The role of conceptual frameworks in epidemiological analysis: A hierarchical approach. *Int J Epidemiol.* 1997;26:224–7.
16. de Almeida MF, Guinsburg R, Martinez FE, Procianny RS, Leone CR, Marba ST, et al. Perinatal factors associated with early deaths of preterm infants born in Brazilian network on neonatal research centers. *J Pediatr (Rio J).* 2008;84:300–7.
17. Gonçalves CV, Cesar JA, Mendoza-Sassi RA. Qualidade e equidade na assistência à gestante: um estudo de base populacional no Sul do Brasil. *Cad Saude Publica.* 2009;25:2507–16.
18. Forabosco A, Percesepe A, Santucci S. Incidence of non-age-dependent chromosomal abnormalities: a population-based study on 88965 amniocenteses. *Eur J Hum Genet.* 2009;17:897–903.
19. Dadkhah F, Kashanian M, Eliasi G. A comparison between the pregnancy outcome in women both with or without threatened abortion. *Early Hum Dev.* 2010;86:193–6.
20. Weiss JL, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Threatened abortion: a risk factor for poor pregnancy outcome, a population-based screening study. *Am J Obstet Gynecol.* 2004;190:745–50.
21. Castles A, Adams K, Melvin CL, Kelsh C, Boulton ML. Effects of smoking during pregnancy Five meta-analyses. *Am J Prev Med.* 1999;16:208–15.
22. Poletini J, Vieira EP, Santos MP, Peraçoli JC, Witkin SS, Silva MG. Interleukin 18 messenger RNA and proIL-18 protein expression in chorioamniotic membranes from pregnant women with preterm prelabour rupture of membranes. *Eur J Obstet Gynecol Reprod Biol.* 2012;161:134–9.
23. Roveran V, Silva MA, Yamano L, Rodrigues LP, Vasquez ML, Piato S. Expressão local do fator de necrose tumoral alfa na ruptura prematura de membranas. *Rev Bras Ginecol Obstet.* 2009;31:249–53.
24. Witt A, Berger A, Gruber CJ, Petricevic L, Worda AP, Husslein P. Increased intrauterine frequency of Ureaplasma urealyticum in women with preterm labor and preterm premature rupture of the membranes and subsequent cesarean delivery. *Am J Obstet Gynecol.* 2005;193:1663–9.
25. Mercer BM, Goldenberg RL, Meis PJ, et al. The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing: the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol.* 2000;183:738–45.
26. Whitehea NS, Callaghan W, Johnson C, Williams L. Racial, ethnic, and economic disparities in the prevalence of pregnancy complications. *Matern Child Health J.* 2009;13:198–205.
27. Feldkamp ML, Reefhuis J, Kucik J, Krikov S, Wilson A, Moore CA, et al. Case-control study of self reported genitourinary

- infections and risk of gastroschisis: findings from the National Birth Defects Prevention Study, 1997-2003. *BMJ*. 2008;336:1420-3.
28. Cagno KC, Pettit JM, Weiss BD. Prevention of perinatal group B streptococcal disease: updated CDC guideline. *Am Fam Physician*. 2012;86:59-65.
29. de Araújo BF, Zatti H, Madi JM, Coelho MB, Olmi FB, Canabarro CT. Analysis of neonatal morbidity and mortality in late-preterm newborn infants. *J Pediatr (Rio J)*. 2012;88:259-66.