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ORIGINAL RESEARCH ARTICLE

Risk factors associated with shortened latency before delivery in outpatients managed for preterm prelabor rupture of membranes

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Abstract

Introduction: Preterm prelabor rupture of membranes (PPROM) occurs in 3% of pregnancies and is the main cause (~30%) of premature delivery. Home care seems to be a safe alternative for the management of patients with PPROM, who have a longer latency than those with PPROM managed with conventional hospitalization. We aimed to identify the risk factors associated with a shortened latency before delivery in women with PPROM managed as outpatients.

Material and methods: The design was a retrospective cohort study and the setting was a Monocentric Tertiary centre (Lille University Hospital, France) from 2009 to 2018. All consecutive patients in home care after PPROM at 24–36 weeks were included. For the main outcome measure we calculated the latency ratio for each patient as the ratio of the real latency period to the expected latency period, expressed as a percentage. The risk factors influencing this latency ratio were evaluated.

Results: A total of 234 patients were managed at home after PPROM. Mean latency was 35.5 ± 20.7 days, corresponding to an 80% latency ratio. In 196 (83.8%) patients the length of home care was more than 7 days. A lower latency ratio was significantly associated with oligohydramnios ($p < 0.001$), gestational age at PPROM ($p = 0.006$), leukocyte count at PPROM more than 12×10^9/L ($p = 0.025$), and C-reactive protein concentration more than 5 mg/L at 7 days after PPROM ($p = 0.046$). Cervical length was not associated with a lower latency ratio.

Conclusions: Women with PPROM managed with home care are stable. The main risk factor associated with a reduced latency is oligohydramnios. Outpatients with oligohydramnios should be informed of the probability of a shortened latency period.

KEYWORDS
home care, latency, oligohydramnios, prematurity, preterm delivery, preterm prelabor rupture of membranes

Abbreviations: CRP, C-reactive protein; PPROM, preterm prelabor rupture of membranes.

1 | INTRODUCTION

Preterm prelabor rupture of membranes (PPROM) occurs in about 3% of pregnancies and is the main cause (~30%) of premature deliveries.[1–4] PPROM is associated with important levels of neonatal morbidity and mortality.[5,6] The risks of PPROM are those associated mainly with prematurity: respiratory distress, sepsis, intraventricular hemorrhage, and necrotizing enterocolitis.[7,8] The risks of prolonged latency (the time between PPROM and delivery) include intrauterine infection, placental abruption, and increased risk of neurodevelopmental impairment,[9] but these risks decrease with increasing gestational age at birth.[10] The risk of intrauterine infection increases with prolonged latency, and studies have reported a benefit of extending the pregnancy to at least 32 weeks of gestation.[6,11] The current practice for treating PPROM is expectant management and induction of labor around 37 weeks of gestation.[12–14] The known factors that can influence the duration of the latency period include cervical length,[15] presence of cervical funneling,[16] amniotic fluid volume,[15,17,18] and gestational age at PPROM.[17–19] These factors have been studied in inpatients and their effects have been measured during the first 7 days after PPROM.

The management of PPROM at home is used in some countries.[13,14] Since 1993, several studies have shown its safety in selected patients[20–29] and its positive effect on increasing the latency period.[30,31] The inclusion criteria vary between studies, but no studies have identified the factors that can influence the latency period as identified in inpatients. The outpatient and inpatient populations may differ because home-care patients have passed the acute phase, which involves hospital management.

The main objective of this study was to identify the risk factors for shortened latency in outpatients managed with home care after PPROM. Our secondary objective was to identify the variable impact of these factors, in subgroups according to term at PPROM onset.

Key message

In a large retrospective cohort study we describe which risk factors lower the latency in patient with preterm prelabor rupture of membranes in home-care management, with a new definition of latency: the latency ratio.

2 | MATERIAL AND METHODS

This was a retrospective monocentric (Lille, France) study from 2009 to 2018 in which all women with PPROM who had been managed as an outpatient were included. The eligibility criteria for home-care management were singleton pregnancy, gestational age between 24 and 35 weeks, absence of intrauterine infection, clinical stability on day 5 after PPROM, cervical dilatation less than 3 cm, and the patient's home located within a 30 minute drive from our center. Patient consent was obtained after information was given to the patient by the obstetrician and home-care service midwife. An appropriate understanding of the situation, as well as the absence of any language barrier were required before the patient was discharged from the hospital after PPROM.

Before 2016, neither the fetal presentation nor the amount of amniotic fluid changed the patient's eligibility for home-care management. Since 2017, we have used three assessment criteria at the time of PPROM to assess the eligibility of each patient for outpatient management: gestational age (>26 weeks or <26 weeks), fetal presentation (cephalic or non-cephalic), and the amount of amniotic fluid (normal or oligohyramnios). The combination of these three unfavorable criteria was an indication for conventional hospitalization.[21] Other exclusion criteria were fetal malformation, multiple pregnancy, delay between the start of home care and labor induction less than 7 days, medically induced abortion, or in utero death. Protocol of follow up was described in previous publications.[21,30]

2.1 | Diagnosis and follow up of PPROM

PPROM was diagnosed based on the visualization of amniotic fluid loss and/or the Actim®PROM test results (Medix Biochemica, Finland). The initial examination included a blood sample with a complete blood count, C-reactive protein (CRP) concentration, and vaginal and urinary bacteriological samples. Examination of the cervix by vaginal touch or ultrasound was recommended only in patients reporting painful contractions. Obstetric ultrasound with fetal biometry and amniotic fluid evaluation were routinely performed. Oligohydramnios was defined as a maximum single vertical pocket less than 20 mm. The position of the placenta was monitored during the ultrasound, and the placenta was considered to have a low implantion when its lower edge was within 20 mm of the internal os of the cervix.

Initial management included hospitalization, antenatal corticosteroid (two intramuscular injections of 12 mg betamethasone, 24 hours apart),[13,32] and prophylactic antibiotics (amoxicillin 1 g every 8 hours for 7 days). Tocolysis was used only in the presence of uterine contractions. After 5–7 days of hospitalization, home care was proposed for patients who met the eligibility criteria. A blood count was repeated 7 days after the rupture and included a complete blood count and CRP concentration. The follow up of outpatients comprised visits by a midwife three times a week. Measurement of blood count and CRP concentration, bacteriological examination of the urine, and a vaginal swab were performed once a week. Every 15 days, a consultation at our center was organized for obstetric ultrasound follow up to assess fetal growth and amniotic fluid volume.

2.2 | Risk factors and outcome

The latency period was defined as the number of days between PPROM and delivery. Each patient was assigned a target term,

which was then defined as the time of induction because of PPROM: 36 weeks until 2016 and 37 weeks from 2017. If labor was induced for a reason unrelated to PPROM (eg preeclampsia, severe intrauterine growth retardation), the target term was set as the day of labor induction. For each patient, we calculated the following variables.

- The expected latency, which corresponded to the number of days between the PPROM date and the target term.
- The real latency, which corresponded to the number of days between the PPROM date and delivery.

We then calculated the latency ratio as the real latency divided by the expected latency, expressed as a percentage.

The main outcome measures were the following potential risk factors for shortened latency and their effects on the latency ratio in PPROM outpatients: smoking status, parity, body mass index, gestational age at PPROM, fetal presentation, amniotic fluid volume, low-lying placenta, cervical sonographic length, leukocyte count, CRP concentration, and bacteriological sample results. The secondary outcome measures were variables related to risk factors in different subgroups classified according to the PPROM onset. We also analyzed whether the same risk factors were associated with a latency greater than 7 days after the beginning of home care.

2.3 | Statistical analyses

Categorical variables are expressed as number (percentage). Continuous variables are expressed as mean (standard deviation) or median (interquartile range). The normality of the data distribution was assessed using histograms and the Shapiro–Wilk test. We first used univariate analysis to examine the associations between risk factors and the latency ratio using the Mann–Whitney *U* test for categorical risk factors and Spearman's rank correlation coefficient for continuous or ordinal risk factors. We also examined the univariate association of risk factors with latency duration treated as a binary variable (latency <7 days after home care vs ≥7 days) using the chi-squared test or Fisher's exact test (when the expected cell frequency was below 5) for categorical risk factors, the Cochran–Armitage trend test for ordinal risk factors, and the Mann–Whitney *U* test for continuous risk factors. Finally, we evaluated the impact of risk factors on the latency ratio according to the gestational phase at PPROM (PPROM term) using nonparametric analysis of covariance for rank-transformed data. This analysis included the risk factors, term of PPROM, and the interaction of risk factor × PPROM term as independent variables. Statistical analyses were performed with a two-tailed α level of 0.05. Data were analyzed using SAS software, version 9.4 (SAS Institute).

2.4 | Ethical approval

This study was approved by the French National Commission on Informatics and Liberty (reference DEC16-210) and by the French Ethics Committee for Research in Gynecology and Obstetrics. (CEROG 2020-OBST-1003), (January 15, 2021).

3 | RESULTS

Among the 370 patients in home care during the study period, 255 were included and 234 were analyzed in this study. Ten patients were excluded because the delay between hospital discharge and induction of labor was less than 7 days, three patients because of medical termination of pregnancy, and eight patients because their records were missing or the missing data were important. The data from 133 patients have already been used in previously published articles.[21,30]

The patient characteristics are presented in Table 1. The mean maternal age was 28.8 years, and 106 patients (45%) were nulliparous. Twelve patients (5%) had a history of PPROM and 24 (10%) had a history of prematurity. The obstetric complications when PPROM was diagnosed were as follows: intrauterine growth restriction in 26 patients (11%), premature labor in 29 (12%) patients, and low-lying placenta in 26 (11%) patients.

The same percentages of patients were diagnosed with PPROM in the three gestational periods 24–28 weeks of gestation, 28–32 weeks of gestation, and >32 weeks of gestation (Table 1). About one-third of patients exhibited a biological inflammatory syndrome and about one-fifth had a positive bacteriological sample at admission for PPROM. The cervical length at admission was less than 25 mm in 41/120 (34%) patients. Oligohydramnios was present in 50 (21%) patients.

The mean theoretical latency after PPROM was 45.2 ± 21.3 days and the mean observed latency after PPROM was 35.5 ± 20.7 days. This corresponded to a latency ratio of 80% (±27%). In 196 (83.8%) patients, the duration of home care was more than 7 days.

The associations between the measured variables and the latency ratio are shown in Table 2. Oligohydramnios ($p < 0.0001$), leukocyte count more than 12×10^9/L at PPROM ($p = 0.025$), and CRP concentration more than 5 mg/L at 7 days after PPROM ($p = 0.046$) were associated with a lower latency ratio. A low-lying placenta was associated with a higher latency ratio ($p = 0.028$). The PPROM term (analyzed as three categories: 24–28, 28–32, and >32 weeks of gestation) correlated significantly with the latency ratio ($r = 0.18$, $p = 0.006$). Higher multiparity was associated with a lower latency ratio ($r = -0.15$, $p = 0.002$). Body mass index did not correlate with the latency ratio ($p = 0.11$).

Figure 1 shows the subgroup analysis according to the PPROM term. In this analysis, a significantly different result means that the risk factor modifies the latency ratio differently between subgroups. The impact of oligohydramnios on the latency ratio differed according to the PPROM term ($p = 0.007$) (Figure 1). The median latency ratio was ~40% for oligohydramnios before 32 weeks of gestation but was 100% after 32 weeks of gestation. The other parameters (leukocyte count >12×10^9/L and CRP >5 mg/L at PPROM) were not significant in this analysis.

TABLE 1 Characteristics of patients

A. Characteristics of the population ($n = 234$)	
Maternal age (years)	28.8 ± 5.9
Smoking	50 (21.7)
BMI (kg/m^2)	24.0 ± 5.6
Nulliparous	106 (45.5)
Obstetric medical history	
Cesarean section	32 (13.7)
Preterm premature rupture of membranes	12 (5.1)
Prematurity	24 (10.3)
Fetal pathology	
Intrauterine growth restriction	26 (11.1)
Fetal malformation	11 (4.7)
Obstetric pathology	
Premature labor	29 (12.4)
Gestational diabetes	21 (9)
Low-lying placenta	26 (11.1)
Invasive procedures	7 (3)
B. Patient characteristics at the time of PPROM	
Gestational age (weeks)	29.8 ± 3.2
24–28	78 (33.3)
28–32	80 (34.2)
>32	76 (32.5)
Inflammatory biological syndrome at admission	
Leukocyte count >12 000/mm^3	73/225 (32.4)
CRP >5 mg/L	73/229 (31.9)
Inflammatory biological syndrome at 7 days	
Leukocyte count >12 000/mm^3	63/181 (34.8)
CRP >5 mg/L	55/210 (26.2)
Positive bacteriological sample at admission	
Vaginal sample	26/229 (11.4)
Urine sample	24/228 (10.5)
≥1 positive sample at admission	45/228 (19.7)
Sonographic cervical length*	
>25 mm	79 (65.8)
15–25 mm	27 (22.5)
<15 mm	14 (11.7)
Fetal presentation	
Cephalic	175 (74.8)
Breech	48 (20.5)
Transverse	11 (4.7)
Oligohydramnios	50 (21.4)
Low-lying placenta	26 (11.1)

Note: The data are presented as number (%) or mean ± standard deviation.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; PPROM, preterm prelabor rupture of membranes.

*Missing data: 114.

TABLE 2 Associations between risk factors and the latency ratio (%)

	N	Value	*p*
Smoking			0.5
No	180	100 (61–100)	
Yes	50	97 (63–100)	
Parity			0.12
Nulliparous	106	100 (63–100)	
Multiparous	127	96 (55–100)	
Leukocyte count at PPROM			0.025
≤12 × 10^9/L	157	100 (66–100)	
>12 × 10^9/L	73	93 (49–100)	
CRP at PPROM			0.075
≤5 mg/L	156	100 (68–100)	
>5 mg/L	73	82 (52–100)	
Bacteriological sample at PPROM			0.084
Both sterile	183	100 (65–100)	
≥1 positive	45	93 (46–100)	
Fetal presentation			0.5
Cephalic	175	100 (60–100)	
Non-cephalic	59	98 (60–100)	
Amniotic fluid			<0.001
Normal	184	100 (71–100)	
Oligohydramnios	50	62 (33–100)	
Leukocyte count at 7 days			0.092
≤12 × 10^9/L	118	100 (69–100)	
>12 × 10^9/L	63	100 (46–100)	
CRP at 7 days			0.046
≤5 mg/L	155	100 (67–100)	
>5 mg/L	55	81 (53–100)	
Invasive procedures			NA
No	227	100 (61–100)	
Yes	7	78 (34–100)	
Scarred uterus			0.14
No	202	100 (63–100)	
Yes	32	82 (41–100)	
Low-lying placenta			0.028
No	208	100 (57–100)	
Yes	26	100 (96–100)	
Cervical length			0.57
≥25 mm	79	100 (49–100)	
<25 mm	41	100 (75–100)	
Term at the time of PPROM	234	0.18	0.006
Parity	233	−0.15	0.022
BMI	101	−0.16	0.11

Note: The data are presented as the median (interquartile range) for categorical variables and Spearman correlation coefficient for continuous variables.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; NA, not applicable; PPROM, preterm prelabor rupture of membranes.

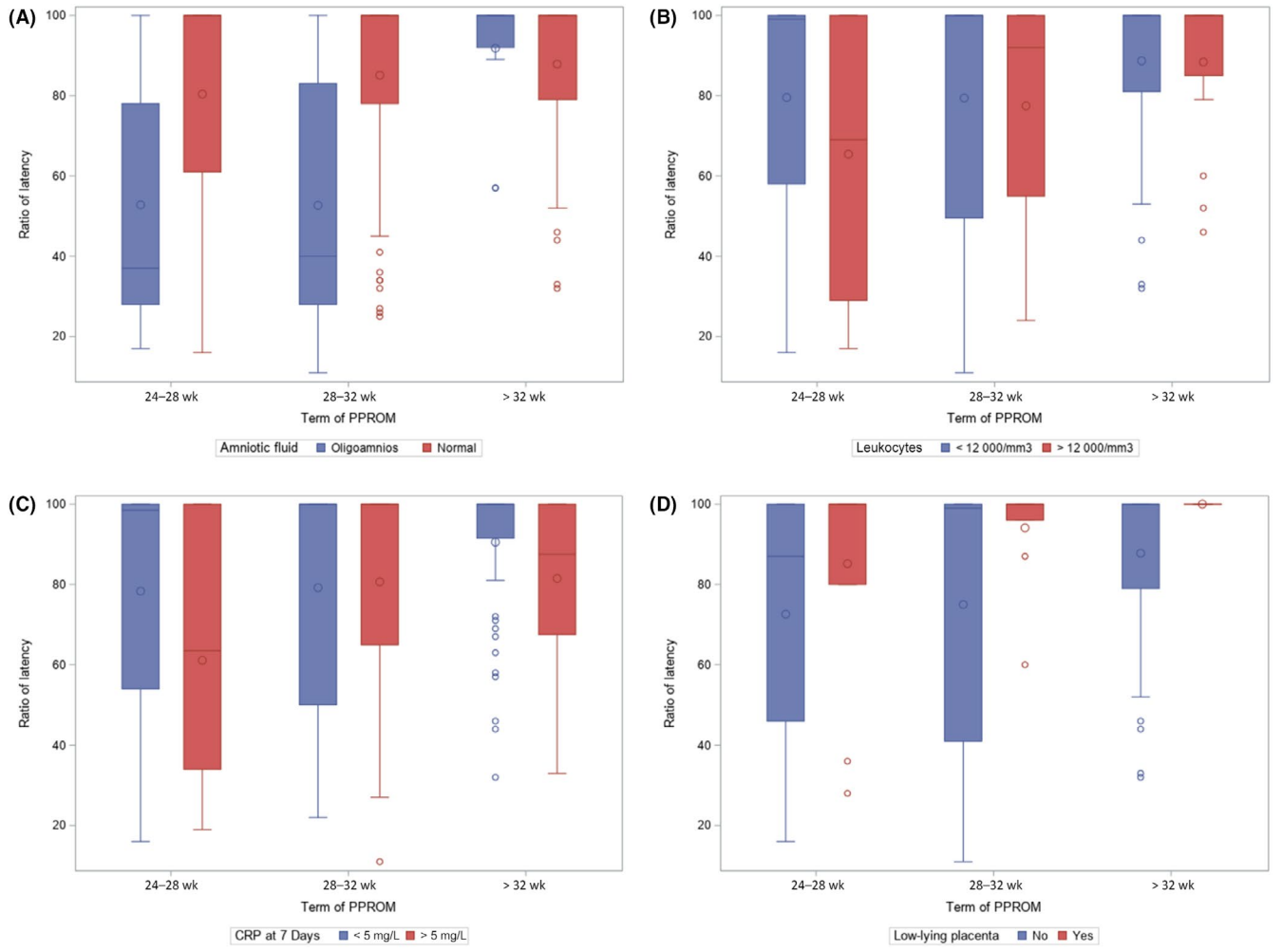

FIGURE 1 Latency ratio according to the term at the time of preterm prelabor rupture of membranes (PPROM). The pairs of boxes represent the repartition of the ratio of latency in the three sub-groups of term (before 28 weeks, 28–32 weeks, and >32 weeks). The boxes represent the Q1 to Q3 range, and the whiskers are delimiting 1.5 × Q1 and 1.5 × Q3. (A) Association with oligohydramnios ($p = 0.0072$). Blue: oligohydramnios; Red: normal amniotic fluid. (B) Association with leukocyte count >12 × 10^9/L at PPROM ($p = 0.63$). Blue: leukocytes <12 × 109/L; Red: leukocytes >12 × 109/L. (C) Association with day 7 C-reactive protein (CRP) >5 mg/L ($p = 0.23$). Blue: CRP at 7 days <5 mg/L; Red: CRP at 7 days >5 mg/L. (D) Associations with low-lying placenta ($p = 0.93$). Blue: normally located placenta; Red: low insertion of placenta.

Sixteen percent (38/234) had a latency after home care of 7 days or less (Table 3). Gestational age at PPROM was the only factor associated with a latency of 7 days or less, with a higher risk for PPROM occurring at a later term of pregnancy ($p = 0.004$).

4 | DISCUSSION

Previous studies have evaluated the risk factors associated with the latency period after PPROM in inpatients. In this study of the risk factors in outpatients, we found that oligohydramnios, leukocyte count at PPROM, and CRP concentration at 7 days after PPROM were associated with a lower latency ratio. In this sample population, cervical length was not associated with a shortened latency ratio.

The main factor associated with a shortened latency ratio was oligohydramnios, as described for inpatients. The results in the literature are concordant on this issue. In a series of 204 patients, Ekin et al. reported an increased risk of latency of less than 72 hours in patients with oligohydramnios.[17] Mehra et al. confirmed this finding in 106 PPROM patients and found that an amniotic fluid index below 5 cm independently predicted delivery within 7 days.[15] Similarly, using a Cox proportional-hazards model in a series of 417 PPROM patients, Melamed et al. found a shorter latency in patients with oligohydramnios.[18] In a previous study of 187 women with PPROM managed as outpatients in our center, oligohydramnios was one of the three criteria that were significantly associated with the risk of severe complications, which was defined as the occurrence of one of the following events: fetal death, placental abruption, umbilical cord prolapse, delivery outside a maternity hospital, or neonatal death.[21] Taken together, these findings suggest that both inpatients and outpatients with oligohydramnios should be informed of the probability of a shortened latency period.

TABLE 3 Risk factors classified according to latency ≤7 days and >7 days of home care after PPROM

	Latency ≤7 days *N* = 38	Latency >7 days *N* = 196	*p*
Smoking	7 (19.4)	43 (22.2)	0.72
Nulliparous	19 (50.0)	87 (44.6)	0.54
Leukocyte count at PPROM >12 000/mm^3	11 (30.6)	62 (32.8)	0.79
CRP at PPROM >5 mg/L	14 (37.8)	59 (30.7)	0.40
Bacteriological sample at PROMM (≥1 positive)	11 (30.6)	34 (17.7)	0.076
Cephalic fetal presentation	31 (81.6)	144 (73.5)	0.29
Amniotic fluid (oligohydramnios)	12 (31.6)	38 (19.4)	0.093
Leukocyte count at 7 days >12 000/mm^3	11 (37.9)	52 (34.2)	0.70
CRP at 7 days >5 mg/L	8 (22.9)	47 (26.9)	0.62
Invasive procedures	0 (0.0)	7 (3.6)	NA
Scarred uterus	6 (15.8)	26 (13.3)	0.68
Low-lying placenta	1 (2.6)	25 (12.8)	0.093
Cervical length (sonographic) <25 mm	8 (42.1)	33 (32.7)	0.43
Term at the time of PPROM (weeks of gestation)			0.004
24–28	5 (13.2)	73 (37.2)	
28–32	15 (39.5)	65 (33.2)	
>32	18 (47.4)	58 (29.6)	

Note: The data are presented as frequency (percentage).

Abbreviations: BMI, body mass index; CRP, C-reactive protein; NA, not applicable; PPROM, preterm prelabor rupture of membranes.

Other factors examined in our study were the presence of a biological inflammatory syndrome, leukocyte count at PPROM, and CRP concentration at 7 days. Ryu et al. reported that a high CRP concentration was an independent risk factor for delivery within 3 days in 72 PPROM patients.[33] Asadi et al. found that maternal serum CRP concentration was a more accurate predictor of chorioamnionitis than procalcitonin concentration and leukocyte count in 75 women with PPROM.[34] Stepan et al. reported that CRP concentration was higher in women with microbial invasion of the amniotic cavity and histological chorioamnionitis in a large cohort of 386 PPROM women. However, this association was observed only for women whose CRP concentration was in the 95th centile and whose PPROM was before 32 weeks of gestation, and the sensitivity of 15% was low.[35] Musilova et al. reported a CRP cut-off value of 17.5 mg/L as best for identifying microbial invasion of the amniotic cavity and intra-amniotic inflammation, with a sensitivity of 47% and a specificity of 96%, in a cohort of 287 PPROM patients.[36] Overall, despite the low sensitivity, CRP concentration seems to be a predictor of intra-amniotic inflammation, which may be responsible for shortening the latency.

A positive bacteriological sample was not related to the latency ratio in our population. We found only a trend in the 24–28 weeks of gestation group, with an average latency ratio of 64% in those with a positive sample vs 99% if all samples are sterile. In the same way, Zilberman et al. reported that endocervical colonization with group B streptococcus did not affect the latency period or increase the risk of intra-amniotic infection in 177 PPROM patients studied between 23 and 34 weeks of gestation.[37] Another possible explanation is the efficacy of the antibiotic treatment. In a large Cochrane meta-analysis of 22 trials involving PPROM patients before 37 weeks of gestation, Kenyon et al. reported that antibiotic treatment reduced the risk of chorioamnionitis and birth within 7 days.[38] In a recent study of 270 patients with PPROM, Kacerovsky et al. found that intravenous therapy with clarithromycin was associated with a reduction in the rate of intra-amniotic infection or sterile intra-amniotic inflammation.[39] Paramel Jayaprakash et al. reported that women with PPROM had mixed abnormal vaginal microbiota but that the microbiome profile at the time of PPROM did not correlate with the latency duration.[40] Taken together, these results suggest that intra-amniotic inflammation influences the latency period in PPROM patients regardless of the microbial infection status of the amniotic cavity documented on microbiological samples.

In our population, a cervical length less than 25 mm was not associated with a lower latency ratio. In a PPROM population managed with conventional hospitalization, Mehra et al. found an increased risk of delivery within 7 days in patients with oligohydramnios or shortened cervical length on ultrasound examination.[15] Rizzo et al. and Gire et al. reported a shortened latency in patients with a cervical length less than 20 mm.[16,41] It is possible that we were unable to identify differences in cervical length because we did not have this value for all patients (ie 114/234 had missing data). It is also possible that ultrasound measurement of cervical length can predict preterm birth during the days following PPROM, but is less informative after the acute phase has past. In our opinion, ultrasound measurement

of cervical length should not be a limiting factor in the selection of women suitable for home care.

Finally, the difference in results between earlier studies and our study may reflect differences between our sample of outpatients and the general PPROM population because we included only patients who had passed the acute phase. This may also explain why, after the beginning of home care, none of the factors studied, except for the PPROM term, increased the risk of delivery within 7 days. The stability of our population was supported by the mean latency of 35 days.

This study is original in its use of the concept of the latency ratio and analysis of the associations between risk factors for a shortened latency in patients grouped according to gestational age. The objective of the care of a patient with PPROM is to deliver as close as possible to 36–37 weeks of gestation to lower the risk of prematurity-associated morbidity.[13,14] The use of the latency ratio seems to be a better way of generalizing this objective to all patients than using a defined number of days. We chose to use an original surrogate outcome marker to generalize the goal to be achieved regardless of the term of rupture, ensuring that each patient extends her pregnancy to the closest possible gestational age of 37 weeks. Neonatal outcomes are not associated with the length of the latency period, but rather with the gestational age at birth, and the use of the latency ratio seemed to us to be more suitable to reflect the term objective to be achieved. In contrast, the use of latency in days as an outcome only reflects the extension of the latency period. Our study included the largest cohort of patients with PPROM managed as outpatients yet reported. However, two main limitations regarding the interpretation and extrapolation of the results should be considered. First, this was a population of clinically stable patients identified using precise criteria for admission to home care, and the results may not apply to all patients with PPROM. Second, we did not include previable ruptures because those who delivered before 24 weeks of gestation would not have been included, which would have caused a significant selection bias, and therefore the results are not relevant to these patients.

Our results confirm the clinical stability of PPROM patients managed in home care. However, oligohydramnios was associated with a shortening of 38% of the median latency ratio, CRP greater than 5 mg/L at 7 days with a shortening of 19%, and leukocyte count at PPROM greater than 12×10^9/L with a shortening of 7%. Cervical length less than 25 mm was not associated with a lower latency ratio in a selected population after the acute phase has past and should not require prolonged hospital monitoring. These results can be used for appropriate patient information when they begin home care and are useful for practitioners to adapt the follow up of each patient.

To improve the selection of eligibility criteria for home care, these results should be confirmed in a randomized study to compare inpatient and outpatient treatment after PPROM.

5 | CONCLUSION

Previous studies have shown that home-care management of PPROM lengthens the latency period. It seems important to identify the risk factors that can influence this latency. By introducing the latency ratio, we have provided a new tool for informing patients with PPROM about their risk of preterm delivery. We found that patients with PPROM managed with home care were stable and had a high latency ratio. However, this ratio was lower in patients with oligohydramnios or inflammatory syndrome at the time of and 7 days after the diagnosis of PPROM, especially if PPROM occurred before 28 weeks of gestation. After 32 weeks of gestation, the median latency was around 100% even in the presence of risk factors. It, therefore, seems reasonable to reassure patients about the lower risk of prematurity once the acute phase of hospitalization after PPROM has passed.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

FP drafted the manuscript, performed the research, acquired the data and wrote the paper. LG, CP, DS, and VHD drafted the manuscript and revised it critically. ED drafted the article and analyzed the data. CG designed and performed the research, interpreted the data and revised the paper critically. All authors gave their final approval of the version to be published and agreed to be accountable for all aspects of the work.

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