

ANALYSIS OF THE FACTORS AFFECTING THE LATENCY PERIOD AND TYPE OF BIRTH IN PATIENTS WITH PRETERM PREMATURE RUPTURE OF MEMBRANES

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ABSTRACT

Purpose: To determine the factors associated with the latent period in patients with preterm premature rupture of membranes (PPROM).

Material and Methods: 53 patients who applied to our clinic within 1 year and were diagnosed with PPRM and met the inclusion criteria participated in this prospective cross-sectional study. Factors thought to affect the latent period in these patients were examined in terms of delivery time and mode.

Results: Latent period; was negatively correlated with dilatation and positively correlated with collum length. The mean latent time of patients with contraction was statistically significantly lower than those without. In another model, gestational week, collum length and birth weight were found to be the most significant factors associated with the latent period. In the latent period groups; Statistically, a significant difference was found in the mean dilatation and collum length. The contraction rate was higher in those with a latency period of 2 days or less.

Conclusion: Latent duration is inversely proportional to dilatation and directly proportional to collum length. Uterine contraction is higher in patients with a latency period of fewer than 2 days. Other statistically significant factors related to the latent period are the gestational week and the fetal weight.

Keywords: fetal membranes, premature rupture, latency

INTRODUCTION

Premature rupture of membranes (PROM) is the loss of amniotic fluid by damage to the chorioamniotic membranes surrounding the fetus, independent of gestational age, before the onset of labor. Preterm premature rupture of membranes (PPROM) is defined as spontaneous rupture of fetal membranes before 37 weeks of gestation and before the onset of labor (1). The period from this stage until birth, which is understood by physical examination, is called the latent period.

PPROM is a common pregnancy complication. Approximately 5-7% of all pregnant women have PPRM (2,3). It is about 20-40% of PROM and its frequency doubles in multiple pregnancies. PPRM is associated with 20-50% of preterm births (4). The most important parameter associated with preterm birth complications is gestational age. Therefore; The length of the latent period from drainage to delivery is of vital importance in order to increase the chance of survival of the fetus and to reduce the complications that may develop.

In our study, we examined the factors affecting the time from diagnosis to delivery in patients with PPRM. This study aimed to examine the factors of age, parity, gestational week, amniotic fluid index, dilatation, collum length, tocolysis, prophylactic antibiotic use, birth weight, presence of contraction, presentation (fetus position) factors in terms of delivery time and shape. Thus, we aimed to highlight the most important factors affecting the latent period.

MATERIAL AND METHODS

This prospective cross-sectional study was started with the approval of the Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (31.10.2017; 1745) and informed consent was obtained from the volunteers. Patients between 28 and 34 weeks diagnosed with PPRM were included in the study between 15.11.2017-15.11.2018. Patients were divided into 3 groups in terms of latent duration, below 2 days, 2-7 days and above 7 days.

Inclusion criteria were accepting informed consent, to be diagnosed with PPRM in physical examination, to be 28-34 weeks pregnant, to have a singleton pregnancy, and to be between the ages of 18-45.

Exclusion criteria were pregnancies less than 28 weeks or more than 34 weeks, multiple pregnancy, being younger than 18 years of age, being older than 45 years of age, pregnant women who did not have a fetal heartbeat at the time of admission, and pregnancies with detected fetal anomaly.

The patients who applied with the complaint of amniotic leakage were evaluated by anamnesis, general physical examination and laboratory tests. For the diagnosis of PPRM, first of all, a sterile speculum examination was performed. The clear discharge from the cervical canal, fluid pooling in the posterior fornix of the vagina and membrane prolapse were evaluated. Litmus Test and PAMG-1 determination (AMNISURE ®) were performed diagnostically except in patients with obvious drainage on examination. Litmus paper was placed on the patient's pad and the color change was considered positive for drainage. In the amnisure test, a sample was taken from the vagina with a cotton swab in the product's box. This sample was again dissolved in the liquid from the box and the test cartridge was placed in the liquid. The double line was considered positive for drainage. All these were evaluated together with fetal ultrasonography and after the diagnosis, the patients were hospitalized.

Factors such as age, parity, amniotic fluid index, dilatation, collum length, tocolysis treatment, prophylactic antibiotic use, birth weight, presence of contraction, presentation (position of the baby), gestational age according to the last menstrual period were recorded. Tocolysis, antibiotic administration, and mode of delivery were determined by the attending physician or physicians. Our preference for antibiotics was: Azithromycin 1 gram orally upon admission, plus Ampicillin 2 grams intravenously every 6 hours for 48 hours, followed by Amoxicillin 875 mg orally every 12 hours or 500 mg orally every 8 hours for an additional five days. If tocolysis was indicated, nifedipine was preferred over current doses.

For amniotic fluid index (AFI), the uterus was divided into 4 equal quadrants on USG and the widest vertical depth in the deepest quadrant was measured and recorded in millimeters.

Cervical dilatation was determined by physical examination and recorded in centimeters.

Collum length was measured with TVUSG under optimum conditions (bladder was empty, cervix was sagittally viewed, the probe did not apply pressure to the cervix, the cervix covered 2/3 of the screen, echogenic cervical mucosa was observed, the anterior and posterior walls of the cervix were equal) by taking at least 3 measurements and the shortest one in millimeters was recorded.

Fetal presentation at the time of diagnosis was evaluated by transabdominal ultrasound and recorded as vertex, breech, or transverse.

Whether the patients had contractions at the time of diagnosis was determined by tocography. Regular contractions of 20 mm/hg and above every 10 minutes were considered positive and recorded as yes/no.

Patients were hospitalized for follow-up until birth or by regular outpatient checks after discharge. Birth patterns, a gestational week at birth, PPRM duration until birth, newborn weight at birth, and fetal sex were recorded.

When evaluating the findings from the study; SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics were number and percentage for categorical variables, mean for numeric variables, standard deviation, minimum, maximum, and median. Since the comparisons of numerical variables in the independent group were

Table 1. General characteristics of the patients

Age Mean±SD (min-max)		27,6±5,5 (18 To 40)
Parity , n (%)	Nulliparous	28 (52,8)
	Multiparous	25 (47,2)
Gestational Week Mean±SD (min-max)		30,3±2,1 (28-34)
Dilatation (cm) Mean±SD (min-max)		1.02±1,36 (0-8)
Collum length (mm) Mean±SD (min-max)		28,4±11,6 (7-49)
Contraction n (%)	Yes	17 (32,1)
	No	36 (67,9)
AFI (mm) AVG.±SD (min-max)		27,4±19,9 (0-83)
Fetal position n (%)	Vertex	37 (69,8)
	Breech	15 (28,3)
	Transverse	1 (1,9)
Tocolysis n (%)	Yes	11 (20,8)
	No	42 (79,2)
Antibiotics use n (%)	Yes	52 (98,1)
	No	1 (1,9)
Latent Period (days) Mean±SD (min-max)		10,0±9,7 (0-34)
Latent Period n (%)	2 days and below	14 (26,4)
	between 2-7 days	11 (20,8)
	7days and above	28 (52,8)
Birth type , n (%)	Vaginal	23 (43,4)
	cesarean section	30 (56,6)
Gender , n (%)	Male	And 20 (37,7)
	Girl	33 (62,3)
Weight (gr) Mean±SD (min-max)		1697,0±727,9 (650-4200)

Table 2. Evaluation of the patients' latent times and other numerical values

	Latent period (days)	
	rho	p
Age	-0,039	0,784
Gestational week	-0,091	0,515
Dilatation (cm)	-0,511	<0,001*
Collum length (mm)	0,731	<0,001*
AFI (mm)	0,071	0,615
Fetal weight (gr)	0,325	0,017 for

* Statistically significant

Table 3. Relationship between factors and latent time-1

		Latent Period (Days)		
		Mean±SD	Median	p
Parity , n (%)	Nulliparous	9,7±9,9	7	0,858
	Multiparous	10,3±9,7	7	
Contraction n (%)	Yes	5,8±8,7	2	0.005*
	No	11,9±9,7	7,5	
Fetal position n (%)	Vertex	9,9±8,7	7	0,341
	Breech	9,9±12,5	4	
	Transverse	12		
Tocolysis n (%)	Yes	12,2±11.4	7	0,575
	No	9,4±9,3	7	
Use of antibiotics , n (%)	Yes	10.2±9,7	7	-
	No	0		
The Type of Birth , n (%)	Vaginal	7,1±7,2	5	0,128
	Cesarean	12,2±10,9	7,5	
Gender , n (%)	Male	10.7±9,2	7	0,303
	Female	9,5±10,2	5	

* Statistically significant

not provided with normal distribution conditions, Mann Whitney U in two groups and the Kruskal Wallis test in more than two groups were performed. Subgroup analysis in more than two groups was performed with The Mann Whitney U test and interpreted with Bonferroni correction. A comparison of the proportions in the groups was made with Ki Square Analysis. Since the relationship between numerical variables was not provided with parametric testing conditions, Spearman correlation analysis was examined. The decisive factors were examined with Linear Regression Analysis. Statistical alpha level $p < 0.05$ was considered significant.

RESULTS

53 patients who met the inclusion criteria were included in the study, and the general characteristics of the patients were presented in Table-1. The evaluation of the patients' latency periods and other numerical values were summarized in Table 2.

The decision to start tocolysis was decided by the following physicians. 20% of patients received tocolysis, 80% did not. 98% of the patients received antibiotics, 2% did not.

Among linear analysis of latent duration and other characteristics of patients; latent duration (days) was

found to be inversely associated with dilatation, and directly associated with cervical length ($p < 0,001$ for both) (Table 3).

In the analysis of the factors affecting latent duration, the mean latent duration of the patients with contraction was statistically significantly lower ($p = 0.005$) compared to patients without uterine contractions (Table 4).

The model created to examine the determinant factors of latent duration (day), gestational week, cervical length (mm) and weight of the fetus (gr) at birth were determined as the most significant factors ($p = 0.006$ $p < 0.001$ $p < 0,001$, respectively). (Table 5)

The mean dilatation and collum length in latent duration groups were statistically significant ($p = 0.001$ $p < 0.001$, respectively). Patients with a latent duration of 7 days or more had statistically significant miscarriages compared to the group with an average dilatation average of 2 days or less ($p = 0.001$). Patients with a latent duration of 7 days or more had a statistically significantly higher collum length than the group with an average length of 2-7 days; and patients with a latent duration between 2-7 days had higher cervical length compared to the group of 2 days or less ($p = 0.001$, $p < 0.001$ $p = 0.008$, respectively) (Table 6).

Table 4. Examination of the latent period and the factors thought to be related with the enter model-backward method

		B	Beta	p
Enter Model	Constant	48,562		
	Age	-0,041	-0,023	0,840
	Parity	-1,310	-0,068	0,545
	Gestational week	-2,331	-0,491	0,008*
	Dilatation (cm)	-1,140	-0,159	0,571
	Collum length (mm)	0,315	0,375	0,018*
	Contraction	0,763	0,037	0,809
	AFI (mm)	0,037	0,075	0,593
	Fetal position	1,404	0,074	0,604
	Tocolysis	-1,760	-0,074	0,541
	Antibiotic use	6,255	0,088	0,661
	Birth type	2,095	0,108	0,485
	Gender	1,928	0,097	0,399
	Weight (gr)	0,008	0,595	0,002*
Backward Method	Constant	46,008		
	Gestational week	-2,151	-0,453	0,006*
	Collum length (mm)	0,361	0,430	<0,001*
	Birth type	3,376	0,173	0,093
	Weight (gr)	0,008	0,598	<0,001*

*: statistically significant

Table 5. Relationship between factors and latent time-2

	Latent period of			p
	2 days and below	between 2-7 days	7 days and above	
	Avg±SD (Median)	AVG.±SD (Median)	AVG.±SD (Median)	
Age	27.0±5,9 (27)	29,2±4,6 (29)	27,4±5,8 (26,5)	0,677
Gestational week	30,1±2,0 (29,5)	31,1±2,1 (32)	30,0±2,0 (29)	0,244
Dilatation (cm)	2.14±2.00 (2)	0.91±0,86 (1)	0,50±0,65 (0)	0,001*
Collum length (mm)	16.6±9,1 (14,5)	25.5±6,4 (26)	35,4±8,9 (36)	<0,001*
AFI (mm)	29.9±21,8 (27,5)	21,2±15,0 (18)	28,6±20,7 (19)	0,628
Weight (GR)	1412,9±633,4 (1460)	1593,6±542,9 (1840)	1879,6±798,3 (2000)	0,107

Dilatation - Collum length 2 days and below etc. 2-7 days p=0.055 p=0.008*

2 days and below vs. 7 days or more p=0.001* p<0.001*

Between 2-7 days vs. 7 days or more p=0.120 p=0.001*

*Statistically significant

Table 6. Relationship between factors and latent time-2

		Latent Period						p
		2 days and below		between 2-7 days		7days and above		
		n	%	n	%	n	%	
Parity	Nulliparous	9	64,3	4	36,4	15	53,6	0,379
	Multiparous	5	35,7	7	63,6	13	46,4	
Contraction	Yes	10	71,4	2	18,2	5	17,9	0,002*
	No	4	28,6	9	81,8	23	82,1	
Fetal position	Vertex	8	57,1	7	63,6	22	78,6	0,338
	Breech	6	42,9	4	36,4	5	17,9	
	Transverse	0	0,0	0	0,0	1	3,6	
Tocolysis	Yes	3	21,4	2	18,2	6	21,4	1,000
	No	11	78,6	9	81,8	22	78,6	
Antibiotics use	Yes	13	92,9	11	100	28	100	0,470
	No	1	7,1	0	0,0	0	0,0	
Type Of Birth	Vaginal	7	50,0	6	54,5	10	35,7	0,478
	Cesarean Section	7	50,0	5	45,5	18	64,3	
Gender	Male	3	21,4	4	36,4	13	46,4	0,287
	Female	11	78,6	7	63,6	15	53,6	

*: statistically significant

A statistically significant difference was found in the contraction rates of latent duration groups (p=0.002). The contraction rate of patients with a latent duration of 2 days and below was significantly higher (Table 6).

DISCUSSION

PPROM is associated with 20-50% of preterm births (4). PROM is the most common cause of premature birth and neonatal complications requiring hospitalization in the neonatal intensive care unit. In the treatment approach; there is a wide range of options from expectant management to emergency birth planning. While trying to prolong the gestational period in order to increase the chance of survival of the fetus; it should be kept in mind that serious complications such as preterm birth, fetal distress, ablatio placenta, cord prolapse, a maternal and fetal infection may develop (5).

The management of PPRM should be carried out by considering the gestational age, the presence of maternal and neonatal risks that will require immediate delivery, and the presence of complications such as intrauterine infection, early separation of the placenta, and fetal distress that may develop during the expected clinical course (3).

In the study of Phupong et al., 231 patients aged 28-34 weeks were analyzed retrospectively. The latency

periods of the patients were divided into 2 days and 2-7 days. It was found to be associated with prophylactic antibiotic use, especially for patients with a latency period of longer than 7 days. In addition, dilatation was found to be associated with the latent period (6). In our study, the dilatation of patients with a latency of 2 days or more was higher compared to 2 days or less, and there was generally a negative linear statistically significant relationship between latent time and dilatation. However, in our study, no relationship was found between antibiotic use and latent time. This may be because antibiotic use was left to the attending physician, and almost all of the patients were started on antibiotics and there was no control group.

In the study of Suwan Mehra et al. in 2015 to predict the latent period, the combination of AFI + TVCL was evaluated, but it was not found to be significant for prediction. However, latent period, gestational week, and short collum lengths were found to be associated with low AFI values (7). In another study, Young-JooLee et al. examined the same combination in 2018, and reduced AFI (the deepest single pocket) and short collum length were found to be associated with a short latent period (8). These findings in both studies were consistent with our study.

In a single-center retrospective study by Stamatios Petousis et al., 313 PPRM cases were examined. In

this study, the small gestational week at presentation and twin pregnancy were associated with a short latent period. (9). In our study, the gestational week was found to be associated with the latent period, but since only singleton pregnancies were accepted in our study, we could not investigate whether multiple pregnancies affected the latent period. Stamatios et al had more cases as they reported their 10-year experience in a single center. Our study was prospective and limited to 1 year.

In a retrospective study by Nir Melamed and his colleagues, late gestational week, nulliparity, >1cm dilatation and oligohydroamniosis were associated with short latent duration in 905 PPROM-diagnosed patients (10). Our study also achieved parallel results, but parity did not make a meaningful difference in our study. This may be due to the smaller number of participants in our study.

In the study by Gidon Test et al., patients were retrospectively examined for 10 years, 1399 patients with PPROM were included in the study, and factors related to the latent period were discussed. Among the factors thought to shorten the latency period, nulliparity, oligohydramnios, gestational week and development of chorioamnionitis were found to be statistically significant (11). We obtained similar results in our study. However, since our study was new and prospective, almost all patients were started on antibiotics to prevent the development of chorioamnionitis, based on the results obtained in previous studies.

The use of tocolytics in patients with PPROM was investigated in the 2011 COCHRANE review. A total of 408 women from 8 studies were included in the review. Seven studies compared the use of tocolytics and those that did not, and one study compared the use of terbutaline and nifedipine. As a result of the review, the use of tocolytics increased the latent period, but significantly increased the risk of chorioamnionitis. No significant difference was found in newborn outcomes (12). In our study, no significant difference was found in terms of tocolytic use. A significant difference can be found when evaluated with larger populations.

Studies on the preterm premature rupture of membranes are few and generally retrospective. The most important aspect of our study is that, since it was designed as a prospective cross-sectional design, it can guide us while providing counseling to pregnant women with preterm premature rupture of membranes, and it guides us in terms of factors that

will further prolong the latent period to obtain better maternal and neonatal outcomes.

The most important limitation of our study was small sample size. The reason for this was the decrease in the number of patients who applied due to the renovation and relocation of our clinic.

CONCLUSION

In conclusion, cervical dilatation, collum length, presence of contraction, gestational week and birth weight were found significantly associated with latent time. Larger prospective trials will elucidate us better about this topic.

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REFERENCES

1. ACOG (American Congress of Obstetricians and Gynecologists). Rupture P. Premature rupture of Membranes Practice Bulletin. 2016;128(4):165–77.
2. ACOG (American Congress of Obstetricians and Gynecologists). Practice bulletins No. 139: premature rupture of membranes. *Obstet Gynecol.* 2013 Oct;122(4):918–30.
3. Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. *Am J Obstet Gynecol.* 2009 Sep;201(3):230–40.
4. Mercer BM, Goldenberg RL, Meis PJ, Moawad AH, Shellhaas C, Das A, et al. The Preterm Prediction Study: Prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. *Am J Obstet Gynecol.* 2000 Sep;183(3):738–45.
5. Van Der Ham DP, Van Der Heyden JL, Opmeer BC, Mulder ALM, Moonen RMJ, Van Beek Hans JJ, et al. Management of late-preterm premature rupture of membranes: The PPROMEXIL-2 trial. *Obstetrical and Gynecological Survey.* 2013 vol: 68 (2) pp: 89-91
6. Phupong V, Kulmala L. Factors associated with

latency period in preterm prelabor rupture of membranes. *J Matern Neonatal Med.* 2015 Oct 20;1–4.

7. Mehra S, Amon E, Hopkins S, Gavard JA, Shyken J. Transvaginal cervical length and amniotic fluid index: can it predict delivery latency following preterm premature rupture of membranes? *Am J Obstet Gynecol.* 2015 Mar 1;212(3):400.e1-9.
8. Mehra S, Amon E, Hopkins S, Gavard JA, Shyken J. Transvaginal cervical length and amniotic fluid index: can it predict delivery latency following preterm premature rupture of membranes? *Am J Obstet Gynecol.* 2015 Mar 1;212(3):400.e1-9.
9. Mehra S, Amon E, Hopkins S, Gavard JA, Shyken J. Transvaginal cervical length and amniotic fluid index: can it predict delivery latency following preterm premature rupture of membranes? *Am J Obstet Gynecol.* 2015 Mar 1;212(3):400.e1-9.
10. Melamed N, Hadar E, Ben-Haroush A, Kaplan B, Yogev Y. Factors affecting the duration of the latency period in preterm premature rupture of membranes. *J Matern Neonatal Med.* 2009 Nov 17;22(11):1051–6.
11. Test G, Levy A, Wiznitzer A, Mazor M, Holcberg G, Zlotnik A, et al. Factors affecting the latency period in patients with preterm premature rupture of membranes. *Arch Gynecol Obstet.* 2011 Apr 20;283(4):707–10.
12. Test G, Levy A, Wiznitzer A, Mazor M, Holcberg G, Zlotnik A, et al. Factors affecting the latency period in patients with preterm premature rupture of membranes. *Arch Gynecol Obstet.* 2011 Apr 20;283(4):707–10.