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Comparison of Maternal and Neonatal Outcomes in Cases of Pre-Viable Preterm Premature Rupture of Membranes (pPPROM) According to Weeks of Gestation

Pre-Viable Preterm Prematür Membran Rüptürü (pPPROM) Olgularında Gebelik Haftalarına Göre Maternal ve Neonatal Sonuçların Karşılaştırılması

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ABSTRACT

AIM: The rupture of the amniotic membrane before 24 weeks gestation is defined as pre-viable preterm premature rupture of membranes (pPPROM). This study aims to compare the maternal and neonatal outcomes of cases of pPPROM detected before and after 22 weeks of gestation.

MATERIAL AND METHOD: This retrospective study evaluated singleton pregnancies with pPPROM between 2014 and 2019. The pPPROM cases were divided into two groups: Group 1 consisted of cases between 12+0 and 21+6 weeks of gestation, while Group 2 consisted of cases between 22+0 and 23+6 weeks of gestation. The obstetric outcomes, maternal complications, and neonatal intensive care unit (NICU) admission rates were compared in both groups. Furthermore, the neonatal outcomes of fetuses with a birth weight of over 500 grams were compared in both groups.

RESULTS: A total of 181 cases of pPPROM were identified, with 45 (24.8%) occurring in Group 2. The latent period duration, age at birth, and maternal complications were found to be higher in Group 2 ($p < 0.05$). Twenty percent of cases resulted in viable outcomes (15/136 vs. 22/45, $p < 0.001$). Higher termination rates were observed in Group 1 ($p<0.001$). However, ongoing pregnancies in this group reached more than 500 grams, these fetuses had higher Apgar scores and lower NICU admission rates ($p < 0.05$).

CONCLUSION: In cases of pPPROM after 22 weeks gestation, the incidence of maternal morbidity was higher, and the NICU admission rate was higher in fetuses born over 500 grams in this group.

Keywords: Pre-viable preterm premature rupture of membranes, neonatal outcomes, maternal outcomes, neonatal intensive care unit, termination of pregnancy

ÖZET

AMAÇ: Amniyotik membranın 24. gebelik haftasından önce rüptüre olması, pre-viable preterm prematüre membran rüptürü (pPPROM) olarak tanımlanır. Bu çalışma, 22. gebelik haftasından önce ve sonra tespit edilen pPPROM olgularının maternal ve neonatal sonuçlarını karşılaştırmayı amaçlamaktadır.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmada 2014-2019 yılları arasında pPPROM'lu tekil gebelikler değerlendirildi ve pPPROM vakaları iki gruba ayrıldı: 12+0 ile 21+6 gebelik haftaları arasındaki vakalardan oluşan Grup 1 ve 22+0 ile 23+6 gebelik haftaları arasındaki vakalardan oluşan Grup 2. Her iki grupta latent dönem süresi, obstetrik sonuçlar, maternal komplikasyonları ve yenidoğan yoğun bakım ünitesine (YYBÜ) yatış oranları karşılaştırıldı. Ayrıca 500 gramın üzerinde ağırlıkla doğan fetüslerin neonatal sonuçları iki grup arasında karşılaştırıldı.

BULGULAR: Grup 2'de 45 (%24,8) olgu olmak üzere toplam 181 pPPROM vakası tespit edildi. Grup 2'de latent dönem süresi, doğum yaşı ve maternal komplikasyonları daha yüksek bulundu ($p <0,05$). Gebeliklerin %20,4'si viable sonuçlandı (15/136 vs. 22/45, $p<0,001$). Grup 1'de daha fazla terminasyon oranları gözlemlendi ($p<0.001$). Ancak, bu grupta devam eden gebelikler 500 gramın üzerine çıktığında, bu fetüslerin Apgar skorları daha yüksekti ve NICU'ya kabul oranları daha düşüktü ($p < 0,05$).

SONUÇ: 22 haftalık gebelikten sonra pPPROM vakalarında, maternal morbidite insidansı daha yüksekti ve bu grupta 500 gramın üzerinde doğan fetüslerde NICU'ya kabul oranı daha yüksekti.

Anahtar Kelimeler: Pre-viable Preterm Premature Membran Rüptürü, neonatal sonuçlar, maternal sonuçları, yenidoğan yoğun bakım ünitesi, terminasyon

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INTRODUCTION

Pre-viable preterm premature rupture of membranes (pPPROM) occurs in 0.4% to 1% of pregnancies before 24 weeks gestation and is defined as a rupture of the amniotic membranes before the onset of labor (1,2). PPROM is associated with high rates of maternal and neonatal morbidity and mortality, including infection-related problems and other associated problems such as pulmonary hypoplasia, fetal malformations, and abruption of placentae. The probability of neonatal death and morbidity associated with premature rupture of membranes (PROM) decreases with prolonged latency and increasing gestational age (1,2,3). Therefore, the gestational week in which PROM occurs affects both neonatal and maternal morbidity and mortality, as well as the management of these cases by clinicians (3).

In the case of pregnancies complicated by pPPROM, the options for women include termination of a pre-viable fetus or expectant management to achieve the viability of the fetus. Although it rarely occurs, critical maternal complications after pPPROM, unfortunately, maternal morbidity is experienced in approximately 14% of cases, which renders expectant management challenging (4). Nevertheless, in cases of PROM detected in the second trimester, the latent periods were observed to be longer than those observed in later gestational ages, however, it was observed that 40-50% of these cases resulted in delivery within the first week, and approximately 70-80% of them resulted in delivery after 2-5 weeks (2,5,6). Furthermore, the survival rates were significantly higher when the rupture of membranes was followed by expectant management after 22 weeks of gestation compared to the rupture of membranes before 22 weeks of gestation (57.7% versus 14.4%, respectively) (2).

The management of PROMs in pre-viable fetuses presents a variety of challenges and crucial processes for the mother, fetus, and obstetrician and one of the most prominent parameters in this process is the rupture of the membranes at which gestational week (1,2,3). This study aims to compare the maternal and neonatal outcomes of these two groups of pPPROM cases detected before and after 22 weeks of gestation.

MATERIAL AND METHOD

This retrospective study identified singleton pregnancies with pPPROM who were admitted to the early pregnancy service between January 2014 and October 2019. The study was conducted on the hospital admission records at our hospital. The study was approved by the local ethics committee on 14/05/2020, with approval number 07. Informed consent was received from all participants.
The study included singleton pregnancies with a definitive clinical diagnosis of pPPROM between 12+0 and 23+6 gestational weeks. The visualization of amniotic fluid passing from the cervical canal or posterior fornix accumulation in cases diagnosed as pPPROM by speculum examination, and pregnant women presenting with a history of vaginal observation of amniotic flow, were included in the study. However, amniotic fluid was not visually observed in speculum examination, but placental alpha microglobulin-1(PAMG-1) test (amniosure) positive and diagnosed as pPPROM were also included. In our clinic, we manage pPPROM cases by the recommendations of the American College of Obstetricians and Gynecologists (ACOG) (1). Multiple pregnancies, cases with PROM detected at <12 and ≥24 weeks gestation, women with labor within 24 hours of rupture, uncertain date of membrane rupture, oligohydramnios or anhydramnios without membrane rupture, membrane rupture within 48 hours of amniocentesis, chorionic villous sampling, or fetal selective reduction, and cases with missing maternal and neonatal data were excluded.

The pregnancies included in the study were divided into two groups, as follows: Group 1 comprised pPPROM cases diagnosed between 12+0 and 21+6 weeks of gestation, and Group 2 comprised pPPROM cases diagnosed between 22+0 and 23+6 gestational weeks. In both groups, demographic characteristics and obstetric factors, ultrasonographic findings such as amniotic fluid index (AFI) and fetal heartbeat (FHB), gestational age at admission, duration of the latent period, birth age, C-reactive protein (CRP), leukocyte count, and medical treatments were compared. Additionally, the rates of cesarean or hysterotomy, transfusion, maternal sepsis, termination, live birth, birth weight, and neonatal intensive care unit (NICU) admission were analyzed. As secondary outcomes, obstetric and neonatal outcomes of fetuses with a live birth over 500 g and fetuses followed in the NICU were subgrouped and compared in both groups.

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 28. The distribution of numerical variables was subjected to a Kolmogorov-Smirnov test. As the data did not demonstrate a normal distribution, all numerical data are presented with median (minimum-maximum) values. Furthermore, percentages (numbers) were employed in the context of categorical variables. The two groups were compared using the chi-square test for categorical variables and the Mann-Whitney U test for numerical variables. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for significant categorical variables. The variables that were found to be significant in the univariate analysis were then evaluated in a multivariate regression analysis. The results were considered statistically significant at the $p< 0.05$.

RESULTS

By the eligibility criteria, a total of 181 (75.1%) cases of pPPROM were identified, with 45 (24.8%) falling within Group 2. There was no difference in age, BMI, or obstetric parameters such as gravida and parity in both groups ($p>0.05$, Table 1).

Table 1: Demographic and obstetric characteristics of the groups

	Group 1	Group 2	
Variables	n=136 (75.18%)	n=45 (24.82%)	p value
	Median (min-max)	Median (min-max)	
Age (years)	32 (17-46)	30 (18-41)	0.278
Body Mass Index (kg/m^2)	26 (21-36)	27 (22-33)	0.527
Gravida (n)	2 (1-9)	2 (1-5)	0.178
Parity (n)	1(0-5)	1 (0-4)	0.636
Previous miscarriages, (n)	0(0-)6	0 (0-3)	0.328
Number of children	1(0-5)	1 (0-4)	0.780
Stillbirth, (n)	0 (0-2)	0 (0-1)	0.732
Ectopic pregnancies, (n)	0 (0-1)	0 (0-0)	0.315
Cesarean birth, (n)	0 (0-3)	0 (0-3)	0.241
Duration of antibiotics (days)	5 (2-30)	7 (3-37)	**<0.001**
C-reactive protein (mg/l)	32 (1-254)	6.5 (1-302)	0.411
Leukocyte count, (x10^9/L)	10.67 (5.10- 25.0)	10.12 (4.71-21.60)	**0.023**
Gestational age at diagnosis (days)	123 (84-152)	165 (154-166)	**<0.001**
Ultrasonographic gestational age (days)	127 (81-165)	166 (136-180)	**<0.001**
Latent period (days)	2 (2-197)	10 (2-93)	**<0.001**
Birth Age (days)	131 (86-278)	175 (157-250)	**<0.001**

Although the CRP values of the groups were similar at admission ($p=0.411$), the leukocyte count was significantly higher in Group 1 ($p=0.023$), but the duration of antibiotic use was significantly longer in Group 2 ($p<0.001$, Table 1). The median duration of the latent period was 2 days (2-197) in Group 1 and 10 days (2-93) in Group 2 (Table 1). The median birth age of Group 2 was 175 days (157-250), while that of Group 1 was 131 days (86-278), as shown in Table 1. The birth ages of these two groups are illustrated in the box plots of Figure 1.

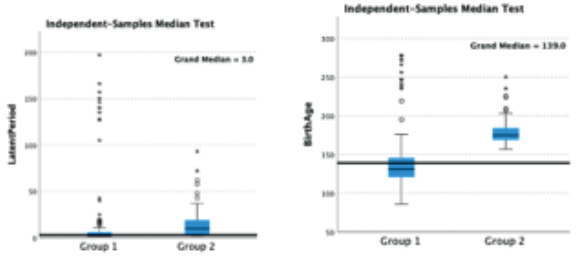

Figure 1: The duration of the latent period (day) and birth age (day) according to the groups in all fetuses.

The significant variables in Table 1, including antibiotic duration, leukocyte count, gestational age, birth age, and latent period were evaluated in a multivariate regression analysis and the results indicated a statistically significant difference at the p < 0.001 level in this model (R=0.806, R2=0.649, and aR=0.639).

A comparison of outcomes of pregnancies in the two groups revealed that 98 cases (72.1%) in Group 1 had been terminated, in contrast to 7 cases (15.6%) in Group 2 (p < 0.001). In addition, 10 cases in Group 1 had resulted in intrauterine fetal death (IUFD), in comparison to 2 cases in Group 2. Furthermore, 8 cases in Group 1 resulted in spontaneous abortion, in contrast to 1 case in Group 2. The live birth rate was 77.8% in Group 2 and 14.7% in Group 1 (p < 0.001). All terminations were conducted via drug-induced abortion, except two cases in Group 1, where the pregnancy was terminated by hysterotomy due to unresponsiveness to medical treatment.

The incidence of postpartum hemorrhage was higher in Group 2 (1 (0.7%) vs. 3 (6.7%), p=0.048, Table 2).

Table 2: Complication rates and other obstetric outcomes of the groups

		Group 1	Group 2			
		n (%) 136 (75.18)	n (%) 45 (24.82)	p value	Odds Ratio	%95 CI
Assisted reproductive techniques	No	131 (96.3)	42 (93.3)	0.256		
	In vitro fertilization	3 (2.2)	3 (6.7)			
	Intrauterine insemination	2 (1.5)	0 (0.0)			
Comorbid systemic disease	No	124 (91.2)	44 (97.8)	0.137		
	Yes	12 (8.8)	1 (2.2)			
Presence of active amniotic flow	No	23 (16.9)	1 (2.2)	**0.012**	8.956	1.174-68.339
	Yes	113 (83.1)	44 (97.8)			
Amniotic fluid index	Oligohydramnios or anhydramnios	118 (86.8)	32 (71.1)	**0.16**	2.663	1.181-6.007
	Normal	18 (13.2)	13 (28.9)			
Termination of pregnancy	No	38 (27.9)	38 (84.4)	**<0.00 1**	0.071	0.029-0.174
	Yes	98 (72.1)	7 (15.6)			
Live birth over 500 g	No	116 (85.3)	10 (22.2)	**<0.00 1**	20.30 0	8.699-47.400
	Yes	20 (14.7)	35 (77.8)			
Cesarean section or hysterotomy	No	123 (90.4)	27 (60.0)	**<0.00 1**	6.308	2.761-14.409
	Yes	13 (9.6)	18 (40.0)			
Gender	Unspecified	114 (83.8)	4 (8.9)	**<0.00 1**		
	Girl	12 (8.8)	18 (40.0)			
	Boy	10 (7.4)	23 (51.1)			
Chorioamnionitis	No	133 (97.8)	39 (86.7)	**0.03**	6.821	1.630-28.533
	Yes	3 (2.2)	6 (13.3)			
Maternal sepsis	No	136 (100.0)	44 (97.8)	.249		
	Yes	0 (0.0)	1 (2.2)			
Abruptio placentae	No	2 (1.5)	2 (4.4)	.239		
	Yes	134 (98.5)	43 (95.6)			
Placental rest	No	132 (97.1)	43 (95.6)	0.625		
	Yes	4 (2.9)	2 (4.4)			
Endometritis	No	134 (98.5)	45 (100.0)	1.000		
	Yes	2 (1.5)	0 (0.0)			
Blood transfusion	No	130 (95.6)	42 (93.3)	0.546		
	Yes	6 (4.4)	3 (6.7)			
Postpartum hemorrhage	No	135 (99.3)	42 (93.3)	**0.048**	9.643	0.977-95.176
	Yes	1 (0.7)	3 (6.7)			

Chorioamnionitis, diagnosed based on the presence of fever, malaise, infective vaginal discharge, and uterine tenderness, was observed significantly more frequent in Group 2 (3 (2.2%) vs 6 (13.3%), p=0.03). Maternal severe sepsis was observed in only one woman at 23+1 weeks in Group 2, resulting in intrauterine fetal death (IUFD). There were no maternal deaths or thromboembolic events in any of the casesistor.

Table 3: Neonatal outcomes of groups in fetuses born over 500 g

		Fetuses live born over 500 g		
		Group 1	Group 2	
		n=20	n=35	p value
Age, years, Median (min-max)		31.5 (21-46)	30 (21-41)	0.508[a]
Gestational age at diagnosis (days), Median (min-max)		122 (84-153)	165 (157-167)	**<0.001[a]**
Latent period (days), Median (min-max)		127 (2-197)	18 (2-93)	**<0.004[a]**
Birth Age (days), Median (min-max)		238 (153-281)	183 (162-250)	**0.019[a]**
Birth weight (gr), Median (min-max)		2265 (500-4330)	930 (545-2410)	0.074[a]
Duration of antibiotics (days), Median (min-max)		7 (2-30)	7 (3-19)	0.745[a]
C-reactive protein, (mg/L), Median (min-max)		15 (3-32)	6.5 (1-305)	0.416[a]
Leukocyte count, (x10³/L), Median (min-max)		12.11 (7.86-18.20)	12.89 (7.93-18.46)	0.414[a]
Amniotic fluid index,n (%)	Oligohydramnios or anhydramnios	5 (25.0)	22 (62.9)	**0.007[b]**
	Normal	15 (75.0)	13 (32.1)	
Cesarean section, n (%)	No	9 (45.0)	17 (48.6)	0.799[b]
	Yes	11 (55.0)	18 (51.4)	
Administration of corticosteroids, n (%)	No	9 (45.0)	0 (0)	**<0.001[b]**
	Yes	11 (55.0)	35 (100)	
Gender, n (%)	Boy	12 (60.0)	15 (42.9)	0.221[b]
	Girl	8 (40.0)	20 (57.1)	
1st-min Apgar score, Median (min-max)		8 (1-9)	6 (1-9)	**<0.001[a]**
5th-min Apgar score, Median (min-max)		9 (2-10)	7 (0-10)	**0.016[a]**
Admission at Neonatal intensive care unit (NICU), n (%)	No (healthy fetüs)	8 (40.0)	1 (2.9)	**0.002[b]**
	Yes	11 (55.0)	30 (85.7)	
	Unresponsive to neonatal resuscitation (death)	1 (5.0)	4 (11.4)	

[a]=Mann Withney U test , [b] = Chi-square test, Bold is statistically significant

Table 3 presents the neonatal outcomes of 55 fetuses (20 vs. 35) born weighing over 500 g and 41 fetuses (11 vs. 30) hospitalized in NICU. There was no significant difference in age, duration of antibiotics, C-reactive protein, leukocyte count, birth weight, cesarean birth rate, and gender of fetuses born over 500 g in both groups (p > 0.05). The detection rate of oligohydramnios or anhydramnios was significantly higher in Group 2 (p=0.007, OR:0.197, 95% CI 0.058-0.669). However, as illustrated in Figure 2

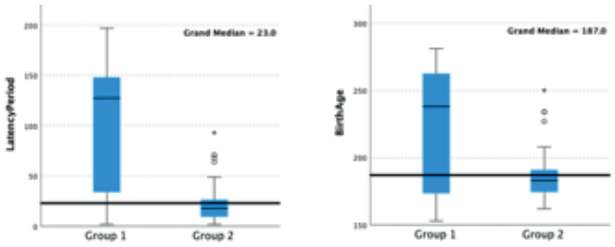

Figure 2: The duration of the latent period (day) and birth age (day) according to the groups of

, in fetuses with a birth weight of over 500 g, there was a significant difference between the groups in median latent period (127 (2-197) vs. 18 (2-93) days, p <0.004) and median birth age (238 (153-281) vs. 183 (162-250) days, p=0.019), with these durations being longer in Group 1, in contrast to all cases, as shown in Figure 1.The significant variables in Table 3, including Apgar 1, Apgar 5, gestational age, and latent period, were evaluated in a multivariate regression analysis and the results indicated a statistically significant difference at the p<0.001 level in this model (R=0.786, R2=0.619, and aR=0.588). Furthermore, the first and fifth-minute Apgar scores were observed to be superior in Group 1 in fetuses with a birth weight of over 500 g (p < 0.05). Consequently, the number of cases admitted to the neonatal intensive care unit (NICU) from fetuses born over 500 g was significantly higher in Group 2 (11 (55.0%) vs. 30 (85.7%), p=0.002). The 41 fetuses admitted to the NICU unit were evaluated in Table 4,

Table 4: Neonatal outcomes of groups in fetuses with Neonatal intensive care unit (NICU) admission

		Fetuses with NICU admission n=41		p value
		Group 1	Group 2	
		n=11	n=30	
Mortality rate, n (%)	No	7 (63.6)	21 (70.0)	0.698[b]
	Yes (death)	4 (36.4)	9 (30.0)	
Postnatal immediate intubation, n (%)	No	4 (36.4)	15 (50.0)	0.438[b]
	Yes	7 (63.6)	15 (50.0)	
Day of hospitalization in the NICU, Median (min-max)		7 (1-126)	59 (1-143)	0.095[a]
Necrotizing enterocolitis, n (%)	No	11 (100.0)	27 (90.0)	0.555[b]
	Yes	0 (0.0)	3 (10.0)	
Transition to total enteral nutrition, n (%)	No	4 (36.4)	5 (16.6)	0.051[b]
	Yes	7 (63.6)	25 (83.3)	
Day of transition to total enteral nutrition, Median (min-max)		6 (0-21)	10 (0-30)	0.127[a]
Patent ductus arteriosus, n (%)	No	6 (54.5)	14 (43.7)	0.711[b]
	Yes	5 (45.5)	16 (53.3)	
	Unknown	0 (0.0)	1 (3.3)	
Respiratory Distress Syndrome, n (%)	No	3 (27.3)	4 (13.3)	0.293[b]
	Yes	8 (72.7)	26 (86.7)	
Number of surfactants given, Median (min-max)		1 (0-2)	1 (0-3)	0.896[a]
Bronchopulmonary dysplasia, n (%)	No	10 (90.9)	23 (76.7)	0.308[b]
	Yes	1 (9.1)	7 (23.3)	
Periventricular/ intraventricular hemorrhage, n (%)	No	10 (90.9)	23 (76.7)	0.308[b]
	Yes	1 (9.1)	7 (23.3)	
Grade of periventricular/ intraventricular hemorrhage, Median (min-max)		0 (0-3)	0 (0-4)	0.308[a]
Retinopathy of the prematüre, n (%)	No	4 (36.4)	8 (26.7)	0.727[b]
	Yes	3 (27.3)	12 (40.0)	
	Not required	4 (36.4)	10 (33.3)	
Stage of retinopathy of the prematüre, Median (min-max)		1 (1-2)	1 (1-3)	0.789[a]
Pulmonary hypoplasia, n (%)	No	10 (90.9)	28 (93.3)	0.762[b]
	Yes	1 (9.1)	2 (6.7)	
Intermittent extubation, n (%)	No	10 (90.9)	16 (53.3)	0.077[b]
	Intermittent oxygen	0 (0.0)	6 (20)	
	Intermittent extubation	1 (9.1)	8 (26.7)	
Neonatal sepsis, n (%)	No	9 (81.8)	28 (93.3)	0.271[b]
	Yes	2 (18.2)	2 (6.7)	

[a]=Mann Withney U test , [b] = Chi-square test, Bold is statistically significant

and no significant differences were observed between groups in mortality rate, day of hospitalization in the NICU, rate of necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), periventricular/intraventricular hemorrhage (P/IVH), retinopathy of prematurity (ROP), and neonatal sepsis were all found to be statistically insignificant (p>0.05).
Consequently, the number of cases resulting in termination or loss of pregnancy in the groups was 121 (89%) and 23 (51.2%), respectively (p < 0.001). Of the 55 surviving fetuses presented in Table 3, 15 (75%) live fetuses remained in Group 1, and 22 (62.8%) live fetuses in Group 2 (p=0.36). In conclusion, only 37 of the fetuses survived, representing 11% of cases in Group 1 and 48.8% of cases in Group 2 (p < 0.001).

DISCUSSION

This study compared maternal and neonatal outcomes of cases with pPPROM before and after 22nd week of gestation. The duration of the latent period, the gestational age at birth, the number of fetuses born over 500 g, and the rate of complications such as chorioamnionitis and postpartum hemorrhage were found to be higher in Group 2. In Group 1, the rate of termination of pregnancy (TOP) was higher, but in fetuses born over 500g, the duration of the latent period and the gestational age at birth were found to be higher. Furthermore, better neonatal outcomes with higher Apgar scores and lower rates of NICU admission were also observed in Group 1.

ACOG recommends that cases of pPPROM be offered immediate delivery and expectant care and that patients receive the most ap-

propriate counseling regarding how management decisions affect the health of the mother and fetus (1). In our early pregnancy service, we provided verbal and written counseling for pPPROM cases by offering both options prélabor managed all cases by considering both the patient's decisions and maternal and fetal factors. Consequently, 58% of all pPPROM cases resulted in TOP, and the number of cases who did not prefer TOP and required expectant management was significantly higher in Group 2 (27.9% vs 84.4%, p < 0.001). As a result, the latency period was longer in Group 2, chorioamnionitis was detected at a higher rate of 6.821 times (95% CI, 1.630-28.533) and postpartum hemorrhage was detected at a higher rate of 9.643 times (95% CI, 0.977-95.176) compared to the other group in this study (p<0.05).

In the study conducted by Sklar et al., which examined 350 cases of pPPROM, 48.1% of cases opted for TOP as the initial management strategy. Women who chose TOP had 4.1 times the odds of developing chorioamnionitis compared to women who chose expectant management (38.0% vs. 9.3%) and the odds of developing chorioamnionitis were 13.0 % (95% CI, 2.03-8.26), while the odds of postpartum hemorrhage were 2.44 times higher (95% CI, 1.13-5.26) (7). Approximately 40% to 50% of women who choose expectant management experience maternal morbidity such as infection, retained placenta, and/or hemorrhage (2,8), and in deliveries of pre-viable pregnancies compared to term pregnancies; this is approximately six times more likely to result in poor outcomes, including chorioamnionitis, blood transfusion, hysterectomy, and/or admission to the maternal intensive care unit (ICU) (9). In this study, no cases of hysterectomy, maternal ICU admission, or maternal death were observed, and no significant differences were identified between the groups in complications, including sepsis, blood transfusion, placental rest, and endometritis.
Several studies have demonstrated that neonatal survival rates in cases of pPPROM range from 0% to 56%, while severe neonatal morbidity rates range from 40% to 100% (3,8,10-13). In this study, the overall neonatal survival rates and the overall survival without serious neonatal morbidity were found to be 20.4% and 4.97%, respectively, in all pPPROM cases. In Group 2, where pPPROM was detected between the 22nd and 24th weeks of gestation, the overall neonatal survival rates were 6.563 times higher than in the other group. Similarly, in the study by Kibel et al. of 140 fetuses diagnosed with pPPROM at 20-24 weeks of gestation, it was found that gestational age at preterm PROM of 22 weeks or greater was significantly associated with overall survival and survival without severe neonatal morbidity. The adjusted odds ratio (aOR) for survival and survival without severe neonatal morbidity with latency periods was found to be 12.2 and 4.8, respectively (10). However, in the study conducted by Lorthe et al. with 427 fetuses (331 singletons and 96 twins) in cases of pPPROM) at 22-25 weeks gestation, 38.8% were survivors at discharge without severe morbidity, and 46.4% were survivors at 2 years without cerebral palsy (13). Although the NICU admission rate was significantly higher in Group 2 (55% vs. 85.7%) for viable fetuses weighing over 500 g (p=0.002), there was no difference in neonatal outcomes between the two groups. This included PDA, P-IVH, ROP, RDS, PBD, neonatal sepsis, and mortality rate (p<0.05).

A number of risk factors for PPROM have been identified (1). Among these are factors that may be amenable to modification, including smoking, a body mass index (BMI) of less than 18.5 kg/m^2, diabetes mellitus, and poor nutrition. Others are related to the maternal obstetric history, including previous preterm labor (PTB), prior cervical conization or a second-trimester short cervical length (CL), and second-trimester vaginal bleeding (14). To date, no preventive treatment for PPROM has been documented. However, a recent study suggests that low-dose aspirin prophylaxis might reduce the prevalence of PPROM in women screened at high risk for preeclampsia (15). A recent study by El-Achi et al. proposed the development of a predictive model for the first trimester, utilizing information currently collected at 11–14 weeks of gestation, though its screening performance was modest. The study found that maternal factors predictive of PPROM included nulliparity, pre-existing diabetes mellitus (DM), maternal age group and BMI category (16). However, further analysis revealed that the uterine artery pulsatility index (UAPI) and biochemical parameters at first-trimester screening (PAPP-A, free βHCG) were not statistically significant (16). The improved early prediction of women at high risk for PPROM is important for further investigation of potential preventive interventions. The prediction and prevention of pPPROM pregnancies are also significant in view of the maternal and fetal consequences. Further studies are required on this subject.

Due to the retrospective design of the study and the pregnancies that resulted in TOP, it was not possible to observe the actual effect of pPPROM in all pregnancies in a prospective manner. Nevertheless, the inclusion of NICU follow-up and results of viable fetuses as a subgroup in pPPROM cases represents a significant strength of this study. Furthermore, the maternal, obstetric, and neonatal outcomes of a considerable number of cases of pPPROM before and after the 22nd week of gestation were compared.

CONCLUSION

A shorter latent period is observed in pPPROM cases before the 22nd week of gestation, which is attributed to a higher rate of TOP. Nevertheless, if a viable live birth weighing over 500 g occurs in this group, birth occurs at an older gestational age with a longer latent period, resulting in fewer NICU admissions with higher Apgar scores. In pPPROM cases between 22 and 24 weeks of gestation, a prolonged latent period was observed due to a lower rate of TOP and a higher rate of maternal complications, including chorioamnionitis and postpartum hemorrhage. Nevertheless, in this group, despite a higher rate of viable live births over 500 g, birth occurs at an earlier gestational age with a shorter latent period, resulting in more NICU admissions with lower Apgar scores. Nevertheless, there was no discernible difference in the neonatal outcomes of the fetuses admitted to the NICU in both groups.

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Author Contributions

YAR: Project Development, Data Collection or Management, Data Analysis, Manuscript Writing/Editing
FBF: Project Development, Data Collection and Management, Data Analysis, Manuscript Writing/Editing
AA, SST: Project Development, Data Collection and Management, Manuscript Writing/Editing
AKÖ: Data Collection and Management, Project Development
SYE, SÖ: Data Management, Data Analysis, Manuscript Writing/Editing
SE, YEÜ: Supervision, Manuscript Writing/Editing
All authors read and approved of the final manuscript.

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