RISK FACTORS ASSOCIATED WITH PRETERM PREMATURE RUPTURE OF MEMBRANES
PRETERM ERKEN MEMBRAN RÜPTÜRÜ ILE İLİŞKİLİ RİSK FAKTÖRLERİ

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ABSTRACT

Preterm premature rupture of membranes is an important obstetric problem that has a profound impact on birth, neonatal mortality and morbidity and therefore requires urgent intervention. In this study, 100 cases and 100 control subjects who applied to a tertiary university hospital were included. Possible risk factors included gravidity, age, smoking, body mass index, time since the previous pregnancy, birth history, socioeconomic status, education level, caffeine consumption, urinary tract infection, and a history of previous abortion. The case and control groups were statistically compared based on risk factors. Based on the results there was a statistically significant difference between the case and control groups with respect toliteracy, obesity, urinary tract infections, history of abortion, multiparity, previous birth was before two years, and history of premature birth (p=0.033, p<0.001, p<0.001, p<0.001, p<0.001, p<0.001, respectively). However, no significant difference was observed regarding age range, number of births, birth type, and coffee use (p=0.334, p=0.131, p=0.057 and p=0.077). As a result of binominal regression analysis, the highest risk was found for obesity (OR=7.63; 95% confidence interval, 1.68–34.66), urinary tract infection (OR=3.57; 95% confidence interval, 1.43–8.93), previous birth less than two years (OR=7.53; 95% confidence interval, 2.85–19.9), previous preterm birth (OR=13.42; 95% confidence interval, 3.62–49.82), smoking/alcohol use (OR=15.97; 95% confidence interval, 4.99–51.1) (p<0.05).Smoking/alcohol consumption and history of previous preterm birth were the most important risk factors.

Keywords: Preterm birth, preterm prematüre rupture of membranes, risk factors.

ÖZ

Preterm prematür membran rüptürü, doğumda neonatal mortalite ve morbidite üzerinde derin etkisi olan ve bu nedenle acil müdahale gerektiren önemli bir obstetrik sorundur. Bu çalışmada üçüncü basamak bir üniversite hastanesine başvuran 100 vaka ve 100 kontrol grubu dahil edildi. Olası risk faktörleri; doğurganlık sayısı, yaş, sigara kullanımı, vücut kitle indeksi, önceki hamilelikten bu yana geçen süre, doğum öyküsü, sosyoekonomik durum, eğitim düzeyi, kafein tüketimi, idrar yolu enfeksiyonu ve önceki kürtaj öyküsü idi. Vaka ve kontrol grupları risk faktörleri açısından istatistiksel olarak karşılaştırıldı. Sonuçlara göre okuma yazma bilmeyen, obezite, idrar yolu enfeksiyonu, kürtaj öyküsü, çok doğum, önceki doğumu iki yıldan önce olan, erken doğum öyküsü olan bu iki grup arasında istatistiksel olarak anlamlı fark vardı (p=0.033, p<0.001, p<0.001, p<0.001, p<0.001, p<0.001). Ancak vaka ve kontrol gruplarında yaş aralığı, doğum sayısı, doğum şekli ve kahve kullanımı açısından anlamlı farklılık gözlenmedi (p=0.334, p=0.131, p=0.057 ve p=0.077). Binominal regresyon analizi sonucunda en yüksek risk obezite (OR=7.63; %95 güven aralığı, 1.68-34.66), idrar yolu enfeksiyonu (OR=3.57; %95 güven aralığı, 1.43 –8.93), iki yıldan az önceki doğum (OR=7.53; %95 güven aralığı, 2.85–19.9), geçirilmiş erken doğum (OR=13.42; %95 güven aralığı, 3.62–49.82), sigara/alkol kullanımı (OR=15.97; %95 güven aralığı, 4.99–51.1) (p<0.05) için bulunmuştur. Araştırma sonuçlarına göre sigara/alkol kullanımı ve daha önce erken doğum yapmış olmak en önemli risk faktörleriydi.

Anahtar kelimeler: Erken doğum, preterm prematür membran rüptürü, risk faktörleri.

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INTRODUCTION

Preterm premature rupture of membranes (PPROM) is defined as the rupture of fetal membranes prior to delivery in preterm pregnancies, complicating 2-5% of all pregnancies.[1,2] PPROM can lead to preterm birth, which increases the risk of neonatal morbidity and mortality, thus necessitating meticulous management and therefore requires careful management.[3] The cause of PPROM is not yet fully understood in current research. However, recent studies have suggested that proinflammatory factors may play a role in its development.[4] It is important to acknowledge that PPROM can be influenced by numerous factors, including a diverse range of conditions andbehaviors. Possible risk factors for PPROM may include a history of PPROM in previous pregnancies, vaginal bleeding before birth, abdominal trauma, previous premature births, smoking, drug use, anemia, low BMI, low socioeconomic status, hypertension history, abortion, cesarean delivery, inadequate prenatal care, parity, multiple pregnancies, polyhydramnios, invasive procedures such as amniocentesis.[5,6]

On the other hand, recent meta-analyses and studies have indicated that low BMI, an interpregnancy interval (IPI) of less than 2 years, a history of previous abortions, previous preterm births, a history of PROM, cesarean delivery, pregnancy-induced hypertension, gestational diabetes mellitus (GDM), abnormal vaginal discharge, reproductive tract infections, malpresentation, increased abdominal pressure, and multiple pregnancies may be associated with a higher risk of preterm premature rupture of membranes (PPROM).

The ongoing significance of this issue as a major public health concern in Türkiye necessitates increased research to address it. For a contemporary perspective on obstetric practices and policies at both national and global levels, it is crucial to conduct further studies in this area.

The purpose of this study is to examine the various factors that may have an impact on the outcome. These factors include parity, age, smoking, BMI, time since the previous pregnancy, birth history, socioeconomic status, education level, caffeine consumption, presence of urinary tract infection, and previous history of curettage.

MATERIALS AND METHODS

The study will focus on women with singleton pregnancies who visited the maternity ward of Niğde Training and Research Hospital between January 2021-2024. Patient history, including systemic and obstetric history as well as sociodemographic characteristics, was obtained from hospital case records after delivery. It is important to note that the study excludes multiple pregnancies, malformed babies, or births that occurred elsewhere.

The study included 100 women with gestational ages ranging from 24 to 37 weeks who were diagnosed with PPROM based on ultrasonographic and clinical examination. Gestational age was calculated using the most recent menstrual cycle and, if available, ultrasonographic data. 100 control women (≥37 weeks' gestation) who did not have any pregnancy issues, such as PPROM, early contractions, or vaginal bleeding, were included in the control group (term birth group). A survey was conducted to obtain information about literacy, socioeconomic status, and negative oral habits such as tobacco and alcohol use.

Statistical Analysis

The statistical analysis was performed using Jamovi software (Version: 2.3.21). Descriptive analysis was conducted, followed by a Chi-square test to compare the PPROM and control groups. Binomial logistic regression analyses were performed to predict PPROM. Significance was established at $p<0.05$.

RESULTS

Those who are illiterate, those who are obese, those who have urinary tract infections, those who have had abortions before, those who have pregnancies more than two, those whose previous birth was before two years, those who had a premature birth before experienced significantly more PPROM ($p=0.033$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, respectively).No significant difference was found between control and PPROM regarding age range, number of births, birth type, and coffee use ($p=0.334$, $p=0.131$, $p=0.057$ and $p=0.077$ respectively) (Table 1).

The model used for the binominal logistic regression analysis of the PPROM explained 51% of the variance ($R^2_{MCF} =0.51$). Obesity (OR=7.63), urinary tract infection (OR=3.57), previous birth which less than two years (OR=7.53), preterm birth before then (OR=13.42), smoking/alcohol use (OR=15.97), and medicine use (OR=3.77) were significant predictors. ($p<0.05$). In the ROC analysis, the cut-off value was set at 0.5, and the constructed model was seen to have 84% sensitivity and 84% specificity (Fig 1, Table 2).

DISCUSSION

PPROM is a condition that gynecologists and obstetricians aim to prevent due to the potential neonatal complications it can cause. It is crucial to identify the risk factors and take appropriate preventive measures to minimize the risk of complications. According to Bouvier et al,[7] inadequate education, infections, and a history of preterm or PPROM are commonly associated with PPROM. Singh et al.[8] noted a significant increase in intrapartum urinary tract infections in cases of PPROM. Our study found that patients with lower education levels and urinary tract infections had a higher incidence of PPROM.

According to Okeke's study, the primigravida group had the highest incidence of preterm PROM at 29.1%.[9] Similarly, the Endale study reported that the highest incidence of PPROM was observed in the primigravida group at 69.7%.[10] Singh identified multiparity as a cause of PPROM.[8] It is worth noting that multiparous women are more susceptible to infections due to the faster cervical dilation process compared to nulliparous women, which may lead to premature rupture of membranes. It has been observed that the connective tissue in multiparous women is relatively looser than in nulliparous women, which may result in a higher likelihood of premature membrane rupture in the former group.[11]

The study conducted by Assefa in Ethiopia suggests that

Table 1. Comparison of control PPROM based on various parameters using the chi-square test.

	Control (N=100)	PPROM (N=100)	p value
age range			0.334
16-25	40 (40%)	34 (34%)	
26-41	60 (60%)	66 (66%)	
education			**0.033**
ılliterate	6 (6%)	17 (17%)	
primary school	37 (37%)	42 (42%)	
high school	30 (30%)	27 (27%)	
university	27 (27%)	14 (14%)	
bmi (kg/m^2)			**< 0.001**
normal	26 (26%)	8 (8%)	
overweight	42 (42%)	38 (38%)	
obese	32 (32%)	54 (54%)	
urinary tract infection			**< 0.001**
none	70 (70%)	30 (30%)	
present	30 (30%)	70 (70%)	
abortion			**< 0.001**
no	46 (46%)	23 (23%)	
yes	54 (54%)	77 (77%)	
number of pregnancies			**< 0.001**
1	30 (30%)	6 (6%)	
2-3	52 (52%)	70 (70%)	
≥4	18 (18%)	24 (24%)	
number of births			0.131
only one	68 (68%)	57 (57%)	
more	32 (32%)	43 (43%)	
previous birth			**< 0.001**
none	0 (0%)	7 (7%)	
<2 years	15 (15%)	52 (52%)	
=>2 years	85 (85%)	41 (41%)	
birth type			0.057
c/s	45 (45%)	58 (58%)	
nvd	55 (55%)	42 (42%)	
premature birth before			**< 0.001**
no	94 (94%)	63 (63%)	
yes	6 (6%)	37 (37%)	
coffee			0.077
no	78 (78%)	66 (66%)	
yes	22 (22%)	34 (34%)	
smoke, alcohol			**< 0.001**
no	92 (92%)	49 (49%)	
yes	8 (8%)	51 (51%)	

bmi: body mass index, c/s: cesarean section, nvd: normal vaginal delivery

there may not be a significant association between PPROM and gravida.[12] However, in our study, we observed that it occurred more frequently in multiparas than in primiparas. Furthermore, previous studies have shown that PPROM is more common in women with maternal obesity,[13-15] which has been linked to elevated systemic inflammation.[16,17] The higher incidence of PPROM in obese women has been attributed to both local infection and systemic inflammation, which is consistent with the current literature. In our sample, it was observed that obese women experienced earlier PPROM and birth compared to non-obese women.[14,16]

It has been observed that the age of the mother can be a significant risk factor for PPROM. If the mother is under 20, the female reproductive organs are not ready for pregnancy, which can affect the formation of the amniotic membranes, making them abnormal. In addition, for those over 35, there is a decrease in the function of the reproductive organs, which affects the process of embryogenesis, causing the amniotic fluid to become thinner and more prone to premature rupture.[18] Furthermore, Hackenhaar et al.[19] reported that women aged 30 years and above may have a higher likelihood of developing PPROM. The study suggests that age may not be a significant factor in the development of PPROM. The occurrence of PPROM was found to be statistically linked to a history of preterm delivery, which is consistent with findings from literature in the US, Canada, and China.[20,21] However, Assefa et al.[12] reported no correlation between PPROM
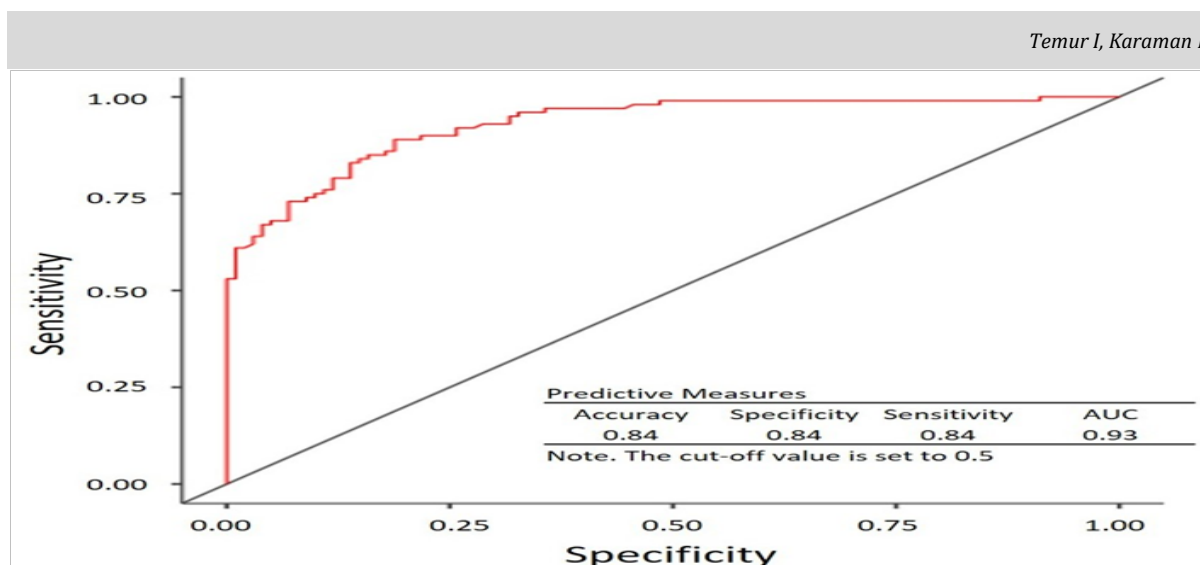
Figure 1. This ROC curve displays the sensitivity and specificity performance of a classification model. The model has an AUC value of 0.93, indicating high predictive accuracy. The threshold value is set at 0.5.

Table 2. Binominal logistic regression analysis that was conducted for the prediction of PPROM

Model 1	R^2_{MCF}= 0.51						
Predictor	Estimate	SE	Z	p	Odds ratio	Lower (95% Cl)	Upper (95% Cl)
intercept	-3.47	1.3	-2.66	**0.008**	0.03	0	0.4
age range:							
26-41 – 16-25	1.06	0.55	1.91	0.056	2.88	0.97	8.54
education:							
primary school – illiterate	0.5	0.76	0.65	0.515	1.64	0.37	7.3
high school – illiterate	0.25	0.76	0.33	0.744	1.28	0.29	5.63
university – illiterate	-0.97	0.85	-1.14	0.254	0.38	0.07	2.01
bmı:							
overweight – normal	1.45	0.75	1.93	0.053	4.24	0.98	18.41
obese – normal	2.03	0.77	2.63	**0.008**	7.63	1.68	34.66
urinary tract infection:							
present – none	1.27	0.47	2.72	**0.007**	3.57	1.43	8.93
abortion:							
yes – no	0.88	0.55	1.6	0.109	2.4	0.82	7.03
number of pregnancies:							
2-3 – 1	0.48	0.92	0.52	0.604	1.61	0.27	9.71
≥4 – 1	0.99	1.06	0.93	0.351	2.69	0.34	21.56
number of births:							
more – only one	-0.56	0.62	-0.91	0.361	0.57	0.17	1.91
previous birth:							
<2 years – ≥2 years	2.02	0.5	4.08	**<.001**	7.53	2.85	19.9
birth type:							
nvd – c/s	-0.86	0.51	-1.69	0.091	0.42	0.16	1.15
premature birth before:							
yes – no	2.6	0.67	3.88	**<.001**	13.42	3.62	49.82
coffee:							
yes – no	-0.41	0.53	-0.78	0.436	0.66	0.23	1.87
smoke, alcohol:							
yes – no	2.77	0.59	4.67	**<.001**	15.97	4.99	51.1

Note. Estimates represent the log odds of "Group = PPROM" vs. "Group = Control", R^2_{MCF}: McFadden's R^2

and a history of preterm birth in Ethiopia. In the present study, we observed that the history of premature birth was associated with PPROM.

Several studies conducted in different countries, including the USA, Lithuania, India, China, and Uganda, have identified a history of abortion as a potential risk factor for PROM.[21-23] In our study, we also found a significant association between abortion history and PPROM. However, we did not find a significant association between cesarean section history and PPROM. During the first trimester, it has been suggested that cigarette use by mothers may be a significant risk factor for PPROM.[24,25] However, based on our study, we did not find a significant association between coffee consumption and PPROM.

According to the study, a shorter birth interval in a previous pregnancy may not have allowed enough time for inflammation at the maternal-fetal interface to heal, which could lead to an increased risk of PPROM in a subsequent pregnancy.[26,27] The research indicates a significant increase in the risk of PPROM in the second pregnancy when the interval between births is less than 24 months. Although the retrospective nature of our study is considered a limitation, as in similar studies in literature, we think that this limitation has been overcome thanks to our strict patient selection criteria. As a result, the risks that may cause PPROM remain unclear, and our study may contribute to the literature at this point.

CONCLUSIONS

Smoking and alcohol use, as well as a history of previous preterm birth, have been identified as the most significant risk factors influencing the risk of PPROM. It is recommended that healthcare professionals evaluate pregnant women who may be at risk for PPROM as they give prenatal care.

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