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To investigate urogenital infections in patients diagnosed with preterm premature rupture of the membranes and their impact on perinatal outcomes

Prematüre membran rüptürü tanısı alan hastalarda ürogenital enfeksiyon ve perinatal sonuçlara etkisi

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ABSTRACT

Aim: To Investigate Urogenital Infections In Patients Diagnosed With Preterm Premature Rupture Of The Membranes (PPROM) And Their Impact On Perinatal Outcomes.

Material and Methods: This retrospective study was conducted at the Perinatology Clinic of Ankara Bilkent City Hospital between June 2020 and December 2023 and included 250 patients diagnosed with PPROM who were followed up and treated in the high-risk pregnancy Vaginal and urine cultures were obtained from each patient, and the impact of culture positivity on perinatal outcomes was assessed.

Results: Among these, 72 patients tested positive on culture, while 178 tested negative. Of the obtained vaginal cultures. Membrane rupture was found to occur at significantly earlier weeks in those with a positive culture test ($p<0.05$) and the latent period was longer in those with a positive culture test ($p<0.001$). While the gestational age at delivery was significantly smaller in the culture positive group compared to the culture negative group ($p<0.05$), the NICU admission was significantly higher ($p<0.05$).In the sperman correlation test, a positive correlation was found between culture positivity and NICU admission (r;0.155, p:0.05).

Conclusion: In conclusion, urogenital infections cause preterm delivery in the early weeks and increase neonatal intensive care unit admission.

Keywords: Candida, preterm premature rupture of the membranes, ürovaginal culture

ÖZ

Amaç: Bu çalışmadaki amacımız pprom tanılı hastalarda ürogenital enfeksiyonu ve bu enfeksiyonun perinatal sonuçlara etkisini incelemektir.

Gereç ve Yöntemler: Bu çalışma Ankara Bilkent Şehir Hastanesi Perinatoloji Kliniğinde Haziran 2020-Aralık 2023 tarihleri arasında retrospektif olarak tasarlandı. Çalışmaya yüksek riskli gebelik bölümünde takip ve tedavi olmuş pprom tanılı 18-45 yaş arası 24-37. gebelik haftalarındaki hastalar dahil edildi. Her hastanın vajinal kültür ve idrar kültür sonucu incelendi.Kültür testi pozitifliğinin perinatal sonuçlara etkisi incelendi.Hastanemizdeki veri tabanı kullanılarak 272 hasta retrospektif olarak tarandı.Bunlardan 22 hastanın kültür sonucuna ulaşılamadığından 250 hasta çalışmaya kabul edildi.

Bulgular: Kültür testi pozitif olan 72 hasta (grup1) ve kültür testi negatif(grup2) 178 hasta tespit edildi. Kültür pozitif olan hasta grubunda Pprom'un gerçekleştiği hafta daha erken olduğu tespit edildi($p<0.05$).Latent periodun da kültür pozitif olan hastalarda daha uzun olduğu tespit edildi($p<0.001$). Kültür pozitif grupta doğumdaki gebelik yaşı kültür negatif gruba göre anlamlı olarak daha küçükken ($p<0.05$), yoğun bakım ünitesine yatış anlamlı olarak daha yüksekti ($p<0.05$). Sperman korelasyon testinde kültür pozitifliği ile yoğun bakım ünitesine yatış arasında pozitif bir korelasyon bulundu.(r;0.155, p:0.05).

Sonuçlar: Sonuç olarak, ürogenital enfeksiyonlar erken haftalarda preterm doğuma neden olmakta ve yenidoğan yoğun bakım ünitesine yatışı artırmaktadır.

Anahtar Kelimeler: Candida, preterm erken membran rüptürü, ürovajinal kültür

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INTRODUCTION

Preterm premature rupture of the membranes (PPROM) is defined as the rupture of membranes before the 37th week of gestation and occurs in approximately 3% of pregnancies [1-3]. The strength and integrity of fetal membranes are composed of extracellular membrane proteins, including collagen, fibronectin, and laminins [4]. Matrix metalloproteinases increase collagen degradation, thereby reducing membrane strength [5]. Various pathological events, such as subclinical or overt infection, inflammation, mechanical stress, and bleeding, can disrupt homeostatic processes and initiate a series of biochemical changes resulting in PPROM [6]. Genital system infection is the most commonly identifiable risk factor for this condition [7].

The likelihood of having pathogenic microorganisms in the amniotic fluid is significantly higher in patients with PPROM These patients also have a higher rate of histological chorioamnionitis, and the frequency of PPROM is significantly higher in those with genital tract infections, especially bacterial vaginosis, compared to non-infected patients [6].

Most microorganisms colonizing the lower genital tract have the capacity to produce phospholipase, which can stimulate prostaglandin production and thereby initiate uterine contractions [8]. In addition, the host's immune response to bacterial invasion of the endocervix and/or fetal membranes can lead to localized weakening of the fetal membranes and the production of multiple inflammatory mediators, which may result in PPROM [9]

This study aimed to investigate urogenital infection in patients diagnosed with PPROM and determine its impact on perinatal outcomes.

MATERIAL AND METHODS

This study was retrospectively designed at the Perinatology Clinic of Ankara Bilkent City Hospital between June 2020 and December 2023 and included patients aged 18 to 45 years diagnosed with PPROM who were followed up and treated in the high-risk pregnancy unit at 24-37 weeks of gestation. Ethical approval for the study was obtained from the Ethics Committee of the hospital (approval number: E2-24-64-68). Informed consent was obtained from each patient before starting the study.

The principles of the Helsinki Declaration were adhered to at every stage of the study.

Patients were diagnosed with PPROM if active leakage of amniotic fluid was observed or if the placental alpha microglobulin-1 (AmniSure®) test was positive. According to our clinic's protocols, urine and servicovaginal cultures are obtained from every patient diagnosed with PPROM before starting prophylactic ampicillin + penicillin treatment. The cultures were stained with gram stain in the microbiology laboratory of our hospital and cultures were inoculated in blood, chocolate, macro and sabouraud agar. The growth in the cultures was photographed at 18th hour and 36th hour. The growth at 36th hour was recorded as the culture result and Nugent scoring was performed.

The Latent Period was determined as the period between the week when pprom occurred and the week of birth. The latent periods of the patients were recorded.

For all patients diagnosed with PPROM under 34 weeks of gestation, two doses of betamethasone were administered 24 hours apart for fetal lung development. Prophylactic antibiotics (ampicillin+penbisin) were started in all patients diagnosed with PPROM.

White blood cell(wbc) and c reactive protein(CRP) levels of each patient at the time of delivery were recorded.

For each patient included in the study, clinical and demographic data, including age, parity, gestational week at PPROM diagnosis, results of vaginal and urine cultures, latent period (time from the week of PPROM diagnosis to delivery), week of delivery, mode of delivery, newborn birth weight, first- and fifth-minute Apgar scores, and the need for neonatal intensive care, were retrospectively obtained from the hospital's database. Patients with multiple pregnancies, those with a gestational age less than 24 weeks, immunosuppressed patients, organ transplant recipients, patients carrying fetuses with known or suspected major structural or genetic anomalies, those with chronic diseases,patients with chronic diseases that are prone to infection and those for whom data was not accessible were excluded from the study.

Statistical analysis

The statistical software SPSS 22.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. The normal distribution of the data was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was employed to compare non-normally distributed variables. Descriptive analyses were conducted using the median and minimum-maximum values for non-normally distributed variables. The chi-square test was utilized to compare categorical variables. Spearman correlation coefficient was used .A p-value less than 0.05 was considered statistically significant.

RESULTS

This study retrospectively examined 272 patients. Twenty-two patients were excluded from the study since the culture result could not be found.Thus, a total of 250 patients were included in the sample. Among these, 72 patients tested positive on culture (Group 1), while 178 tested negative (Group 2). Of the obtained vaginal cultures, 46 patients were identified as culture-positive. Among these culture-positive cases, Candida was detected in 36 patients (78%) (Table 2) Additionally, 32 patients had positive results on urine culture. The distribution of microorganisms in urine cultures revealed that 21 patients (65%) had results indicating diverse species (Table 3).

Table I presents the clinical and demographic data, as well as the biochemical results of the patients included in the study, pregnancy details, delivery information, and newborn outcomes for both groups. There was no statistical difference between the gravida, parity,birth weight,wbc,crp, 1st and 5th minute apgar scores of both groups (p>0.05) (Table 1). Age was found to be significantly younger in the culture test positive group (p<0.05) (Table 1).

Membrane rupture was found to occur at significantly earlier weeks in those with a positive culture test (p<0.05) and the latent period was longer in those with a positive culture test (p<0.001) (Table 1).

While the gestational age at delivery was significantly smaller in the culture positive group compared to the culture negative group (p<0.05), the NICU admission was significantly higher (p<0.05) (Table 2). In the sperman correlation test, a positive correlation was found between culture positivity and NICU admission (r;0.155, p:0.05) (Table 4).

No statistically significant differences were found between Group 1 and Group 2 in terms of gravidity, parity, white blood cell (WBC) count, C-reactive protein (CRP), newborn outcomes, or mode of delivery (p>0.05).

DISCUSSION

In this study, genitourinary culture results were analyzed in PPROM patients. The most common microorganism detected in

Table 1. Clinicodemographic data of the patients and newborn outcome

Variables	Group 1 (n = 78)	Group 2 (n = 172)	*p* value
Maternal Age	25.0 (17-39)	27.0 (16-44)	0.02
Gravida	2.0 (1-6)	2.0 (1-8)	0.27
Parity	0.00 (0-5)	1.0 (0-7)	0.26
Latent period	10 (0-98)	3 (0-80)	0.00
Week of PPROM	32.00 (24-36)	33.10 (24-37)	0.04
WBC	11.18(5.13-19.54)	11.07(5.27-24.63)	0.85
CRP	0.06(0.65-53.56)	1.55(0.00-96.40)	0.86
Birth Week	34.65(27-35.4)	35.1(27.3-36.2)	0.03
Birth Weight	2370(1070-2840)	2535(985-2890)	0.25
First-minute Apgar score	7 (1-9)	7 (0-9)	0.18
Fifth-minute Apgar score	8 (1-9)	8 (0-10)	0.17
NICU	30 (48.4%)	63 (42.9%)	0.45

Group 1: culture-positive patients, Group 2: culture-negative patients, PPROM: preterm premature rupture of the membranes, White blood cell(wbc) ,c reactive protein(CRP)

Table 2. Distribution of microorganisms in vaginal culture results

Number of patients	46
Candida	36 (78%)
Klebsiella	1 (2.1%)
Gram-negative bacillus	2 (4.3%)
Mixed flora	2 (4.3%)
Proteus mirabilis	1 (2.1%)
Escherichia coli	2 (4.3%)
Pseudomonas aeruginosa	1 (2.1%)
Candida + Klebsiella	1 (2.1%)

Table 3. Distribution of microorganisms in urine culture results

Number of patients	32
Escherichia coli	5 (15%)
Candida	2 (6%)
Multiple different species	21 (65%)
Proteus mirabilis	1 (3.1%)
Ureaplasma	1 (3.1%)
Klebsiella	1 (3.1%)
Streptococcus agalactiae	1 (3.1%)

Table 4. Spearman correlation of the Culture test and NICU

Variables	NICU	
	r	p
Culture test	0.155	0.05

r : correlation coefficient
NICU: neonatal intensive care unit
p<0.05 statistically significant

genitourinary culture results was candida. NICU admission was higher in patients with positive culture test than in patients with negative culture test.

PPROM occurs in 3% of pregnancies and causes one third of all spontaneous preterm deliveries [10].

Genital tract infection is the most common identifiable risk factor for PPROM[6].

The important role of genitourinary infections in the etiology of PPROM formed the basis of this study.

Lactobacillus species, which are the predominant vaginal bacteria in the majority of women, keep the vaginal environment acidic (ph: 3.5-4.5) with hydrogen peroxide produced by Lactobacillus species, preventing the overgrowth of pathogenic microorganisms and improving both the health status of the woman and the pregnancy outcomes in pregnancy. When this balance is disrupted, it has been found to contribute to the overgrowth of pathogens that cause complex vaginal infections such as bacterial vaginosis (BV), sexually transmitted infections (STIs) and vulvovaginal candidiasis (VVC) [11]. The increased estrogen level during pregnancy stimulates the transformation of Candida species, a member of the vaginal flora, from yeast to yeast and the production of glycogen in the vaginal epithelium. As a result, it creates a carbon source that colonized Candida species can easily use. For this reason, the incidence of Candida increases in pregnant women [12-15]. In a study in which data from many countries were analyzed, it was determined that Candida was the most common microorganism in pregnant women [16].

Although Candida is commonly colonized in healthy people, it is also responsible for mucosal infections and serious invasive diseases [17]. Candida causes intrauterine inflammation leading to various adverse pregnancy outcomes such as premature rupture of membranes, which is an important cause of preterm delivery [18]. A study examining cases of Candida-associated chorioamnionitis found that the most common predisposing condition was rupture of membranes [19].

In another study of patients with PPROM below 32 weeks of gestation whose postpartum placenta was sent to pathology, Candida infection was detected in 8% of patients [20].

Studies have found that morbidity and mortality in PPROM are primarily associated with preterm birth [21]. Prematurity poses a potential risk in newborns because many organs, including the central nervous system, lungs and cardiovascular system, fail to complete full development [22].

In our study, the reason for NICU admission was preterm birth.

The limitations of this study were that it was a single-center retrospective cohort study.

In conclusion, candida is the most common microorganism detected in urogenital infections and urogenital infections cause preterm delivery in the early weeks and increase neonatal intensive care unit admission.

Ethics Committee Approval: Approval for the study was obtained from the Ethics Committee of the hospital (number: E2-24-6468). The principles of the Declaration of Helsinki were followed at every stage of the study.

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Conflict of Interest: The authors state no conflicts of interest.

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