

Relationship between Urogenital Culture Positivity and Threatened Preterm Labor in Pregnant Women

Gebe Kadınlarda Ürogenital Kültür Pozitifliği ile Erken Doğum Tehdidi İlişkisi

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ÖZ

Amaç: Erken doğumla sonuçlanan preterm eylem tehdidi (TPL), gebelik komplikasyonları ve yenidoğan morbiditesinin en sık görülen sebeplerinden biri olarak bilinmektedir. Bu çalışmada, TPL olan hastalarda pozitif ürogenital kültür ile erken doğum eylemi arasındaki ilişki araştırılmıştır.

Araçlar ve Yöntem: 2018 ile 2022 yılları arasında TPL nedeniyle takip edilen hastaların tıbbi dosyaları değerlendirildi. Demografik verileri, gestasyonel hikayeleri, vaginal swab ve idrar örneklerinin sonuçları kaydedildi. Transvaginal ultrasonografi (TVUS) ile preterm ve term doğum sırasındaki servikal uzunluk ölçümleri yapılarak, <25mm, <20mm ve <15mm olarak derecelendi. İstatistiksel analizler Chi square, Mann Whitney U ve Pearson's korelasyon (r) testleri ile yapıldı. P<0.05 değeri anlamlı olarak kabul edildi.

Bulgular: TPL ile takip edilen 202 hasta çalışmaya dahil edildi. Hastaların yaklaşık yarısında (%40-50) vaginal kültür pozitif bulunurken, bu oran idrar kültüründe çok daha az (%10-15) idi. Erken preterm, geç preterm ve term doğum yapan hastalar arasında hem vaginal hem de idrar kültürleri açısından bir farklılık saptanmadı (p>0.05). Bununla birlikte, erken ve geç preterm doğumlarda, servikal uzunluğun kısalmasına paralel olarak (CL<15mm) pozitif kültür sonuçlarının arttığı tespit edildi (p<0.05). Candida, Staphylococcus ve Escherichia türleri en sık olarak izole edildi.

Sonuç: TPL olan hastalarda ürogenital kültür sonuçları preterm ve term doğumlar açısından anlamlı farklılık göstermemekle birlikte (r=0.19), servikal uzunluktaki azalma ile paralel şekilde artış gösteren kültürde üremenin (r=0.74) erken eylemi başlatma potansiyeli göz ardı edilmemelidir.

Anahtar Kelimeler: erken doğum tehdidi; idrar kültürü; preterm eylem; ürogenital enfeksiyon; vaginal kültür

ABSTRACT

Purpose: Preterm labor (TPL), which can result in preterm birth, is known as one of the most common causes of pregnancy complications and neonatal morbidities. This study investigates the relationship between positive urogenital culture and preterm labor in patients with TPL.

Materials and Methods: Between 2018 and 2022, medical records of patients monitored due to threatened preterm labor (TPL) were reviewed. Demographic data, gestational histories, and results of vaginal swabs and urine samples were recorded. Transvaginal ultrasound was used to measure cervical length during preterm and term births, categorized as <25mm, <20mm, and <15mm. Statistical analyses were conducted using Chi-square, Mann-Whitney U, and Pearson's correlation (r) tests. A significance level of P<0.05 was considered statistically significant.

Results: A total of 202 patients monitored for TPL were included. Approximately half of the patients (40-50%) tested positive for vaginal culture, whereas this rate was much lower in urine culture (10-15%). There was no significant difference in terms of both vaginal and urine cultures among patients who had early preterm, late preterm, and term births (p>0.05). However, it was observed that positive culture results increased parallel to cervical length shortening (CL<15mm) in both early and late preterm births (p<0.05). Candida, Staphylococcus, and Escherichia species were the most frequently isolated organisms.

Conclusion: In patients with TPL, urogenital culture results did not show significant differences between preterm and term births (r=0.19). However, it is crucial not to overlook the potential of culture positivity (r=0.74) increasing in parallel with cervical length reduction to initiate early labor.

Keywords: preterm delivery; threatened preterm labor; urine culture; urogenital infection; vaginal culture

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INTRODUCTION

Threatened preterm labor (TPL) is defined as advanced cervical dilatation and ripening caused by regular uterine contractions before pregnancy week 37 that can result in a preterm birth. Preterm birth is the most common cause of neonatal morbidity and mortality worldwide, and it constitutes over 80% of total fetus death rates.¹ It occurs in up to 20% of pregnancies, and is a common cause of hospital admissions during the antenatal period.^{1,2} To prolong gestation and to improve neonatal outcomes, several management methods for preterm labor have been extensively studied, i.e., corticosteroids, antibiotics and tocolytics.³ However, its incidence continues to rise largely due to its pathophysiology that is not yet understood and the scarce of effective treatment.⁴

Patients with a history of preterm labor, pregnancy with twins or other multiplies, placental and amniotic fluid problems or vaginal bleeding, and some other chronic problems may aggravate preterm birth.^{4,5} Demographic features, stressful events during gestation and urogenital infections are also among risk factors.⁵ Although evidence that research for vaginal and urinary infections in women admitted for TPL is helpful to identify those at increased risk of preterm birth, there are also many recent publications suggesting no clinical significances of the positivity of disease causing bacteria from urinary tract as a predictor of preterm birth and its outcome.^{6,7} Therefore, even the prevalence seems to be very high, value of urogenital infection screening is still debatable.

In current study, we aimed to study women admitted to our clinics due to TPL to investigate probable effects of positive urogenital culture on pregnancy and the overall outcome.

MATERIALS and METHODS

The present study was approved by the Clinical Research Ethics Committee of S. B. U. Istanbul Training and Research Hospital (dated 24.03.2023 and numbered 82). Patient charts of patients who were hospitalized for TPL between January 2018 and December 2022 were reviewed. Demographics, gestational and maternal history, and culture results of both vaginal swab and urine sample of each

patient with TPL were recorded at Excel program (1997, Illionis, US) for data evaluation. Transvaginal ultrasonographic (TVUS) measurement of cervical lengths (in millimeters, mm) were done in each patient during preterm or term delivery, and graded as <25mm, <20mm and <15mm. Patients with early membrane rupture and those with missing information in their files (TVUS findings, urine culture or vaginal culture results, etc.) were excluded from the study. Patients with multiple gestations, previous preterm labor, active infections and cervical surgery were also excluded.

TPL was defined as any symptom of possible uterine contractions including crampy belly pain, low lying back pain or a feeling of pelvic pressure leading to cervical advancement for which women were admitted before 37 weeks of gestation. After confirmation of diagnosis, management was started as bed rest, magnesium sulfate, antibiotics and tocolytics. Despite these measures, preterm delivery (<37 weeks of gestation) was inevitable in some patients, and these were classified as: early preterm delivery <34 weeks and late preterm delivery at or >34 weeks. Normal term delivery was defined as giving birth at or after 37 weeks of gestation.

Statistical Analysis

SPSS (Statistical Package for Social Sciences, version 13, IBM Corp., Armonk, NY, USA) was used for all statistical analyses. Descriptive statistics were reported as number (N), percentage (%), median value with standard deviation (SD). The Chi-square test was employed for nominal and categorical variables, while the Kolmogorov-Smirnov test was used to compare non-parametric variables. Group comparisons were conducted using the Mann-Whitney U test to identify differences between groups, and Pearson's correlation test (correlation coefficient, r) was used to examine relationships between variables. The sample size was determined based on a pilot study of 50 cases, which revealed a 13% positive culture rate of the genitourinary tract, with a confidence level of 95% and a margin of error of 5%. A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

Both vaginal and urine culture were available in 202 out of 239 patients with TPL. Maternal age and gestational history including parity were not different statistically (each, $p>0.05$). Gestational week at admission due to TPL was 30

to 32 weeks of pregnancy, but measures taken were sufficient to ensure term delivery in 91 patients (45%). However, preterm delivery was inevitable in 111 (54.9%), and almost half of them gave birth before pregnancy week of 34 (Table 1).

Table 1. Gestational history of patients with threatened preterm labor (TPL) resulting in preterm or term delivery.

Variables	Preterm (n=111)		Term (n=91)
	Early † (n=56)	Late †† (n=55)	
Gestational week at admission	30.7±3.1	32±3.2	32±3.1
Gestational week at delivery	31.6±2.4	35.4±2.9	8.6±3.3
Maternal age (years, mean±SD)	27.2±6.9	26.9±7.1	28.05±8.6
Parity (n, %)			
Multiparity	26 (46.4%)	25 (45.4%)	38 (41.7%)
Nulliparity	30 (53.5%)	30 (54.5%)	53 (58.2%)
Risk factors and comorbidities			
Smoking	6 (7.1%)	5 (9%)	10 (10.9%)
Obesity (BMI>25)	6 (7.1%)	4 (7.2%)	9 (9.8%)
Diabetes mellitus	1 (1.7%)	2 (3.6%)	4 (4.3%)
Hypertension	2 (3.5%)	1 (1.8%)	3 (3.2%)

Preterm: delivery <37 week; †Early preterm: delivery <34 week; ††Late preterm: delivery at or >34 week; Term: delivery at or >37 week; n: number, %: percent, SD: standard deviation; BMI: body mass index

While the number of patients with and without positive vaginal culture was close to each other ($p>0.05$), in majority of patients with TPL, urine culture was negative ($p<0.01$). Furthermore, both vaginal and urine culture results showed no statistical difference among patients with early preterm, late preterm and term deliveries ($p>0.05$, $r=0.19$, Table 2). On the other hand, positive culture rate was seen to significantly increase in parallel with a decrease in cervical length (CL<15mm at late preterm delivery with positive vaginal swab and CL<15mm at early preterm delivery with

positive urine sample; each, $p<0.05$, $r=0.74$). Growth in urine culture of late preterm deliveries was also remarkable, but statistically insignificant

Most commonly isolated microorganisms from vaginal swabs were *Candida (albicans) spp.*, *Staphylococcus (hemolyticus) spp.*, *Streptococcus spp.*, *Enterobacteria* and *Klebsiella spp.* (each, $p<0.05$), while those growing in urine samples were *Escherichia coli* ($p<0.01$) and *Staphylococcus spp* ($p<0.05$) (Table 3).

Table 2. Culture results in different cervical lengths.

Variables	Preterm (n=111)		Term (n=91)
	Early † (n=56)	Late †† (n=55)	
Positive vaginal culture	22 (39.2%)	21 (38.1%)	43 (47.2%)
CL<25mm	8 (36.3%)	3 (14.2%)	15 (34.8%)
CL<20mm	7 (31.8%)	5 (23.8%)	15 (34.8%)
CL<15mm	7 (31.8%)	13 (61.9%)*	13 (30.2%)
Negative vaginal culture	34 (60.7%)	34 (61.8%)	48 (52.7%)
CL<25mm	11 (32.3%)	11 (32.3%)	16 (33.3%)
CL<20mm	13 (38.2%)	9 (26.4%)	17 (35.4%)
CL<15mm	10 (29.4%)	14 (41.1%)	15 (31.2%)
Positive urinary culture	8 (14.2%)	6 (10.9%)	9 (9.8%)
CL<25mm	1 (12.5%)	1 (16.6%)	3 (33.3%)
CL<20mm	1 (12.5%)	2 (33.3%)	3 (33.3%)
CL<15mm	6 (75%)*	3 (50%)	3 (33.3%)
Negative urinary culture	48 (85.7%)**	49 (89%)**	82 (90.1%)**
CL<25mm	15 (31.2%)	13 (26.5%)	27 (32.9%)
CL<20mm	15 (31.2%)	7 (34.6%)	30 (36.5%)
CL<15mm	18 (37.5%)	19 (38.7%)	25 (30.4%)

Preterm: delivery <37 week; †Early preterm: delivery <34 week; ††Late preterm: delivery at or >34 week; Term: delivery at or >37 week; CL: cervical length in millimeters (mm) measured by ultrasound; n: number, %: percent, SD: standard deviation; BMI: body mass index, * $p<0.05$: statistically significant, ** $p<0.01$: statistically very significant

Table 3. Cultured microorganisms in vaginal swabs and urine samples.

Variables	Vaginal culture (n=86)	Urinary culture (n=20)
Candida spp.	17 (19.7%)*	
Candida albicans	11 (12.7%)*	
Staphylococcus spp.	17 (19.7%)*	4 (20%)*
Staphylococcus hemolyticus	14 (16.2%)*	
Streptococcus spp.	11 (12.7%)*	3 (15%)*
Escherichia coli	9 (10.4%)	9 (45%)*
Klebsiella spp.	3 (3.4%)	2 (10%)
Enterobacteria spp.	2 (2.3%)	1 (5%)
Others	2 (2.3%)	1 (5%)

*p<0.05: statistically significant, **p<0.01: statistically very significant, spp.: species

DISCUSSION

There are many conditions and risk factors known to be associated with TPL and preterm birth, such as young maternal age, non-white race, fetal and uterine malformations, polyhydramnios, high blood pressure, diabetes, stress, smoking, multifetal gestations, placenta previa, shortened cervix, vaginal bleeding, being underweight or obese, gestation resulting from in vitro fertilization (IVF), previous preterm labors, clotting or bleeding problems, certain vaginal infections, sexually transmitted diseases (STDs) and urinary tract infections (UTIs), etc.^{4,5} Some of these risk factors are modifiable, meaning they might be changed or treated to reduce the overall risk. One of them is urogenital bacterial colonization and subsequent infection. Recent studies have confirmed a relationship between bacterial vaginosis and TPL, with adjusted odds ratios between 1.5 and 7.⁸ It has also been reported that diagnosing and managing the patients having urogenital infections at a stage, where it has not shown clinical findings, will decrease the percentage of TPL and might improve perinatal outcome.⁹ Although several recent studies have investigated the role of screening for bacterial vaginosis in asymptomatic patients and many more studies evaluated vaginal and urinary infections in women with TPL, none of these focused on the possible role of micro-biological specimens as a predictive tool in those patients admitted for TPL.^{10,11} On the other hand, there are increasing number of recent studies interrogating the association between urogenital bacterial colonization and preterm birth, as well.^{6,7}

In the present study, we detected a positive vaginal culture in nearly half of the patients with TPL (40 to 50%), while those with positive urine culture was significantly fewer

(10 to 15%). Furthermore, both vaginal and urine culture results showed no statistical difference among patients with early preterm, late preterm and term deliveries. These results should make one think that there is no relationship between preterm birth and urogenital colonization, as suggested in previous studies of Giraldo et al and Silio et al.^{7,12} However, the most interesting finding in our study was significantly higher rates of positive cultures in parallel with a decrease in cervical length (CL<15mm), as a marker of labor induction, at early and late preterm deliveries. There should be multiple mechanisms by which urogenital colonization leads to preterm birth, but the exact pathway remains speculative. Bacterial induction of cytokines and prostaglandin release or bacterial endotoxin that is introduced into the amniotic water leading to cytokine release may start spontaneous labor.¹³ Moreover, as stated by Mancuso et al, changes in the cervical matrix may result in a shorter mid-trimester cervical length, which is recognized widely as a sign of TPL.⁸ Similarly, Cram et al have found that symptomatic bacteriuria, gonococcal cervicitis and vaginosis are strongly related with preterm delivery.¹⁴ The authors have also suggested that uterine contractions may be induced by cytokines and prostaglandins, which are stimulated by these microorganisms.

Abnormal vaginal colonization, which replaces regional floral lacto-bacillus during gestation, includes vaginosis or aerobic infections.¹⁵ Whereas bacterial vaginosis is defined by anaerobic over-growth, aerobic vaginitis is dominated by several microorganisms such as Escherichia coli, group B streptococci, or Enterococcus spp.^{15,16} There are significant differences in isolated microorganisms from vaginal swabs in different parts of the world. In Son et al's study, it has been shown that Klebsiella species are

the dominant vaginal colony.¹⁵ However, main microorganism that has been shown in Lajos et al's study was Group B Streptococcus.¹⁷ In our study, we observed both of these species, but *Candida* and *Staphylococcus* groups were found to be much more dominant. There are no significant differences in urine culture results, regarding the literature, and *Escherichia* species are isolated frequently.

Main limitation of the current study is its retrospective design and observational nature leaving the possibility of residual confounding. Follow-up examinations after delivery are also missing. However, investigation of the culture results in both vaginal and urine samples reflecting whole urogenital system and in a large number of patients, over 200 women, is its main strength.

Conclusion

In conclusion, even the urogenital culture results seem to be not significantly different in patients with TPL for preterm and term deliveries, induction of labor is still possible considering the significantly higher rates of positive cultures in parallel with a decrease in cervical length (CL<15mm, $r=0.74$, $p<0.05$). Sonographic measurements of CL in these high risk patients should be done more carefully and closely.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

The study was approved by the Clinical Research Ethics Committee of S. B. U. Istanbul Training and Research Hospital (dated 24.03.2023 and numbered 82).

Authors' Contributions

Concept/Design: AF, NU. Data Collection and/or Processing: AF, NU. Data analysis and interpretation: DCK, NU. Literature Search: AF, DCK. Drafting manuscript: AF, DCK. Critical revision of manuscript: DCK, NU.

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