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Evaluation of Vaginal Flora of Pregnant Women Using Fosfomycin*

Fosfomisin Kullanan Gebe Kadınların Vajinal Florasının Değerlendirilmesi

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Abstract: Objective: The objective of this investigation is to elucidate the influence of fosfomycin on the composition and stability of the vaginal microbiota during pregnancy. Methods: All last-trimester pregnant women who presented to Karabük Training and Research Hospital (KEAH) for delivery between August 15, 2020, and January 15, 2021, were included in this case-control study. The study group consisted of 40 pregnant women who used fosfomycin and 40 control participants who met the following criteria: Turkish-speaking, no intellectual disability, intact membranes, no vaginal bleeding, no vaginal examination within the previous 24 hours, and a negative Covid-19 test. An informed consent form was administered to all pregnant women admitted for delivery. Vaginal culture samples were obtained in the lithotomy position using transport swabs from the upper lateral walls of the mucosal membranes or fornices. Samples were inoculated into culture media in the KEAH Microbiology Laboratory on the same day under sterile conditions. Results: A statistically significant difference was found between pregnant women using fosfomycin and those not using fosfomycin in terms of pathogenic microorganism growth in the vaginal flora (p=0.002). Conclusion: The study determined that the use of fosfomycin during pregnancy leads to the growth of pathogenic microorganisms in the vaginal flora. Since antibiotics used during pregnancy do not possess toxicity exclusively toward the target pathogen, they also affect the vaginal flora. Pregnant women should be educated on maintaining vaginal flora through healthy dietary habits, proper hygiene practices, and safe sexual intercourse.
Keywords: Fosfomycin, Pregnancy, Vaginal microbiota, Vaginal culture.

Öz: Amaç: Bu araştırmanın amacı, fosfomisinin gebelik sırasında vajinal mikrobiyota kompozisyonu ve stabilitesi üzerindeki etkisini açıklığa kavuşturmaktır. Gereç ve Yöntem: Karabük Eğitim ve Araştırma Hastanesi'ne (KEAH) doğum yapmak üzere 15 Ağustos 2020 ile 15 Ocak 2021 tarihleri arasında başvuran son trimesterdeki tüm gebeler bu vaka-kontrol çalışmasına dahil edildi. Çalışma grubu, fosfomisin kullanan 40 gebe ile aşağıdaki kriterleri karşılayan 40 kontrol olgudan oluşturuldu: Türkçe konuşan, zihinsel engeli olmayan, zarları intakt, vajinal kanaması olmayan, son 24 saat içinde vajinal muayene yapılmamış ve Covid-19 testi negatif olan. Doğum amacıyla hastaneye başvuran tüm gebelere bilgilendirilmiş onam formu uygulandı. Vajinal kültür örnekleri, litotomi pozisyonunda mukozal membranların veya fornikslerin üst lateral duvarlarından transport çubukları kullanılarak alındı. Örnekler aynı gün KEAH Mikrobiyoloji Laboratuvarı'nda steril koşullarda besiyerlerine ekildi. Bulgular: Fosfomisin kullanan gebeler ile kullanmayanlar arasında vajinal florada patojen mikroorganizma üremesi açısından istatistiksel olarak anlamlı bir fark bulundu (p=0,002). Sonuç: Çalışma, gebelikte fosfomisin kullanımının vajinal florada patojen mikroorganizmaların üremesine yol açtığını göstermiştir. Gebelikte kullanılan antibiyotikler yalnızca hedef patojene özgü toksisite göstermediğinden vajinal florayı da etkilemektedir. Gebelere, sağlıklı beslenme alışkanlıkları, uygun hijyen uygulamaları ve güvenli cinsel ilişki yoluyla vajinal floranın korunması konusunda eğitim verilmelidir.
Anahtar Kelimeler: Fosfomisin, Gebelik, Vajen florası, Vajen kültürü.

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Introduction

The communities of microorganisms that inhabit the healthy human body, coexisting without causing harm and often providing beneficial functions, are collectively referred to as the normal microbial flora. The microbial community present in the vagina is known as the vaginal flora, within which *Lactobacillus species* predominate in healthy individuals (Nsereko et al., 2021).

During pregnancy, several physiological changes take place within the endocrine, immunological, and vascular systems. These alterations can increase a pregnant individual's susceptibility to infections (Gestels and Vandenplas, 2023). Pregnancy is considered a period in which susceptibility to vaginal infections increases. Disturbance of the vaginal flora during this time may contribute to intrauterine infection, fetal growth restriction, premature rupture of membranes, preterm labor, low birth weight, and puerperal infections (Yu et al., 2018).

Physiological changes that occur during pregnancy, combined with additional risk factors, increase the incidence of urinary tract infections (UTIs), including bacteriuria, cystitis, and pyelonephritis. Maternal complications associated with UTIs in pregnancy may include septic shock, maternal mortality, intrapartum fever requiring antibiotic therapy, postpartum infections requiring antibiotic treatment, pyelonephritis, preeclampsia, cesarean delivery, endometritis, chorioamnionitis, and premature rupture of membranes (Azami et al., 2019; Lee et al., 2019). Fetal complications associated with UTIs during pregnancy include sepsis, low birth weight, prematurity, premature rupture of membranes, infected amniotic fluid, intrauterine growth restriction, and perinatal mortality. Additional potential complications encompass cerebral palsy, neonatal encephalopathy, chronic lung disease, intraventricular hemorrhage, necrotizing enterocolitis, neonatal seizures, intrapartum bleeding, and congenital cardiac malformations (Azami et al., 2019). Therefore, early diagnosis and treatment of UTIs during pregnancy are essential. Owing to its high sensitivity, ease of administration, and favorable safety profile, fosfomycin is commonly preferred in the management of uncomplicated UTIs during pregnancy (Aktün et al., 2018; Çeken and Avcı, 2019; Mannucci et al., 2019).

Fosfomycin, owing to its distinctive pharmacological properties and broad antimicrobial spectrum, is a targeted antibiotic recommended for the treatment of uncomplicated UTIs. It demonstrates a broad-spectrum and rapid bactericidal activity against on many gram-positive bacteria, such as *E. faecalis* isolated from uncomplicated UTIs, as well as most gram-negative bacteria, including *E. coli* (Aşgın et al., 2018). First derived from *Streptomyces cultures* in Spain in 1969 and initially named phosphonomycin, fosfomycin trometamol has been used for many years in the treatment of various infections, primarily UTIs. Despite its long-standing clinical use, it remains one of the few antibiotics worldwide with an exceptionally low incidence of *E. coli* resistance (approximately 1%). In addition to low resistance rates, fosfomycin possesses several noteworthy attributes, including favorable pharmacokinetic and pharmacodynamic properties, strong in vitro activity, proven clinical efficacy, and high tolerability and safety. It is classified as a "Category B" drug by the FDA, although antibiotic resistance patterns can vary considerably among different countries (Uzun et al., 2012; Aktün et al., 2018).

Literature studies have demonstrated that vaginal flora undergoes alterations during pregnancy and that antibiotic use can influence its composition. However, research investigating the effects of antibiotics on the structure and function of the vaginal flora remains limited. This study aims to address this gap by evaluating the effects of fosfomycin exposure on the growth of pathogenic microorganisms within the vaginal microbiota.

Methods

This case-control study was conducted between August 15, 2020, and January 15, 2021, at Karabük University Training and Research Hospital. The study population consisted of all pregnant women in their last trimester (28–40 weeks of gestation) who presented to the hospital for delivery during this period.

The study group included 40 pregnant women at Karabük University Training and Research Hospital who met the inclusion criteria and had used fosfomycin during pregnancy. The control group comprised an equal number of pregnant women, randomly selected from those meeting the inclusion criteria during the same period. Pregnant women were excluded from the study if they met any of the following criteria: difficulty speaking or understanding Turkish, intellectual disabilities, intact membranes or bleeding, vaginal examination within the previous 24 hours, declining to participate in the study, a positive COVID-19 test.

Approval for this study was obtained from the Karabük University Non-Interventional Clinical Research Ethics Committee (Decision No: 7/7, Date: 11/11/2019). The samples were collected from pregnant women who provided written informed consent. To minimize anxiety in the participants, sample collection was synchronized with the routine vaginal examination at the time of hospital admission for delivery, as recommended by the attending obstetrician. Samples were obtained by the investigator with participants in the lithotomy position on a gynecological examination table, using Cultiplast® transport swabs to collect mucosal specimens from the upper lateral vaginal walls or fornices. The samples were sent to the Microbiology Laboratory, inoculated into BD Blood Agar, BD Eosin Methylene Blue (EMB) Agar, and RTA Sabouraud Dextrose Agar (SDA), and incubated at 35°C for 24–48 hours. Bacterial species were then identified using the BD Phoenix system after determining the growth densities in the cultures.

The data were analyzed using SPSS 25.0 software (IBM Corporation, Armonk, NY, USA). The normal distribution of the data was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was applied to compare two independent groups for non-normally distributed quantitative data. For categorical variables, the Chi-square test, Fisher's exact test, and Fisher-Freeman-Halton exact test were used. Quantitative variables are presented as medians (25th–75th percentile), and categorical variables as percentages (n%). All analyses were conducted at a 95% confidence level, and p-values <0.05 were considered statistically significant.

Results

The case and control groups did not differ significantly in terms of sociodemographic characteristics. Smoking was reported by 9 participants in the case group and 2 in the control group. Similarly, no significant differences were observed between the groups regarding chronic disease status or gestational diabetes (Table 1).

When comparing the hygiene habits of pregnant women in the case and control groups, 43.3% of women using cotton underwear belonged to the case group, while 56.7% were in the control group. The use of antiseptic solutions and vaginal douches was higher in the case group (71.4% and 28.6%, respectively) than in the control group (56% and 44%, respectively). Additionally, the rates of engaging in sexual intercourse and using sanitary pads were higher in the case group (66.7% and 44.1%, respectively) (Table 2).

Among the 20 pregnant women with pathogenic microorganisms in their vaginal cultures, 7 had used an antiseptic solution; however, no statistically significant association was observed. Among the 20 pregnant women who did not use cotton underwear, 6 had pathogenic microorganism growth. Similarly, among the 30 women who changed their underwear every two days, 6 exhibited pathogenic microorganism growth. Among the 25 women who practiced vaginal douching, 9 had pathogenic microorganisms in their vaginal culture samples. Additionally, of the 21 women who engaged in sexual intercourse within the last 48 hours, 3 had pathogenic microorganism growth. Finally, among the 19 women who used sanitary pads, 6 showed pathogenic microorganism growth in their vaginal cultures (Table 3).

Table 1: Comparison of the Case and Control Groups in Terms of Pregnant Women's Demographic Characteristics

	N	Case Group	Control Group	Test Statistics	p-value
Age (Median, Q1-Q3)	80	26.4 (20.0-31.0)	27.4 (23.0-30.0)	692.500	0.300[a]
Number of pregnancies (Median, Q1-Q3)	80	2.0 (1.0-2.0)	2.2 (1.0-3.0)	634.500	0.092[a]
Number of births (Median, Q1-Q3)	53	1.5 (1.0-2.0)	1.3 (1.0-2.0)	330.500	0.777[a]
Miscarriages/Abortions (Median, Q1-Q3)	53	0.3 (0.0-0.00)	0.7 (0.0-1.0)	330.000	0.719[a]
Gestational weeks (Median, Q1-Q3)	80	38 (37.0-39.0)	38.1 (36.0-40.0)	784.000	0.876[a]
Education level (n, %)					0.654[b]
Below high school	38	18 (47.4)	2 0 (54.6)	0.201	
High school and above	42	22 (52.4)	20 (47.6)		
Employment status (n, %)					1.000[b]
Employed	70	35 (50.0)	35 (50.0)	0.000	
Unemployed	10	05 (50.0)	05 (50.0)		
Smoking status (n, %)					
Yes		11	09 (81.8)	02 (18.2)	
No		69	31 (44.9)	38 (55.1)	
Alcohol use (n, %)					1.000[c]
No	80	40 (50.0)			
Yes	00	00 (0.0)			
Chronic disease status (n, %)					0.412[b]
Yes	17	07 (41.2)	10 (58.8)	0.672	
No	63	33 (52.4)	30 (47.6)		
Gestational diabetes diagnosis (n, %)					1.000[c]
Yes	2	01 (50.0)	01 (50.0)	0.000	
No	78	39 (50.0)	39 (50.0)		

[a]Mann-Whitney U test; Q1: 25th Percentile, Q3: 75th Percentile; [b] Chi-square testi; [c] Fisher's Exact testi

Among the 40 pregnant women who used fosfomycin antibiotics, pathogenic microorganisms were detected in the vaginal flora of 16 participants. These 16 women comprised the case group (fosfomycin users), while 4 women constituted the control group (non-users) (Table 4).

The pathogens identified in the vaginal flora were *Candida albicans*, *Escherichia coli*, *Streptococcus agalactiae*, and *Stenotrophomonas maltophilia*. It was determined that out of 10 cases where *Candida albicans* were identified, 9 of them were in the case group. Among the 6 cases with *E. coli* growth, 4 were in the case group. All the 2 cases where *Streptococcus agalactiae* was identified were in the case group. Regarding the 2 cases with *Stenotrophomonas maltophilia* growth, 1 of them was in the case group (Table 5).

Table 2: Comparison of Hygiene Habits Between the Case and Control Groups (n=80)

	Total n (%)	Case Group n (%)	Control Group n (%)	Test Statistics	p-value
Cotton underwear usage					
Yes	60 (100.0)	26 (43.3)	34 (56.7)	4.267	0.039[a]
No	20 (100.0)	14 (70.0)	06 (30.0)		
Frequency of changing underwear					
Every day	50 (100.0)	25 (50.0)	25 (50.0)	0.000	1.000[a]
Every two days	30 (100.0)	15 (50.0)	15 (50.0)		
Antiseptic solution usage					
Yes	14 (100,0)	10 (71,4)	04 (28,6)	3,117	0,077[a]
No	66 (100.0)	30 (45.5)	36 (54.5)		
Vaginal douching					
Yes	25 (100.0)	14 (56.0)	11 (44.0)	0.524	0.469[a]
No	55 (100.0)	26 (47.3)	29 (52.7)		
Sexual intercourse					
Yes	21 (100.0)	14 (66.7)	07 (33.3)	3.164	0.075[a]
No	59 (100.0)	26 (44.1)	33 (55.9)		
Pad usage					
Yes	19 (100.0)	12 (63.2)	07 (36.8)	1.726	0.189[a]
No	61 (100.0)	28 (45.9)	33 (54.1)		

[a]*Chi-square test*

Discussion

In our study, among the vaginal culture samples in which pathogenic microorganisms were isolated, *Candida albicans* was identified in 50% of cases, *Escherichia coli* in 30%, *Streptococcus agalactiae* in 10%, and *Stenotrophomonas malt*ophilia in 10%. Elevated estrogen levels during pregnancy are known to increase glycogen deposition in the vaginal epithelium, thereby creating a favorable environment for the proliferation of *C. albicans*. These findings are consistent with previously published research. Balaka et al. (2003) reported *Candida albicans* in 33.3% and *Escherichia coli* in 10.9% of vaginal cultures obtained from 306 pregnant women at 29–32 and 33–36 weeks of gestation. Similarly, Di Bartolomeo (2001) detected *C. albicans* in 34.3% and *Streptococcus agalactiae* in 4.5% of samples collected from 198 pregnant women. Kaźmierczak et al. (2004) identified *C. albicans* in 42.0% of cultures obtained from 450 pregnant women in Poland. In a larger cohort study, Yu et al. (2018) examined vaginal microecological factors in 751 pregnant women and found that 32.62% had genital tract infections, with *C. albicans* present in 14.91% of case.

Cengiz et al. (2004) reported that among women presenting with vaginal discharge, *Candida albicans* was isolated in 39.8% of cases, while *Escherichia coli* was identified in 12.4%. Similarly, in a study of 121 women with uncomplicated pregnancies, Çelen et al. (2012) found that 14.9% had positive vaginal cultures. The most frequently isolated microorganisms were *E. coli* (5.8%), *C. albicans* (2.5%), and *Streptococcus agalactiae* (0.8%), representing the three predominant pathogens.

Table 3: The Impact of Hygiene Habits on Vaginal Culture Results (n=80)

	Total n (%)	Pathogenic Growth (+) n (%)	No Pathogenic Growth (-) n (%)	Test Statistics	p-value
Cotton underwear usage					
Yes	60 (100.0)	14 (23.3)	46 (76.7)	0.356	0.551[a]
No	20 (100.0)	06 (30.0)	14 (70.0)		
Frequency of changing underwear					
Every day	50 (100.0)	14 (28.0)	36 (72.0)	0.640	0.424[a]
Every two days	30 (100.0)	06 (20.0)	24 (80.0)		
Antiseptic solution usage					
Yes	14 (100.0)	07 (50.0)	07 (50.0)		0.025[b]
No	66 (100.0)	13 (19.7)	53 (80.3)		
Vaginal douching					
Yes	25 (100.0)	09 (36.0)	16 (64.0)	2.347	0.126[a]
No	55 (100.0)	11 (20.0)	44 (80.0)		
Sexual intercourse					
Yes	21 (100.0)	03 (14.3)	18 (85.7)	1.743	0.187[a]
No	59 (100.0)	17 (28.8)	42 (71.2)		
Pad usage					
Yes	19 (100.0)	06 (31.6)	13 (68.4)		0.448[b]
No	61 (100.0)	14 (23.0)	47 (77.0)		

[a]*Chi-square test;* [b]*Fisher's Exact test*

Table 4: Comparison of Case and Control Groups in Terms of Vaginal Culture Results (n=80)

	Total n (%)	Case Group n (%)	Control Group n (%)	Test Statistics	p-value
Culture outcome					
Pathogenic growth (+)	20 (100.0)	16 (80.0)	4 (20.0)	9.600	0.002[a]
No pathogenic growth (-)	60 (100,0)	24 (40.0)	36 (60.0)		

[a]*Chi-square test*

Previous studies have consistently demonstrated that in vaginal cultures obtained from pregnant women in their third trimester, *Candida albicans* is the predominant pathogen, followed by *Escherichia coli* and *Streptococcus agalactiae*. The findings of our study parallel these reports, further supporting the high prevalence of *C. albicans* during late pregnancy. Notably, *Stenotrophomonas maltophilia* was isolated in 10% of cases, a rate that is relatively uncommon in the existing literature and may warrant closer clinical attention. This observation underscores the need for future research involving larger study populations to better characterize the epidemiological significance and potential clinical implications of this microorganism in pregnant women.

Table 5: Pathogenic Microorganisms Cultured in the Case and Control Groups (n=20)

	Total n (%)	**Case Group n (%)**	**Control Groub n (%)**
Candida albicans	10 (100.0)	09 (90.0)	01 (10.0)
Escherichia coli	06 (100.0)	04 (66.7)	02 (33.3)
Streptococcus agalactiae	02 (100.0)	02 (100.0)	00 (0.0)
Stenotrophomonas maltophilia	02 (100.0)	01 (50.0)	01 (50.0)

During pregnancy, the use of antiseptic solutions for vulvovaginal hygiene has been associated with alterations in the vaginal flora and the proliferation of pathogenic microorganisms (Okumuş and Demirci, 2014). Oh et al. (2002) reported that among adolescents, 79% used a water–vinegar mixture, 17% used povidone–iodine, and 14% used baking soda for vaginal cleansing. Similarly, Rajamanoharan et al. (1999) demonstrated that the use of antiseptic agents disrupts the normal vaginal microbiota and contributes to the development of bacterial vaginosis. Ergün et al. (2020) found that among 268 participants, 17.9% used soap, 18.3% used shower gel, and 5.6% used antiseptic solutions for genital hygiene. In line with previous research, the present study showed that the use of antiseptic solutions was significantly associated with the growth of pathogenic microorganisms in the vaginal flora of pregnant women ($p=0.025$).

Vaginal douching is known to introduce various pathogenic microorganisms into the vagina, thereby disrupting the normal vaginal flora (Çalışkan, 2005). This practice decreases the number of Lactobacilli, elevates vaginal pH, and consequently increases the risk of genital infections (Nsereko et al., 2021). Sakru et al. (2006) reported higher frequencies of Group B *Streptococcus*, *Enterococcus* spp., and *Candida albicans* among pregnant women who practiced vaginal douching. In a pilot study, Brotman et al. (2008a) found that discontinuing vaginal douching reduced the occurrence of bacterial vaginosis (BV). In a subsequent study, Brotman et al. (2008b) further demonstrated that vaginal douching disrupts the vaginal microbiota and increases the risk of BV. Similarly, Drugbo et al. (2015) showed in a Nigerian cohort that vaginal douching performed by 34 women disrupted the normal vaginal flora and elevated the risk of BV. However, a study conducted by Yıldırım et al. (2020) in Türkiye did not observe significant effects of vaginal douching on the vaginal flora. In another study, Yurttaş Akar (2020) reported that women who practiced vaginal douching experienced a higher frequency of vaginal infections, although no significant association was found between vaginal douching and alterations in the vaginal flora (p=0.126).

Smoking has been shown to reduce *Lactobacillus* species and disrupt the normal vaginal flora (Brotman et al., 2014). In a study including 20 smokers and 20 non-smokers, Brotman et al. (2014) reported significantly lower levels of *Lactobacillus* species among smokers. Similarly, Nelson et al. (2018), in their study of 17 smokers and 19 non-smokers, observed decreased *Lactobacillus* species in smokers, which increased their susceptibility to urogenital infections and vaginal odor. In the present study, microbial growth was detected in the vaginal cultures of 4 out of 11 smokers; however, this finding was not statistically significant.

The use of cotton underwear is recommended to support genital hygiene, as synthetic fabrics tend to retain moisture and create an environment conducive to the development of infections (Cangöl and Tokuç, 2013). However, Klebanoff et al. (2010), in their study of 3,620 women, reported that wearing cotton underwear did not influence the composition of the vaginal flora. In a hospital-based study of 714 pregnant women, Pınar et al. (2009) investigated factors affecting abnormal vaginal discharge and found that the use of cotton underwear was significantly associated with fewer complaints of abnormal discharge. Conversely, Cangöl et al. (2013) reported that cotton underwear use did not have an impact on genital infections. In the present study, microbial growth was detected in 14 out of 60 women who wore cotton underwear; however, this finding was not statistically significant.

The frequency of changing underwear is considered an important hygiene practice (Cangöl and Tokuç, 2013). In their study of 402 women, Cangöl and Tokuç (2013) reported that 58.9% changed their underwear daily, and this practice had no effect on genital infections. Similarly, Pınar (2009) found that the frequency of changing underwear did not influence the occurrence of abnormal vaginal discharge. In the present study, 62.5% of pregnant women reported changing their underwear every day; however, the impact of this practice on the growth of pathogenic microorganisms in the vaginal flora was not statistically significant.

Results and Recommendations

Of the 20 women with positive vaginal cultures, 16 were in the study group (those who used fosfomycin) and 4 were in the control group (those who did not use fosfomycin). A statistically significant difference was observed between the two groups in the growth of pathogenic microorganisms in vaginal culture samples ($p=0.002$).

Disruptions in the vaginal flora during pregnancy are known to be associated with adverse outcomes such as intrauterine infections, fetal growth restriction, premature rupture of membranes, preterm labor, low birth weight, and puerperal infections. Based on our findings regarding fosfomycin use—particularly in relation to antiseptic exposure and the presence of pathogenic microorganisms—midwives and nurses should provide evidence-based supportive care to pregnant women during pregnancy, childbirth, and the postpartum period. Although this study did not directly evaluate the effects of hygiene practices, diet, or sexual behavior on pathogenic growth, these factors remain essential components of routine antenatal education.

This study found that pathogenic microorganisms were more frequently detected in the vaginal cultures of women who received fosfomycin; however, due to the observational nature of the research, causality cannot be established. As no comparable studies were identified in the literature, further research into larger sample sizes is recommended. Additionally, comparative studies involving different antibiotics or analyses conducted across various trimesters should be considered to enhance the evidence base.

Ethical Consideration: Approval for this study was obtained from the Karabük University Non-Interventional Clinical Research Ethics Committee (Decision No: 7/7, Date: 11/11/2019).

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References

Aktün, LH., Karaca, N., & Alpak, YK. (2018). Gebelik dönemindeki asemptomatik bakteriüri: prevalansı, antibyotik duyarlılığı ve demografik faktörlerle ilişkisi. *Bezmialem Science*, 6(3), 163-167.

Aşgın, N., Eroğlu, S. & Çakmaklıoğulları EK. (2018). Gebelikte üriner sistem infeksiyonlarının ampirik tedavisinde hangi antibiyotikler ilk seçenek olmalıdır. *ANKEM Dergisi*, 32(3), 94-102. https://doi.org/10.5222/ankem.2018.1820

Azami, M., Jaafari, Z., Masoumi, M., Shohani, M., Badfar, G., Mahmudi, L., & Abbasalizadeh, S. (2019). The etiology and prevalence of urinary tract infection and asymptomatic bacteriuria in pregnant women in Iran: a systematic review and Meta-analysis, *BMC Urology*. 19(1), 43. https://doi.org/10.1186/s12894-019-0454-8

Balaka, B., Agbere, A. D., Baeta, S., Kessie, K., & Assimadi K. (2003). Bacterial flora in the genital tract the last trimester of the pregnancy. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction*, 32(6), 555-561.

Brotman, R. M., Ghanem, K. G., Klebanoff, M. A., Taha, E. T., Scharfstein, D. O., & Zenilman, J. M.(2008a). The effect of vaginal douching cessation on bacterial vaginosis: a pilot study. *American Journal of Obstetrics and Gynecology*, 198(6), 628.e1-7. https://doi.org/10.1016/j.ajog.2007.11.04

Brotman, R. M., He, X., Gajer, P., Fadrosh, D., Sharma, E., Mongodin, E. F., Ravel, J., Glover, E. D., & Rath, J. M. (2014). Association between cigarette smoking and the vaginal microbiota: a pilot study. *BMC Infectious Diseases*, 14(1), 471. https://doi.org/10.1186/1471-2334-14-471

Brotman, R. M., Klebanoff, M. A., Nansel, T. R., Andrews, W. W., Schwebke, J. R., Zhang, J., Yu, K. F., Zenilman, J. M., & Scharfstein, D. O. (2008b). A longitudinal study of vaginal douching and bacterial vaginosis – A marginal structural modeling analysis, *American Journal of Epidemiology*, 168(2), 188-196. https://doi.org/10.1093/aje/kwn103

Cangöl, E. & Tokuç, B. (2013). Jinokoloji polikliniğine başvuran kadınlarda genital enfeksiyon sıklığı ve genital hijyen davranışları. *Florence Nightingale Journal of Nursing*, 21(2), 85-91.

Cengiz, S. A., Cengiz, L., & Us, E. (2004). Gebe kadınların vajinal akıntılarından üretilen mikroorganizmaların dağılımı ve antibakteriyellere duyarlılıkları antibiyotik direnci. *Journal Of Experimental and Clinical Medicine*, 21(2), 84-89. https://dergipark.org.tr/tr/pub/omujecm/issue/20394/215891

Çalışkan, D. (2005). Geleneksel intravaginal uygulama "vajinal duş, lavaj" yapılmalı mı? yapılmamalı mı? *Sürekli Tıp Eğitimi Dergisi*, 14(1): 15-18.

Çeken, N. & Avcı, E. (2019). Tam idrar tetkiki ve idrar kültürünün gebe popülasyonunda karşılaştırılması. *ANKEM Dergisi*, 33(1), 6-11. https://doi.org/10.5222/ankem.2019.192

Çelen, Ş., Özcan-Temizkan, R., Yapar-Eyi, E. G., Seçkin, T., Saygan, S., & Özkan, M. Ş. (2012). Preterm eylem ve erken membran rüptüründe servikal kültür sonuçlarının karşılaştırılması. *Erciyes Medical Journal*, 34(4): 174-177. https://doi.org/10.5152/etd.2012.47

Di Bartolomeo, S., Rodríguez, M., Sauka, D., & de Torres, R. A. (2001). Perfil microbiológico en secreciones genitales de embarazadas sintomáticas, en el Gran Buenos Aires, Argentina. *Enfermedades Infecciosas y Microbiología Clínica*, 19(3), 99-102. https://doi.org/10.1016/s0213-005x(01)72577-3

Durugbo, I. I., Nyengidiki, T. K., Bassey, G., & Wariso, K. T. (2015). Bacterial vaginosis among women with tubal factor infertility in Nigeria. *International Journal of Gynecology & Obstetrics,* 131(2), 133-136. https://doi.org/10.1016/j.ijgo.2015.05.031

Ergün, S., Gök, G., Karlıdağ, E. G., & Er-Güneri, S. (2020). Kadınların genital hijyen davranışlarının belirlenmesi. *Turkish Journal of Family Medicine and Primary Care*, 14(4), 540-547. Doi:10.21763/tjfmpc.706830

Gestels, T. & Vandenplas, Y. (2023). Prenatal and perinatal antibiotic exposure and long-term outcome. *Pediatric Gastroenterology, Hepatology & Nutrition*, 26(3), 135-145. https://doi.org/10.5223/pghn.2023.26.3.135

Kaźmierczak, W., Wnek, M., & Kamiński, K. (2004). Czestość zakazeń Pochwy Ciezarnych Hospitalizowanych w Klinice Perinatologii i Ginekologii, Zabrzu. *Ginekologia Polska*, 75(12), 932–936. https://pubmed.ncbi.nlm.nih.gov/15751213/

Klebanoff, M. A., Nansel, T. R., Brotman, R. M., Zhang, J., Yu, K. F., Schwebke, J. R., & Andrews, W. W. (2010). Personal hygienic behaviors and bacterial vaginosis. *Sexually Transmitted Diseases*, 37(2), 94–99. https://doi.org/10.1097/OLQ.0b013e3181bc063c

Lee, A. C., Mullany, L. C., Quaiyum, M., Mitra, D. K., Labrique, A., Christian, P., Ahmed, P., Uddin, J., Rafiqullah, I., DasGupta, S., Rahman, M., Koumans, E. H., Ahmed, S., Saha, S. K., Baqui, A. H., & Projahnmo Study Group in Bangladesh (2019). Effect of population-based antenatal screening and treatment of genitourinary tract infections on birth outcomes in Sylhet, Bangladesh (MIST): a cluster-randomized clinical trial. *The Lancet Global Health*, 7(1), e148–e159. https://doi.org/10.1016/S2214-109X(18)30441-8

Mannucci, C., Dante, G., Miroddi, M., Facchinetti, F., D'Anna, R., Santamaria, A., Lenti, M. C., Vannacci, A., Calapai, F., Perone, M., Migliardi, G., Alibrandi, A., Navarra, M., & Calapai, G. (2019). Vigilance on use of drugs, herbal products, and food supplements during pregnancy: focus on fosfomycin. *The Journal of Maternal-Fetal and Neonatal Medicine*, 32(1), 125–128. https://doi.org/10.1080/14767058.2017.1373761

Nelson, T. M., Borgogna, J. C., Michalek, R. D., Roberts, D. W., Rath, J. M., Glover, E. D., Ravel, J., Shardell, M. D., Yeoman, C. J., & Brotman, R. M. (2018). Cigarette smoking is associated with an altered vaginal tract metabolomic profile. *Scientific Reports*, 8(1), 852. https://doi.org/10.1038/s41598-017-14943-3

Nsereko, E., Moreland, P. J., Dunlop, A. L., Nzayirambaho, M., & Corwin, E. J. (2021). Consideration of Cultural Practices When Characterizing the Vaginal Microbiota Among African and African American Women. *Biological Research for Nursing*, 23(1), 91–99. https://doi.org/10.1177/1099800420940788

Oh, M. K., Merchant, J. S. & Brown, P. (2002). Douching behaviour in high-risk adolescents. What do they use, when and why do they douche? *Journal of Pediatric and Adolescent Gynecology*, 15(2), 83-88. https://doi.org/10.1016/S1083-3188(01)00148-6

Okumuş, F. & Demirci, N. (2014). Türkiye'de vajinal duş gerçeği. *Florence Nightingale Journal of Nursing*, 22(1), 53-62.

Pınar, T., Çakmak, Z. A., Saygun, M., Pınar, G., & Ulu, N. (2009). Gebelikte anormal vajinal akıntı üzerine etkili risk faktörleri. *Tıp Araştırmaları Dergisi*, 7(2), 79-86.

Rajamanoharan, S., Low, N., Jones, S. B., & Pozniak, A. L. (1999). Bacterial vaginosis, ethnicity, and the use of genital cleaning agents: a case control study. *Sexually Transmitted Diseases*, 26(7), 404–409. https://doi.org/10.1097/00007435-199908000-00008

Sakru, N., Inceboz, T., Inceboz, U., Zeren, I., Karakus, M., & Kirca, U. (2006). Does vaginal douching affect the risk of vaginal infections in pregnant women? *Saudi Medical Journal*, 27(2), 215–218. https://pubmed.ncbi.nlm.nih.gov/16501679/

Uzun, A., Gülen, D., Tanrıverdi, Y. & Kaya, A. D. (2012). Fosfomisin ve bazı antimikrobiyal ajanların üriner *Escherichia coli* izolatlarına in vitro etkinliğinin değerlendirilmesi. *Klimik Dergisi*, 23(2), 77-80. https://doi.org/10.5152/kd.2012.21

Yıldırım, R., Vural, G., & Koçoğlu, E. (2020). Effect of vaginal douching on vaginal flora and genital infection. *Journal of the Turkish German Gynecological Association*, 21(1), 29–34. https://doi.org/10.4274/jtgga.galenos.2019.2018.0133

Yu, F., Tang, Y. T., Hu, Z. Q. & Lin, X. N. (2018). Analysis of the vaginal microecological status and genital tract infection characteristics of 751 pregnant women. *Medical Science Monitor*, 24, 5338–5345. https://doi.org/10.12659/MSM.909051

Yurttaş Akar, Ç. B. (2020). Bir aile sağlığı merkezi'ne kayıtlı 15-49 yaş kadınlar arasında vajinit prevalansı ve etkileyen faktörlerin belirlenmesi. *Journal of Midwifery and Health Sciences*, 3(2), 100-114. https://dergipark.org.tr/tr/pub/esbder/issue/56656/731500