BACTERIAL MORPHOTYPES OF BACTERIAL VAGINOSIS

Drage Dabeski
University Clinic for Gynecology and Obstetrics in Skopje, Republic of North Macedonia,
drdabeski@yahoo.com, dr.dabeski@gmail.com
Aneta Sima
University Clinic for Gynecology and Obstetrics in Skopje, Republic of North Macedonia,
aneta_sima@yahoo.com

Abstract: Bacterial vaginosis is a disorder in the composition of the vaginal flora that leads to a decrease in the number of hydrogen peroxide-producing lactobacilli and a predominance of various anaerobic bacteria. A retrospective cohort study, performed on a series of 192 patients aged 20 to 59 years, divided into two groups: examined and control. The study group included 128 sexually active women with a Pap smear that showed the presence of a squamous intraepithelial lesion or squamous invasive cervical cancer. The control group included 64 sexually active women with a normal PAP smear. All women have a Nugent score system. The most common bacterial morphotype of bacterial vaginosis in women in the study group was Gardnerella vaginalis (96.43%; 54/56), followed by descending order: Bacteroides species (69.64%; 39/56), Mobiluncus species (51,78%; 29/56), Prevotella species (50.00; 28/56) and Lactobacillus species (19.64%; 11/56). The most common bacterial morphotype detected in patients with normal cervical cytology was Lactobacillus species (96.87%; 62/64), followed by descending order: Gardnerella vaginalis (28.12%; 18/64), Bacteroides species (23.44%; 15/64) and Mobiluncus species and Prevotella species (with 9.37% each; 6/64). Bacterial vaginosis was detected in 43.75% of patients with squamous cell abnormalities of the cervix and in 12.50% of patients with normal cervical cytology. Data analysis showed: correlation between the presence of bacterial vaginosis and the occurrence of squamous cell abnormalities of the cervix (chi-square test = 4.19, $p < 0.05$); increase in the presence of bacterial vaginosis in parallel with an increase in the cytopathological degree of cervical lesion (chi-square test = 12.19, $p < 0.05$) and that bacterial vaginosis was most common in patients under 30 years of age (57, 14%; 16/28). Our study showed that Gardnerella vaginalis is the most common bacterial morphotype of bacterial vaginosis.
Keywords: bacterial morphotype, bacterial vaginosis, Gardnerella vaginalis

1. INTRODUCTION

Bacterial vaginosis is a disorder in the composition of the vaginal flora that leads to a decrease in the number of hydrogen peroxide-producing lactobacilli and a predominance of various anaerobic bacteria (Gad, 2014).

Bacterial vaginosis is not considered a serious disease. It is not considered a classic infection due to the absence of signs of inflammation. There is still controversy about how to label it, as a changed vaginal condition or as a vaginal syndrome (Djukic, 2011). What most researchers agree on is that bacterial vaginosis is a change in the microecology of the lower female genital tract, so that microorganisms that are present in small numbers in the vagina during a woman's reproductive period begin to dominate the lactobacilli (Djukic, 2000).

The composition of the vaginal flora in women with bacterial vaginosis differs significantly from that of normal flora. The first sign that is observed is the predominance of aerobic and anaerobic bacteria in the vaginal secretions of women with bacterial vaginosis. Less than 10^7 bacteria per gram of secretion are found in women with normal vaginal flora, while in women with bacterial vaginosis more than 10^{11} bacteria per gram of secretion are isolated (Forsum, 2005). Women with bacterial vaginosis have more gram-negative aerobic and anaerobic bacteria than those with normal vaginal flora. However, it is impossible to single out one of these bacterial species as a cause of bacterial vaginosis, given that they are all part of the vaginal flora of healthy women, although in much smaller quantities (Yan, 2009).

Although bacterial vaginosis was first described in 1895, the focus of attention, as a major concern for women's genital health, is in the early 1980s. Bacterial vaginosis, meanwhile, has not found a place in the core arsenal of syndromes treated by medical staff, nor has an adequate pathophysiological explanation been given. It is still a serious problem for both doctors and researchers of its etiology. Nowadays it requires a bigger and more detailed investigation. The rapid development of molecular-biological methods facilitates the detection of bacterial vaginosis (Eriksson, 2011).

For the past few years, researchers have been examining the virulent factors of Gardnerella vaginalis compared to other bacteria associated with bacterial vaginosis. Patterson et al. studied the adhesion, biofilm formation, and in vitro cytotoxicity of Gardnerella vaginalis species isolated from women with bacterial vaginosis as well as other bacteria associated with bacterial vaginosis, including Prevotella and Mobiluncus. They showed that, of all these

microorganisms, only Gardnerella vaginalis demonstrated the three virulence factors and suggested that other microorganisms may be relatively avirulent opportunists who colonize after the onset of Gardnerella vaginalis infection (Patterson, 2010). Machado et al. showed that in vitro, among the bacteria associated with bacterial vaginosis, Gardnerella vaginalis had the greatest capacity to attach to epithelial cells in the presence of Lactobacillus crispatus (Machado, 2013).

The objectives of the study were: to detect the most common bacterial morphotypes of bacterial vaginosis; to determine the prevalence of bacterial vaginosis in women with and without squamous cell abnormalities of the cervix; to determine the most affected age group of patients and to prove the existence of a connection between bacterial vaginosis and squamous cell abnormalities of the cervix.

2. MATERIAL AND METHODS

Study design: The study is a retrospective cohort study.

Material: Material is 192 patients aged 20 to 59 years, divided into two groups: examined and control. The study group included 128 sexually active women with abnormal cervical cytological findings, ie Pap smear, which shows the presence of squamous intraepithelial lesion or squamous invasive cervical cancer. The control group included 64 sexually active women with normal cervical cytological findings, ie PAP test.

Exclusion criteria: The study did not include: pregnant women, women with previous cervical surgery (conization, carbon dioxide laser vaporization and total hysterectomy), with previous abnormal cytological and histopathological findings of the cervix, women during bleeding, women who have been or are on topical or systemic antibiotic therapy for the last six weeks, and women who have had sex or had a vaginal toilet for the last two days.

Period of realization: The study was conducted in the period from January 2018 to June 2019.

Location of the study: The study was performed at the University Clinics for Gynecology and Obstetrics and at the Institute of Public Health of the Republic of North Macedonia in Skopje.

Methods: In all women we donw: Nugent score system.

Cytological analysis: All samples for cytological analysis were taken using Thin Prep PAP test and processed in the cytology laboratory of the University Clinic for Gynecology and Obstetrics in Skopje by a cytopathologist. Cytological results were classified according to the revised Bethesda classification (Zerat, 2002; Solomon 2002) as: ASC-US-Atypical Squamous Cells of Undetermined Significance; ASC-H-Atypical Squamous Cells cannot exclude a High-grade squamous intraepithelial lesion; LSIL-Low grade Squamous Intraepithelial Lesion (CIN 1-Cervical Intraepithelial Neoplasia Grade 1); HSIL-High grade Squamous Intraepithelial Lesion (CIN 2-Cervical Intraepithelial Neoplasia Grade 2, CIN 3-Cervical Intraepithelial Neoplasia Grade 3, CIS-Carcinoma In Situ) and squamous invasive carcinoma.

Nugent score system: For the development and interpretation of the Nugent score system (Nugent, 1991), vaginal secretions were taken from the posterior fornix of the vagina using a sterile, cotton swab at one end, and the vagina was escalated with a sterile, non-slim tube. at the University Clinic for Gynecology and Obstetrics in Skopje. It was processed in the Laboratory of Microbiology of the Institute of Public Health of the Republic of North Macedonia in Skopje by a microbiologist. A preparation was made on a Gram-colored subject glass and analyzed under a light microscope Olympus BH-2 (USA) at 1000 times magnification of the field of view. The presence or absence of normal bacterial vaginal flora was detected, the most common bacterial morphotypes (Lactobacilli, Gardnerella vaginalis, Bacteroides, Mobiluncus, Prevotella) were detected and a Nugent score system was developed, on the basis of which the bacterial diagnosis was diagnosed. The interpretation of the Nugent score was in the following order: a score of 0-3, meaning the presence of normal vaginal flora (predominance of Lactobacilli-negative for bacterial vaginosis); a score of 4-6 means reduction of normal vaginal flora (negative for bacterial vaginosis) and a score of 7-10, according to the Nugent criteria, means dominance of pathogenic vaginal flora (positive for bacterial vaginosis), the 'gold standard' for presence of bacterial vaginosis.

Statistical analysis: Data were entered into standard database software (Excel). The statistical analysis of the formed statistical series was conducted with the statistical program Statistical Package for Social Sciences (SPSS), version 23.0 and consists of a descriptive and analytical phase. The descriptive phase consisted of analyzing the structure of statistical series and examining the normality of data distributions in numerical series. The structure of statistical series with attributive traits was analyzed by determining proportions and rates. The structure of numerical features was analyzed by determining central tendency measures and dispersion measures. The normality of the numerical series was assessed using a chi-square test. Analysis of relationships between two series with attributive variables was done using a chi-square test. Analysis of relationships between two series with numerical variables was done using regression analysis and linear correlation coefficient. The testing of the differences between the compared groups was done with the help of Student's t-test. Data with p value <0.05 were considered statistically significant. The results are presented in a table.

3. RESULTS

Table 1. Distribution of patients by age groups

Age group	Examined group		Control group	
	Number	(%)	Number	(%)
20-29	28	(21.87)	13	(20.31)
30-39	38	(29.69)	22	(34.38)
40-49	30	(23.44)	18	(28.12)
50-59	32	(25.00)	11	(17.19)
Total	128	(100)	64	(100)

The mean age of the patients in the study group was 40.50 ± 10.85 years, and the mean age of the patients in the control group was 39.34. 9.70 years (Table 1). According to the t-test, the percentage difference between the mean ages between the two groups is statistically insignificant for $p>0.05$ ($p = 0.47$, $t = 0.72$, 95% CI: -2.01-4.32). *Examined group*

Table 2. Distribution of bacterial vaginosis in relation to cytopathological diagnosis

Bacterial Vaginosis	Examined group Cytopathological diagnosis							
	ASC-US (n=13)	ASC-H (n=7)	LSIL (n=31) CIN1 (n=31)	HSIL (n=56) CIN2 (n=20)	CIN3 (n=21)	In situ squamous cell carcinoma (n=15)	Invasive squamous cell carcinoma (n=21)	Total (n=128)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Presence	1 (7.69)	4 (57.14)	12 (38.71)	7 (35.00)	11 (52.38)	7 (46.67)	14 (66.67)	56 (43.75)
Absence	12 (92.31)	3 (42.86)	19 (61.29)	13 (65.00)	10 (47.62)	8 (53.33)	7 (33.33)	72 (56.25)

Legend: n, number; CIN, cervical intraepithelial neoplasm; ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells cannot exclude a high-grade squamous intraepithelial lesion; LSIL, a low-grade squamous intraepithelial lesion; HSIL, a high-grade squamous intraepithelial lesion
Out of a total of 128 patients, bacterial vaginosis was found in 56 (43.75%) patients.
Data analysis showed an increase in the presence of bacterial vaginosis in parallel with an increase in the cytopathological degree of cervical lesion; from 7.69% (1/13) in ASCUS, 38.71% (12/31) in LSIL, 46.03% (29/63) in HSIL to 66.67% (14/21) in squamous invasive carcinoma (chi-square test = 12,198, $p = 0.01$, $p<0.05$).
Data analysis showed an association between the presence of bacterial vaginosis and the occurrence of squamous intraepithelial lesions and squamous invasive cervical cancer (chi-square test = 4.19, $p = 0.04$, $p <0.05$).

Table 3. Distribution of bacterial vaginosis by age groups in 128 patients

Bacterial Vaginosis	Age group							
	20-29		30-39		40-49		50-59	
	Number	(%)	Number	(%)	Number	(%)	Number	(%)
Presence	16	(57.14)	13	(34.21)	12	(40.00)	15	(46.87)
Absence	12	(42.86)	25	(65.79)	18	(60.00)	17	(53.13)
Total	28	(21.87)	38	(29.69)	30	(23.44)	32	(25.00)

Data analysis showed that bacterial vaginosis is most common in patients under 30 years of age (57.14%; 16/28) (Table 3)

Table 4. Diagnosis of bacterial vaginosis with Nugent score

Nugent score Points	Number	(%)
0 - 3	53	(41.41)
4 - 6	19	(14.84)
7 - 10	56	(43.75)
Total	128	(100)

Interpretation of the Nugget score showed that out of a total of 128 patients in the study group, 53 (41.41%) patients had normal vaginal flora, 19 (14.84%) had a reduction in normal vaginal flora, and 56 (43.75%) patients with bacterial vaginosis present (Table 4).
The distribution of the most common bacterial morphotypes in 128 patients in the study group is shown in Table 5.

Table 5. Distribution of bacterial morphotypes in 128 patients

Bacterial morphotypes	With Bacterial Vaginosis (n=56)		No Bacterial Vaginosis (n=72)	
	n	(%)	n	(%)
Gardnerella vaginalis	54	(96.43)	18	(25.00)
Bacteroides species	39	(69.64)	15	(20.83)
Mobiluncus species	29	(51.78)	8	(11.11)
Prevotella species	28	(50.00)	7	(9.72)
Lactobacillus species	11	(19.64)	60	(83.33)

Legend: n, number

Gardnerella vaginalis was the most common bacterial morphotype in patients with bacterial vaginosis present (54/56), and Lactobacillus species in patients with absent bacterial vaginosis (60/7) (Table 5).
The most common bacterial morphotype of bacterial vaginosis was Gardnerella vaginalis (96.43%; 54/56), followed by descending order: Bacteroides species (69.64%; 39/56), Mobiluncus species (51.78%; 29/56), Prevotella species (50.00; 28/56) and Lactobacillus species (19.64%; 11/56) (Table 5).
Control group
The distribution of bacterial vaginosis in 64 patients with normal cervical cytology (PAP test) is shown in Table 6.

Table 6. Distribution of bacterial vaginosis in 64 patients with normal cytological findings

Bacterial Vaginosis	Control group Cytological diagnosis Normal finding (n=64)	
	n	(%)
Presence	8	(12.50)
Absence	56	(87.50)

Legend: n, number

Bacterial vaginosis was detected in 8 (12.50%) patients.
There is a statistically significant correlation between the modalities, the presence of bacterial vaginosis and the absence of bacterial vaginosis between the examined and the control group (chi-square test = 18.75, p=0.000015, p<0.05).
According to the t-test, the percentage difference between the modalities of presence of bacterial vaginosis and absence of bacterial vaginosis between the examined and the control group is statistically insignificant for p>0.05 (p = 0.18, t = 1.97, 95% CI = -138 ,82-54,32).
Data analysis showed that bacterial vaginosis was most common in patients under 30 years of age (30.77%; 4/13) (Table 7).

Table 7. Distribution of bacterial vaginosis by age groups in 64 patients

Bacterial Vaginosis	Age group							
	20-29		30-39		40-49		50-59	
	Number	(%)	Number	(%)	Number	(%)	Number	(%)
Presence	4	(30.77)	2	(9.09)	1	(5.56)	1	(9.09)
Absence	9	(69.23)	20	(90.91)	17	(94.44)	10	(90.91)
Total	13	(20.31)	22	(34.37)	18	(28.13)	11	(17.19)

Out of a total of 64 patients in the control group, 38 (59.38%) patients had normal vaginal flora, 18 (28.12%) had a reduction of normal vaginal flora and 8 (12.50%) patients had bacterial vaginosis present (Table 8).

Table 8. Diagnosis of bacterial vaginosis with Nugent score

Nugent score Points	Number	(%)
0 - 3	38	(59.38)
4 - 6	18	(28.12)
7 - 10	8	(12.50)
Total	64	(100)

The most common bacterial morphotype detected in patients with normal cervical cytology was Lactobacillus species (96.87%; 62/64), followed by descending order: Gardnerella vaginalis (28.12%; 18/64), Bacteroides species (23.44%; 15/64) and Mobiluncus species and Prevotella species (with 9.37%; 6/64 each) (Table 9).

Table 9. Distribution of bacterial morphotypes in 64 patients with normal cervical cytological findings

Bacterial morphotypes	Normal cervical cytological finding (n=64)	
	број	(%)
Lactobacillus species	62	(96.87)
Gardnerella vaginalis	18	(28.12)
Bacteroides species	15	(23.44)
Mobiluncus species	6	(9.37)
Prevotella species	6	(9.37)

4. DISUSSION

Bacterial vaginosis is a common vaginal syndrome in a woman's reproductive period. It may be associated with a number of obstetric and gynecological complications, such as preterm delivery, chorioamnionitis, caesarean section endometritis, pelvic inflammatory disease, postoperative infections after hysterectomy, and with abnormal cervical findings (Gad, 2014; Morris, 2014).

In our study, bacterial vaginosis was detected in 43.75% of the patients in the study group and in 12.50% of the patients in the control group. This percentage of bacterial vaginosis in patients with squamous intraepithelial lesion and squamous invasive cervical cancer corresponds to some previously published studies; in a study by Caixeta et al. since 2015, working on 251 women with abnormal cervical cytological findings, bacterial vaginosis was detected in 103 (41.00%) women (Caixeta, 2015), in a US study by Behbakht et al. since 2002, in the group of women with intraepithelial lesion of the cervix, bacterial vaginosis was detected in 49.02% of patients (Behbakht, 2002), the Italian study by Vetrano et al. since 2007, working on 504 women with dysplastic changes of the cervix, showed a prevalence of 41.67% (Vetrano, 2007). In the study by Discacciati et al. since 2006, in patients with normal cervical cytology, bacterial vaginosis has been detected in 12.00% of women (Discacciati, 2006). The prevalence of bacterial vaginosis of 12.2% was shown in a study by Kero et al. since 2017, worked on 329 women with a normal Pap test (Kero, 2017).

In our study, the highest percentage of bacterial vaginosis of 57.14% was found in the young population under 30 years of age. This is probably due to the sexual behavior (promiscuity) of the young population. A high percentage of bacterial vaginosis in the young population has also been found in some previously published studies: in the Danish screening study by Klopm et al. since 2008, 67.40% of bacterial vaginosis has been detected in the young population (Klomp, 2008); the Brazilian study of Murta et al. since 2000, showed a bacterial vaginosis of 64.10% (250/390) in women under 30 years of age, with a positive Pap smear for squamous intraepithelial lesion of the cervix (Murta, 2000).

A number of previously published studies present a different association between bacterial vaginosis and squamous intraepithelial lesions and squamous invasive cervical cancer. An association between bacterial vaginosis and squamous cell abnormalities of the cervix, as in our study (p = 0.04), has been found in some previously published studies; the Italian study by Vetrano et al. since 2007, working on 504 women with squamous intraepithelial lesions of the cervix, showed a positive correlation between bacterial vaginosis and squamous intraepithelial lesions of the cervix (p<0,0001) (Vetrano, 2007), a Belgian meta-analysis by Gillet et al. since 2012 has shown an association between bacterial vaginosis and cervical intraepithelial neoplasm (OR = 1.51; 95% CI: 1.24–1.83) (Gillet, 2012), a positive correlation between bacterial vaginosis and squamous cell abnormalities of the cervix showed the Korean studies of Nam et al. from 2009 (p = 0.043) and Oh et al. from 2015 (p = 0.007) (Nam, 2009). In the study of Antovska et al., Bacterial vaginosis was found more in the subgroup of women with malignant lesions of the cervix (6.3%) than in the subgroup of benign lesions of the cervix (2.1%) (Antovska, 2012). Several hypotheses explain the association between bacterial vaginosis and intraepithelial lesions of the cervix. One suggests that mucin-degrading enzymes are on the rise in women with bacterial vaginosis. These enzymes, such as sialidases (neuraminidases), play a major role in degrading the protective layer of the cervical epithelium, causing microabrasions or changes in epithelial cells leading to the destruction of the protective mucosal barrier (Briselden, 1992).

In our study, a correlation was found between bacterial vaginosis and the degree of cervical lesion (p = 0.04). An association between bacterial vaginosis and the degree of cervical lesion was detected in a study by Roeters et al. from 2009 (p<0.05) with OR: 7-12 for HSIL (Roeters, 2009); in the Dutch study by Verbruggen et al. from 2006 (OR: 1.62; 95% CI: 1.10-2.38) (Verbruggen, 2006), as well as in the Korean study by Oh et al. from 2015 (p<0.0001) (Oh, 2015).

The most common bacterial morphotype of bacterial vaginosis in patients with squamous cell abnormalities of the cervix was Gardnerella vaginalis (96.43%), followed by descending order: Bacteroides species (61.64%) and Mobiluncus species (51.78%), Prevotella species (50.00%) and Lactobacillus species (19.64%). In a Paraguayan study by Mongelos P. et al. since 2015, working on 181 women with squamous cell abnormalities of the cervix, Gardnerella vaginalis has been detected in 96.5% of women (Mongelos, 2015). A similar percentage (95.00%) of Gardnerella vaginalis was shown in the Bosnian study by Numanovic F. et al. since 2008, working on 200 sexually active women from Tuzla Canton (Numanovic, 2008). In a Korean study by Oh et al. since 2015, Bacteroides species have been detected in 64.28% of patients with CIN (Oh, 2015). A 2005 Turkish study by Bahar H. noted a 49.00% frequency of Mobiluncus species in women with bacterial vaginosis (Bahar, 2005). While in the American study of Srinivasan et al. since 2012, the percentage of Lactobacillus species women with bacterial vaginosis has been 17.9% (Srinivasan, 2012).

In our study, the most common bacterial morphotype detected in patients with normal cervical cytological findings was Lactobacillus species (96.87%), followed by descending order: Gardnerella vaginalis (28.12%), Bacteroides species (23.44%) and Mobiluncus and Prevotella species (with 9.37% each). These results correspond to some previously published studies; in an American study by Livengood et al. since 2009, Gardnerella vaginalis has been detected in 96.00% (20/21) of women with normal cervical cytology (Livengood, 2009), study by Nzomo et al. from 2013, performed on 193 women aged 18 to 49 years with a normal PAP test, showed the presence of the following bacterial morphotopes in descending order: Gardnerella vaginalis (67.70%), Bacteroides species (23.00%) and Mobiluncus species (9.30%) (Nzomo, 2013).

5. CONCLUSION

Our study showed: that Gardnerella vaginalis is the most common bacterial morphotype of bacterial vaginosis; there is an association between bacterial vaginosis and squamous cell abnormalities of the cervix; the most affected age group was the young population under 30 years of age and bacterial vaginosis was detected in 43.75% of patients with cervical squamous cell abnormalities and in 12.50% of patients with normal cervical cytology.

LITERATURE

Avery, K.N.L., Bosch, J.L.H.R., Gotoh, M., Naughton, M., Jackson, S., Radley, S.C., et al. (2007). Questionnaires to assess urinary and anal incontinence: review and recommendations. J Urol.;177:39–49

Antovska, V., Basheska, N., Grncarova, Z, & Aleksioska N. (2012). Relationship among bacterial vaginosis, local inflammatory response and presence of cervical intraepithelial neoplasia in women with and without human papillomavirus infection. Korean J Obstet Gynecol, 55:468-476.

Antovska, V., Bahar, H., Torun, M. M., Ocer, F. & Kocazejbek, B. (2005). Mobiluncus species in gynaecological and obstetric infections: antimicrobial resistance in a Turkish population, 25(3):268-271.

Behbakht, K., Friedman, J., Heimler, I., Aroutcheva, A. & Simoes, J. (2002). Role of the vaginal microbiological ecosystem and cytokine profile in the promotion of cervical dysplasia: a case-control study. Infect Dis Obstet Gynecol, 10:181-186.

Briselden, A. M., Moncla, B. J., Stevens, C. E, & Hillier S. L. (1992). Sialidases (neuraminidases) in bacterial vaginosis and bacterial vaginosis-associated microflora. J Clin Microbiol, 30:663-6.

Caixeta, R. C., Ribeiro, A. A., Segatti, K. D., Saddi, V. A., Figueiredo Alves, R. R., Dos Santos Carneiro, M. A. & Rabelo-Santos, S. H. (2015). Association between the human papillomavirus, bacterial vaginosis and cervicitis and the detection of abnormalities in cervical smears from teenage girls and young women. Diagn Cytopathol, 43(10):780-5.

Discacciati, M. G., Simoes, J. A., Lopes, E. S., Silva, S. M., Montemor, E. B., Rabelo-Santos, S. H. & Westin, M. C. (2006). Is bacterial vaginosis associated with squamous intraepithelial lesion of the uterine cervix? Diagn Cytopathol, 34(5):323-5.

Djukic, S., Opavski, N., Mijac, V. & Ranin, L. (2011). Current knowledge of bacterial vaginosis. Srp Arh Celok Lek, 139(5-6):402-8.

Djukic, S. (2000). Bakterijska vaginoza u trudnoci. Beograd: Univerzitet u Beogradu.

Eriksson, K. (2011). Bacterial Vaginosis: Diagnosis, Prevalence and Treatment. Linkoping, Sweden: Unitryck.

Forsum, U., Holst, E., Larsson, P. G., Vasques, A., Jakobsson, T. & Mattsby-Baltzer, I. (2005). Bacterial vaginosis-a microbiological and immunological enigma. APMIS, 113:81-90.

Gad, G. F. M., El-Adawy, A. R., Mohammed, M. S., Ahmed, A. F. & Mohammed, H. A. (2014). Evaluation of different diagnostic methods of bacterial vaginosis. IOSP-JDMS, 13:15-23.

Gillet, E., Meys, J. F. A., Verstraelen, H., Verhelst, R., De Sutter, P., Temmerman, M. & Broeck, D. V. (2012). Association between Bacterial Vaginosis and Cervical Intraepithelial Neoplasia: Systematic Review and Meta-Analysis. PLoS ONE, 7(1):45201.

Kero, K., Rautava, J., Syrjanen, K., Grenman, S. & Syrjanen S. (2017). Association of asymptomatic bacterial vaginosis with persistence of female genital human papillomavirus infection. Eur J Clin Microbiol Infect Dis, 36(11):2215-2219.

Klomp, J. M., Boon, M. E., Van Haaften, M. & Heintz, P.M. (2008). Cytologically diagnosed Gardnerella Vaginalis infection and cervical (pre)neoplasia as established in population-based cervical screening. Am J Obstet Gynecol, 199:480.

Kurman, R. J., Carcangin, M. L., Herrington, C. S., & Young, R. H. (2014). World Health Organization Classification of Tumors of Female Reproductive Organs. 4th ed. Lyon, France: IARC Press.

Livengood, C.H. (2009). Bacterial vaginosis: an overview for 2009. Rev Obstet Gynecol, 2:28-37.

Mongelos, P., Mendoza, L.P., Rodrguez-Riveros, I., Castro, A., Gimenez, G., Araujo, P., Paez, M., Castro, W. & Basilleti J. (2015). Distribution of human papillomavirus (HPV) genotypes and bacterial vaginosis presence in cervical samples from Paraguayan indigenous. Int J InfecDis, 39:44-9.

Machado, A., Jefferson, K.K. & Cerca, N. (2013). Interactions between Lactobacillus crispatus and bacterial vaginosis (BV)-associated bacterial species in initial attachment and biofilm formation. Int J Mol Sci, 14:12004-12.

Morris, M., Nicoll, A. & Simms, I. (2001). Bacterial vaginosis: a public health review. Br J Obstet Gynaecol, 108:439-50.

Murta, E. F., Souza, M. A., Argujo Junior, E. & Adad, S. J. (2000). Incidence of gardnerella vaginalis, candida and human papillomavirus in cytological smears. Sao Paulo Med J, 118:105-8.

Nam, K. H. (2009). Association between bacterial vaginosis and cervical intraepithelial neoplasia. J Gynecol Oncol, 1:39-43.

Nugent, R. P., Krohn, M. J. & Hillier, S. L. (1991). Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. J Clin Microbiol, 29:297-301.

Numanovic, F., Hukic, M., Gegic, M., Nukic, M., Delibegovic, Z., Pasic, S & Cicko E. (2008). Bacterial vaginosis presence in sexually active women in Tuzla Canton area. Bosn J Basic Med Sci, 8(4):322-30.

Nzomo, J., Waiyaki, P. & Waihenya, R. (2013). Bacterial vaginosis and correlates in women of reproductive age in thika, Kenya. Advances in Microbiology, 3:249-254.

Oh, H. Y., Kim, B. S., Seo, S. S., Kong, J. S., Lee, J. K., Park, S. Y., Hong, K. M., Kim, H. M. & Kim, M. K. (2015). The association of uterine cervical microbiota with an increased risk for cervical intraepithelial neoplasia. Clin Microbiol Infect, 21(7):674.

Patterson, J. L., Stull-Lane, A., Girerd, P. H. & Jefferson, K. K. (2010). Analysis of adherence, biofilm formation and cytotoxicity suggests a greater virulence potential of Gardnerella vaginalis relative to other bacterial vaginosis-associated anaerobes. Microbiology, 156:392-9.

Roeters, A. M., Boon, M. E., Van Haaften, M., Vernooij, F. & Bontekoe, T. R. (2009). Inflammatory events as detected in cervical smears and squamous intraepithelial lesions. Diagn Cytopathol, 38:85-93.

Solomon, D., Davey, D., & Kurman, R. (2002). The 2001 Bethesda System. Terminology for reporting results of cervical cytology. JAMA; 287:2114-19.

Srinivasan, S., Hoffman, N. G. & Morgan M. T. (2012). Bacterial communities in women with bacterial vaginosis: high resolution phylogenetic analysis reveal relationships of microbiota to clinical criteria. PloS One, 7:37818.

Verbruggen, B. S., Boon, M. E. & Boon, L. M. (2006). Dysbacteriosis and squamous (pre)neoplasia of immigrants and Durch women as established in population-based cervical screening. Diagn Cytopathol, 34:377-381.

Vetrano, G., Pacchiarott,i A., Lombardi, G., Cimellaro, V. & Verrico, M. (2007). Correlation between squmous intraepithelial lesions and bacterial vaginosis. Eur J Gynaecol Oncol, 28:310-312.

Yan, D. H., Lu, Z. & Su, R. J. (2009). Comparison of main Lactobacillus species between women and women with bacterial vaginosis. Chin Med J, 122:2748-51.

Zerat, L. (2002). La nouvelle terminologie de Bethesda: quellschangements? Rev Prat Gynecol Obstet. Numero Special, 3-10.