

# Association Between Bacterial Vaginosis and Cytological Abnormalities in Cytopathological Exams Analyzed in a Laboratory School of Goiânia-GO

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*Associação entre Vaginose Bacteriana e Anormalidades Citológicas nos Exames Citopatológicos Analisados em um Laboratório Escola de Goiânia-GO*

*Asociación entre Vaginosis Bacteriana y Anormalidades Citológicas en Exámenes Citopatológicos Analizados en una Escuela de Laboratorio de Goiânia-GO*

Isabelly Ribeiro Barbosa<sup>1</sup>; Denes Santos Rodrigues<sup>2</sup>; Luiz Henrique Alves Ferreira<sup>3</sup>; Leonardo Luiz Borges<sup>4</sup>; Andrea Alves Ribeiro<sup>5</sup>

## ABSTRACT

**Introduction:** *Gardnerella vaginalis* facilitates human papillomavirus (HPV) infection. **Objective:** To verify the association between cytological abnormalities and the presence of *Gardnerella vaginalis* in cervicovaginal smears sent to the Clinical Laboratory of the Pontifical Catholic University of Goiás (LAC/PUC Goiás) stratified by age range. **Method:** Cross-sectional study carried out at LAC/PUC Goiás from January 2013 to December 2015. For statistical analysis, the variable age was categorized as  $\leq 39$  years and  $>40$  years, using the IBM SPSS Statistics program (Version 2.0, 2011<sup>®</sup>) for the chi-square test ( $X^2$ ), with a 95% confidence interval and  $p < 0.05$ . **Results:** 4,558 cytopathological exams were analyzed, most of them with the presence of *Lactobacillus* spp (46.97%). The prevalence of pathogens was *Gardnerella vaginalis* (79.6%), followed by *Candida* spp. (16.8%), *Trichomonas vaginalis* (2.2%), *Herpes simplex* (0.4%) and *Chlamydia trachomatis* (0.1%). Cytological abnormalities were observed in 9.1%, being atypical squamous cells of undetermined significance (ASC-US) 2.57%, low grade squamous intraepithelial lesion (LSIL) 1.78%, atypical squamous cells of undetermined significance cannot exclude high grade squamous intraepithelial lesion (ASC-H) 3.52%, high grade squamous intraepithelial lesion (HSIL) 1.08%, atypical endocervical cells, neoplastic favor (AGC-NEO) 0.22% and carcinoma 0.02%. There was a significant association between severe cytological abnormalities and women  $>40$  years old OR 3.01 (95% CI 2.0-4.58) ( $p < 0.0001$ ). Women  $\leq 40$  years old showed the presence of *Gardnerella vaginalis* ( $p < 0.0004$ ). **Conclusion:** A high prevalence of *Gardnerella vaginalis* was found and its association with cytological abnormalities, especially in sexually active women.

**Key words:** Papanicolaou Test; Gardnerella vaginalis; Vaginosis, Bacterial; Vaginal Smears; Pathology.

## RESUMO

**Introdução:** A *Gardnerella vaginalis* facilita a infecção pelo papilomavírus humano (HPV). **Objetivo:** Verificar a associação entre anormalidades citológicas e presença de *Gardnerella vaginalis* nos esfregaços cervicovaginais encaminhados ao Laboratório Clínico da Pontifícia Universidade Católica de Goiás (LAC/PUC Goiás) estratificadas por faixa etária. **Método:** Estudo transversal realizado no LAC/PUC Goiás entre janeiro de 2013 a dezembro de 2015. Para análises estatísticas, a variável idade foi categorizada em  $\leq 39$  anos e  $>40$  anos, utilizando o programa IBM SPSS Statistics (Versão 2.0, 2011<sup>®</sup>) para o teste de qui-quadrado ( $X^2$ ), com intervalo de confiança de 95% e valor  $p < 0,05$ . **Resultados:** Foram analisados 4.558 exames citopatológicos, a maioria com presença de *Lactobacillus* spp. (46,97%). A prevalência dos agentes patogênicos foi a *Gardnerella vaginalis* (79,6%), seguida de *Candida* spp. (16,8%), *Trichomonas vaginalis* (2,2%), *Herpes simplex* (0,4 %) e *Chlamydia trachomatis* (0,1%). As anormalidades citológicas foram observadas em 9,1%, sendo *atypical squamous cells of undetermined significance* (ASC-US) 2,57%, *low grade squamous intraepithelial lesion* (LSIL) 1,78%, *atypical squamous cells of undetermined significance cannot exclude high grade squamous intraepithelial lesion* (ASC-H) 3,52%, *high grade squamous intraepithelial lesion* (HSIL) 1,08%, *atypical endocervical cells, favor neoplastic* (AGC-NEO) 0,22% e *carcinoma* 0,02%. Houve uma associação significante entre anormalidades citológicas graves e mulheres  $\geq 40$  anos, OR 3,01 (IC 95% 2,0-4,58) ( $p < 0,0001$ ). Mulheres  $\leq 40$  anos mostraram significância à presença de *Gardnerella vaginalis* ( $p < 0,0004$ ). **Conclusão:** Uma elevada prevalência de *Gardnerella vaginalis* foi encontrada associada com as anormalidades citológicas, principalmente em mulheres sexualmente ativas.

**Palavras-chave:** Teste de Papanicolaou; Gardnerella vaginalis; Vaginose Bacteriana; Esfregaço Vaginal; Patologia.

## RESUMEN

**Introducción:** *Gardnerella vaginalis* facilita la infección por el virus del papiloma humano (VPH). **Objetivo:** Verificar la asociación entre anormalidades citológicas y la presencia de *Gardnerella vaginalis* en frotis cervicovaginales enviadas al Laboratorio Clínico de la Pontifícia Universidad Católica de Goiás (LAC/PUC Goiás) estratificadas por grupo de edad. **Método:** Estudio transversal realizado en LAC/PUC Goiás desde enero de 2013 hasta diciembre de 2015. Para el análisis estadístico, la edad variable se clasificó como  $\leq 39$  años y  $>40$  años, utilizando el programa IBM SPSS Statistics (Versión 2.0, 2011<sup>®</sup>) para la prueba de chi-cuadrado ( $X^2$ ), con un intervalo de confianza del 95% y  $p < 0,05$ . **Resultados:** Se analizaron 4.558 exámenes citopatológicos. La prevalencia de *Lactobacillus* spp. con 46,97%. Los patógenos como *Gardnerella vaginalis* fueron 79,6%, *Candida* spp. 16,8%, *Trichomonas vaginalis* 2,2%, *Herpes simplex* 0,4%, y *Chlamydia trachomatis* 0,1%. Se observaron anormalidades citológicas en 9,1%, con células escamosas atípicas de significado indeterminado (ASC-US) 2,57%, lesión intraepitelial escamosa de bajo grado (LSIL) 1,78%, células escamosas atípicas de significación indeterminada no pueden excluir lesión intraepitelial (ASC-H) 3,52%, lesión intraepitelial escamosa de alto grado (HSIL) 1,08%, células endocervicales atípicas, favor neoplásico (AGC-NEO) 0,22% y carcinoma 0,02%. Hubo una asociación significativa entre anormalidades citológicas severas y mujeres  $>40$  años OR 3,01 (IC 95% 2,0-4,58) ( $p < 0,0001$ ). Las mujeres  $\leq 40$  años mostraron la presencia de *Gardnerella vaginalis* ( $p < 0,0004$ ). **Conclusión:** Se encontró una alta prevalencia de *Gardnerella vaginalis* y su asociación con anomalías citológicas, especialmente en mujeres sexualmente activas.

**Palabras clave:** Prueba de Papanicolaou; Gardnerella vaginalis; Vaginosis Bacteriana; Frotis Vaginal; Patología.

<sup>1-5</sup>Catholic University of Goiás (PUC Goiás). School of Medical, Pharmaceutical and Biomedical Sciences. Goiânia (GO), Brazil.

<sup>1</sup>E-mail: isabelly.rbarbosa@gmail.com. Orcid iD: <https://orcid.org/0000-0002-2621-7035>

<sup>2</sup>E-mail: denesrodrigues13@hotmail.com. Orcid iD: <https://orcid.org/0000-0001-5870-8181>

<sup>3</sup>E-mail: luiz132012@gmail.com. Orcid iD: <https://orcid.org/0000-0001-6060-5739>

<sup>4</sup>E-mail: leonardoquimica@gmail.com. Orcid iD: <https://orcid.org/0000-0003-2183-3944>

<sup>5</sup>E-mail: andrea.ribeiro13@gmail.com. Orcid iD: <https://orcid.org/0000-0002-1692-7025>

**Corresponding author:** Andrea Alves Ribeiro. PUC Goiás. Escola de Ciências Médicas, Farmacêuticas e Biomédicas. Avenida Universitária, 1440 – Setor Universitário. Goiânia (GO), Brazil. CEP 74605-010. E-mail: andrea.ribeiro13@gmail.com



## INTRODUCTION

Vaginal microbiota classified as normal and abnormal is a complex ecosystem of more than 200 bacterial species influenced by genes, ethnicity origin, environmental and behavioral factors<sup>1,2</sup>. *Lactobacillus spp.* are predominant in healthy women in gestational age and promote the maintenance of the vaginal homeostasis through the production of lactic acid, hydrogen peroxide, bacteriocins and other substances that block the colonization and growth of adverse microorganisms including the responsible for sexually transmitted infections (STI)<sup>3,4</sup>.

*Lactobacillus spp.* form a natural biofilm that inhibits the adherence, growth, and proliferation of other alien microorganisms to the vaginal mean through different mechanisms, including secretion of organic acids and production of antimicrobial substances (hydrogen peroxide, bacteriocins and biosurfactants). Lactic acid, responsible for low pH values results from the fermentation of carbohydrates by breakdown of glycogen present in the vaginal epithelium<sup>5,6</sup>.

The imbalance of the vaginal ecosystem characterized by the substitution of the normal lactobacilli microbiota by relatively large concentrations of other bacteria, anaerobic mainly, triggers a phenomenon called bacterial vaginosis (BV). This affects the lower genital female tract with accentuated reduction of the normal vaginal microbiota formed predominantly by lactobacilli and there is an overgrowth of pathogenic anaerobic variety as *Gardnerella vaginalis*, the *Mobiluncus sp.*, the *Bacteroides spp.* and the *Mycoplasma hominis*, followed by an elevation of the pH (>4.5).

BV causal agents are present in great part of the female population without symptoms and clinical manifestations are due to the imbalance of the vaginal microbiota when an excessive growth of preexisting anaerobic endogenous bacteria occurs<sup>4</sup>. This is the most common cause of vaginal discharge with prevalence ranging between 8.3% and 31.9%, it can be asymptomatic or with foul odor<sup>7-9</sup>.

It is already well established that human papillomavirus is the etiologic agent for the development of cervical cancer<sup>0</sup>. BV can be a risk factor both for HPV infection and progression towards an invasive carcinoma<sup>11</sup>.

This can be explained by the fact that anaerobic bacteria present in BV are able to produce enzymes that destroy the protective biofilm of the cervicovaginal epithelium, facilitating the entry of HPV. These bacteria have metabolites that destroy the innate immune system in the vaginal environment causing increase of the cytokines levels (IL-2, IL-6 and IL-12). This occurs by the production of sialidases and prolidases that degrade IgA<sup>12,13</sup>. Therefore, the local immune response reduces,

facilitating the persistent HPV infection causing cytologic abnormalities and consequently, cervical cancer<sup>14,15</sup>.

The cytopathological exam is valuable as a screening test and is widely disseminated in Brazil because is included in the National Cervical Prevention Program<sup>16</sup>. Although the cytopathological exam is not the test of choice to detect cervicovaginal infections, this method presented specificity between 93% and 98% to detect BV<sup>17</sup>.

The objective of this study was to verify the association between cytologic abnormalities and the presence of *Gardnerella vaginalis* in the cervicovaginal smears referred to the Clinical Laboratory of the Catholic University of (LAC/PUC Goiás) stratified by age range.

## METHOD

Cross-sectional study conducted in LAC/PUC Goiás. Cervicovaginal satisfactory cytologic smears were utilized from January 2013 to December 2015. LAC/PUC Goiás cytologic sector has a strict internal quality control as the quick analysis of 10%, verifying 10% of the previously classified smears as negatives from 30 seconds to two minutes, all unsatisfactory after the routine screening. The negative smears are considered as results and released while the suspects are submitted to thorough review analyzed by a cytologist who did not participate of the routine review. The concordant results are considered as results. After a thorough review, a third cytologist analyzes the discordant results and the result is defined upon consensus. Unsatisfactory cytologic smears are excluded because due to the small sample, they would not interfere in the statistical analyzes. This model was stratified per age range in: 14-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80-90 years for the calculation of the prevalence<sup>18</sup>. The Institutional Review Board of PUC Goiás approved the study, protocol number 235,376.

The result of the cytopathological test was categorized according to the Brazilian Nomenclature of Cervical Reports, which is based in the cytopathological criteria defined in the Bethesda System of Reporting Cervicovaginal Cytopathology<sup>19</sup>. The possible results of the cervical reports are: negative for intraepithelial lesion or malignancy – NILM, atypical squamous cells of undetermined significance – ASC-US or cannot exclude high grade squamous intraepithelial lesion – ASC-H, atypical glandular cells – AGC, low grade squamous intraepithelial lesion – LSIL, high grade squamous intraepithelial lesion – HSIL, and squamous carcinoma<sup>19</sup>.

The bacterial microbiota was evaluated from stained cytologic smears by Papanicolaou methodology, classified

in negative or positive microbiota for BV, according to Discacciati et al.<sup>20</sup> defined standards.

The variable age in the statistical analyzes was categorized in individuals  $\leq 39$  years and  $\geq 40$  years based in the mean age of women of 39 years old analyzed. The software IBM SPSS Statistics (version 2.0, 2011<sup>®</sup>) was utilized for chi-square test ( $X^2$ ), with confidence interval of 95% and value of  $p < 0.05$ .

## RESULTS

4,558 satisfactory cytopathological lab tests were reviewed. 39 years old was the mean age among women. The prevalence for the microbiota was *Lactobacillus spp.* with 46.97% (2,141/4,558), followed by *Bacillus sp.* 6.63% (302/4,558), bacilli and cocci, 4.64% (253/4,558) and bacilli and *Lactobacillus sp.* 0.81% (37/4,558). For women between 30 and 39 years, higher prevalence of *Lactobacillus spp.*, 13.36% (609/4,558) was observed and in women aged 50 to 59 years, the results of cocci were 1.66% (76/4,558) (Table 1).

For pathogens, *Gardnerella vaginalis* was diagnosed with 79.6% (1141/1,433), standing out women from 30 to 39 years with higher prevalence of 26.7% (305/1,433); *Candida spp.* infection was 16.8% (253/1,433), more prevalent in women in gestational age between 20 and 39 years, with 25.3%. *Trichomonas vaginalis* represented 2.2% (32/1,433) of the diagnostic, the other results of *Herpes simplex* and *Chlamydia trachomatis* were noticed with lower prevalence, 0.4% (6/1,433) and 0.1% (1/1,433), respectively (Table 2).

In relation to the cytological abnormalities, 9.1% (415/4,558) were diagnosed. These abnormalities were ASC-US 2.57% (117/4,558); LSIL 1.78% (81/4,558);

ASC-H 3.52% (160/4,558); HSIL 1.08% (48/4,558); AGC-NEO 0.22% (10/4,558) and invasive carcinoma 0.02% (1/656). Three patients presented ASC-H and AGC-NEO concomitantly. In the age range from 14 to 39 years, it was observed a total of 46.51% (2,120/4,558) negative results, 1.6% (73/4,558) ASC-US, 1.58% (72/4,558) LSIL, 1.56% (71/4,558) ASC-H, 0.63% (29/4,558) HSIL, 0.06% (3/4,558) AGC-NEO and no record of invasive carcinoma was found. In the age range from 40 to 49 years, 44.38% (2,023/4,558) negative results were observed, 1.95% (89/4,558) ASC-H, 0.96% (44/4,558) ASC-US, 0.44% (20/4,558) HSIL, 0.2% (9/4,558) LSIL, 0.16% (7/4,558) AGC-NEO and 0.02% (1/4,558) invasive carcinoma (Table 3).

Table 4 shows that in the present study there was statistically significant association between severe cytological abnormalities and women  $\geq 40$  years (OR 3.01 CI 95% 2.0-4.58  $p < 0.0001$ ); that is, older women have three-fold more odds of presenting cytological abnormalities considered precursor lesions of cervical cancer when compared with younger women.

Table 5 demonstrates the relation between cytological abnormalities and presence or absence of *Gardnerella vaginalis*, when stratified in age ranges between 14 and 39 years and above 39 years. Women younger than 40 years showed statistically significant difference, that is, more odds of presenting cytological abnormalities associated with the presence of *Gardnerella vaginalis* in relation to women  $\geq 40$  years ( $p < 0.0004$ ).

## DISCUSSION

The predominant microbiota in the present study consisted of *Lactobacillus spp.* (46.97%) in women in

Table 1. Prevalence of the microbiota of women consulted at the Clinical Laboratory of the Catholic University of Goiás. Goiânia, 2013-2015

Age range (Years)	Microbiota											
	Bacilli		Cocci		Lactobacillus sp		Bacilli and Cocci		Bacilli and Lactobacillus sp ssp		Total	
	n	(%)	n	(%)	N	(%)	n	(%)	n	(%)	n	(%)
14-19	104	2.28	1	0.02	127	2.78	51	1.11	6	0.13	289	6.34
20-29	275	6.03	7	0.15	482	10.57	170	3.72	20	0.43	954	20.93
30-39	302	6.63	6	0.13	609	13.36	176	3.86	32	0.70	1,125	24.68
40-49	232	5.08	13	0.28	530	11.62	170	3.72	24	0.52	969	21.26
50-59	152	3.33	76	1.66	291	6.38	253	4.64	37	0.81	809	17.75
60-69	47	1.03	54	1.18	81	1.77	134	2.93	10	0.21	326	7.15
70-79	9	0.19	15	0.32	21	0.46	32	0.70	2	0.04	79	1.73
80-90	1	0.02	4	0.17	0	0.00	2	0.04	0	0	7	0.15
<b>Total</b>	<b>1,122</b>	<b>24,62</b>	<b>176</b>	<b>3,86</b>	<b>2,141</b>	<b>46,97</b>	<b>988</b>	<b>21,68</b>	<b>131</b>	<b>2,87</b>	<b>4,558</b>	<b>100</b>

**Table 2.** Stratified prevalence per age range of the pathogenic microbiological agents in relation to the total number of patients consulted at the Clinical Laboratory of the Catholic University of Goiás. Goiânia, 2013-2015

Age range	Microbiological Agents											
	<i>Gardnerella vaginalis</i>		<i>Candida sp.</i>		<i>Trichomonas vaginalis</i>		<i>Herpes Simplex</i>		<i>Chlamydia trachomatis</i>		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
14-19	109	9.6	32	12.6	1	3.1	3	0.5	0	0	145	10.1
20-29	282	24.7	64	25.3	6	18.8	0	0	0	0	352	24.5
30-39	305	26.7	64	25.3	12	37.5	3	0.5	0	0	384	26.8
40-49	238	20.9	53	20.9	7	21.9	0	0	0	0	298	20.8
50-59	160	14.0	28	11.1	5	15.6	0	0	1	1	195	13.6
60-69	40	3.5	10	4.0	1	3.1	0	0	0	0	51	3.5
70-79	6	0.5	2	0.8	0	0	0	0	0	0	8	0.6
80-90	1	0.1	0	0	0	0	0	0	0	0	1	0.1
<b>Total</b>	<b>1,141</b>	<b>79,6</b>	<b>253</b>	<b>100</b>	<b>32</b>	<b>100</b>	<b>6</b>	<b>100</b>	<b>1</b>	<b>100</b>	<b>1,433</b>	<b>100</b>

**Table 3.** Prevalence of the cytopathological results analyzed at the Clinical Laboratory of the Catholic University of Goiás. Goiânia, 2013-2015

Age range	Negative		ASC-US		LSIL		ASC-H		HSIL		AGC-NEO		Invasive carcinoma		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
14-19	248	5.44	13	0.29	22	0.48	4	0.09	0	0	2	0.04	0	0	289	6.34
20-29	850	18.65	27	0.59	35	0.77	30	0.66	12	0.26	0	0	0	0	954	20.93
30-39	1,022	22.42	33	0.72	15	0.33	37	0.81	17	0.37	1	0.02	0	0	1,125	24.68
40-49	900	19.75	21	0.46	4	0.09	32	0.7	10	0.22	3	0.07	0	0	969	21.26
50-59	738	16.19	16	0.35	4	0.09	39	0.86	9	0.2	4	0.09	1	0.02	809	17.75
60-69	305	6.69	5	0.11	0	0	16	0.35	0	0	0	0	0	0	326	7.15
70-79	73	1.6	2	0.04	1	0.02	2	0.04	1	0.02	0	0	0	0	79	1.73
80-90	7	0.15	0	0	0	0	0	0	0	0	0	0	0	0	7	0.15
<b>Total</b>	<b>3,902</b>	<b>85,61</b>	<b>117</b>	<b>2,57</b>	<b>81</b>	<b>1,78</b>	<b>160</b>	<b>3,51</b>	<b>49</b>	<b>1,08</b>	<b>10</b>	<b>0,22</b>	<b>1</b>	<b>0,02</b>	<b>4,558</b>	<b>100</b>

**Captions:** ASC-US: atypical squamous cells of undetermined significance; LSIL: low grade squamous intraepithelial lesion; ASC-H: atypical squamous cells – possible high-grade lesion; HSIL: high-grade squamous epithelial lesion; AGC-NEO: atypical glandular cells.

**Table 4.** Association between the age range and less severe (ASC-US and LSIL) and severer cytologic abnormalities (ASC-H, AGC-NEO, HSIL and IC) in the cytopathological tests conducted at the Clinical Laboratory of the Catholic University of Goiás. Goiânia, 2013-2015

Age range (years)	ASC-US and LSIL	ASC-H, AGC-NEO, HSIL and CA	OR	CI 95%	P
14 ≥ 39	145	103			
40 > 90	53	114	3.01	2.0-4.58	0,0001
<b>Total</b>	<b>198</b>	<b>217</b>			

**Captions:** ASC-US: atypical squamous cells of undetermined significance; LSIL: low grade squamous intraepithelial lesion; ASC-H: atypical squamous cells – possible high-grade lesion; AGC-NEO: atypical glandular cells; HSIL: high-grade squamous epithelial lesion; IC: invasive carcinoma; OR: *odds ratio*; CI: confidence interval.

**Table 5.** Association between age range and cytopathological abnormalities with presence or absence of bacterial vaginosis in the cytopathological tests at the Clinical Laboratory of Catholic University of Goiás. Goiânia, 2013-2015

Age range (years)	Positive Cytologic Abnormality + BV Present	Age range (years) + VB Absent	p
14 ≥ 39	135	32	
40 > 90	161	87	0.0004
<b>Total</b>	<b>296</b>	<b>119</b>	

**Caption:** BV: bacterial vaginosis.



gestational age from 30 to 39 years. The predominance of *Lactobacillus sp.* able to produce  $H_2O_2$  and lactic acid contributed for the inhibition of the growth of several other organisms obnoxious to the vaginal mucosa<sup>21</sup>. In the vaginal microbiota without agents, it was demonstrated that the prevalence per age range was modified from a lactobacilli pattern to a non-lactobacilli pattern with predominance of coccoid bacteria in ageing women.

In the age range from 14 to 39 years, the prevalence of cocci and bacilli was of 8.69% and cocci, 0.3%. In women aged 40 years or more, the prevalence was 12.03% and 3.61%, respectively. Some women in menopause, for suffering depletion of *Lactobacillus spp.* are colonized by an adverse microbiota, possibly causing urinary infection and BV<sup>22</sup>.

Among the pathogenic agents, *Gardnerella vaginalis* was more prevalent corresponding to 79.6%. Similar to the results of this study, Rivers et al.<sup>23</sup> reported *Gardnerella vaginalis* diagnosed in 72.5% of the participants. Among women from 30 to 39 years, a prevalence of 26.7% was found, followed by women from 20 to 29 years (24.7%) and of women from 40 to 49 years (20.9%). Toninato et al.<sup>9</sup> encountered higher frequency of *Gardnerella vaginalis* in the age range of 40 to 49 years (38.96%), followed by the group from 30 to 39 years (32.47%). However, it has been proved in a previous study that the prevalence of BV varies from 10% to 64%<sup>24</sup>.

Actually, higher number of sexual partners and first sexual intercourse at a younger age are risk factors for BV<sup>25</sup>. This, associated to behavioral changes with sexual life beginning each time earlier, justifies more prevalence of BV in younger women. Therefore, they are more vulnerable to HPV infections and cytological abnormalities are more frequent, in addition to evolving to more abnormalities earlier<sup>26</sup>.

In the present study, the less severe cytologic abnormalities (ASC-US and LSIL) are more frequent in younger women (<40 years) and the severer abnormalities (ASC-H, AGC and CA) are more frequent in older population ( $\geq 40$  years). As demonstrated, association between severer lesions in women older than 40 years exists (OR=3.01 CI 95%, 2.0-4.58,  $p < 0.001$ ). The distribution of the diagnosis per age-range is similar to other studies<sup>10,25</sup>, with diagnosis of severer lesions encountered in older women and transitory lesions in younger women<sup>26</sup>. A prospective cohort study demonstrated that in the age-range from 40 to 50 years in a group of HPV positive women initially without cytologic abnormalities, 25% of them developed cytologic abnormalities after five years and 35% after ten years. In HPV positive women too and cytologic abnormalities free but in the age range from 22 to 32 years, 18% developed

cytologic abnormalities after five years and 25% after ten years<sup>27</sup>. These results confirm the characteristic of transitoriness of HPV in younger women and its higher persistence and virulence in women older than 40 years.

Women in the age range from 14 to 39 years presented significant association between cytologic abnormalities and BV, compared to women older than 40 years ( $p < 0.0004$ ). Caixeta et al.<sup>12</sup> found in HPV infected adolescents and younger women with BV, significantly results associated with positive cytologic abnormalities (OR=2.59; CI 95%: 1.09-6.20;  $p = 0.032$ ), and Furtado et al.<sup>13</sup>, a statistically significant association among women infected by *Gardnerella vaginalis* and cytologic abnormalities (OR=2.40, CI 95%: 1.1-6.37,  $p < 0.04$ ). This can be explained due to evidences that pathogenic bacteria present in BV can change the immune signs reducing the capacity of the immune system to protect the host leaving the mucosa more susceptible to HPV infection and cytologic abnormalities<sup>15,28</sup>.

A systematic review and meta-analysis associating BV and cervical intraepithelial neoplasia (CIN) confirmed a significant association among them, with OR=1.51; CI 95%: 1.24-1.83,  $p < 0.05$ <sup>29</sup>. However, the cytologic abnormalities were found more frequently in women who presented vaginal microbiota disorders, suggesting a possible connection between BV and cervical cancer.

## CONCLUSION

Association between BV and cytologic abnormalities was found in sexually active women mainly, which reinforces the efficacy of BV diagnostic in cytopathological tests and their relationship with HPV infections and consequently with cytologic abnormalities.

Health programs including reproductive, sexual education and public policies for the implementation of preventive measures should be disclosed to women who seek health services. They must be guided about the importance of the cytopathological test for cervical cancer prevention and when detected the pathogens agents, mainly *Gardnerella vaginalis*, to submit to the correct treatment avoiding cytologic abnormalities.

## CONTRIBUTIONS

Isabelly Ribeiro Barbosa and Leonardo Luiz Borges contributed substantially for the study conception and/or design, gathering, analysis and/or interpretation of the data. Denes Rodrigues da Silva and Luiz Henrique Alves Ferreira contributed for the wording and critical review. Andrea Alves Ribeiro contributed substantially for the study conception and/or design, gathering, analysis and/

or interpretation of the data, wording, and critical review. All the authors approved the final version to be published.

#### DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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