

# Profile of women with cervical changes from a city in the Northeast Brazil

## *Perfil das mulheres com alterações cervicais em uma cidade do nordeste brasileiro*

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### ABSTRACT

**Introduction:** In Brazil, cervical cancer is the fourth leading cause of cancer death. It reached 5,430 deaths in the year 2013, with estimated 16,370 new cases by 2018. Its occurrence has been associated with previous human papillomavirus (HPV) infection for the development of intraepithelial lesions; however, several factors can influence this appearance, including number of sexual partners and infections by other microorganisms. **Objective:** The profile of women from the city of Caruaru, Pernambuco, Brazil, with atypia, cervical intraepithelial lesions and cancer, was verified. **Material and method:** Documentary, analytical, retrospective study, carried out through the collection of information in the database of the State Department of Health of Pernambuco, by TabNet, referring to the tests in the laboratory of the municipality of Caruaru, Pernambuco, Brazil. **Results:** During the study period, 18,466 tests were evaluated. From the samples evaluated, 735 (4.31%) were squamous and glandular atypia, 167 (0.98%) intraepithelial lesions, and one (0.005%) cancer. Coccus, *Gardnerella vaginalis* and Lactobacilli were the most evident agents in cervical alterations. **Discussion:** Studies demonstrate the intimate relationship between infectious agents and the development of cervical lesions and cancers. *Gardnerella vaginalis* was the most frequent agent in the presence of abnormalities was identified as a facilitator of HPV penetration. **Conclusion:** Women infected by *Gardnerella vaginalis* and older than 30 years of age are more exposed to the development of alterations. Guidelines on prevention and screening should be continuous strategies in public services. Understanding these risk factors is a paramount concern because they are involved in the prevention and etiology process of cervical lesions and cancer.

**Key words:** risk factors; carcinoma of the uterine cervix; sexually transmitted diseases; papillomavirus infections.

### RESUMO

**Introdução:** No Brasil, o câncer do colo do útero é a quarta causa de morte por câncer. Atingiu 5.430 mortes no ano de 2013, com estimativa de 16.370 novos casos para 2018. Sua ocorrência tem sido associada à infecção prévia pelo papilomavírus humano (HPV) para o desenvolvimento de lesões intraepiteliais, no entanto, vários fatores podem influenciar esse aparecimento, por exemplo, número de parceiros sexuais e infecções por outros microrganismos. **Objetivo:** Verificou-se o perfil das mulheres do município de Caruaru, Pernambuco, Brasil, com atípias, lesões intraepiteliais cervicais e câncer. **Material e método:** Estudo documental, analítico, retrospectivo, realizado por meio do levantamento de informações no banco de dados da Secretaria Estadual de Saúde de Pernambuco, pelo TabNet, referentes aos exames no laboratório do município de Caruaru, Pernambuco, Brasil. **Resultados:** No período do estudo foram avaliados 18.466 exames. Das amostras avaliadas, 735 (4,31%) foram atípias escamosas e glandulares; 167 (0,98%), lesões intraepiteliais; e uma (0,005%), câncer. Cocos, *Gardnerella vaginalis* e lactobacilos foram os agentes mais evidentes nas alterações cervicais. **Discussão:** Estudos comprovam relação íntima dos agentes infecciosos com o desenvolvimento de lesões e cânceres cervicais. *Gardnerella vaginalis* foi o agente mais frequente na presença de anormalidades, sendo identificada como facilitadora da penetração do HPV. **Conclusão:** Mulheres infectadas por *Gardnerella vaginalis* com idade acima de 30 anos representam maior exposição ao desenvolvimento de alterações. Orientações quanto à prevenção e ao rastreamento devem ser

*estratégias constantes nos serviços públicos. Entender esses fatores de risco é primordial, porque eles envolvem o processo de prevenção e etiologia das lesões e do câncer cervical.*

*Unitermos: fatores de risco; neoplasias do colo do útero; doenças sexualmente transmissíveis; infecções por papilomavírus.*

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## RESUMEN

**Introducción:** En Brasil, el cáncer de cuello de útero es la cuarta causa de muerte por cáncer, con 5.430 muertes en 2013 y previsión de 16.370 nuevos casos para 2018. Su aparición se asocia a la infección previa por el virus del papiloma humano (VPH) para el desarrollo de lesiones intraepiteliales; no obstante, diversos factores pueden influenciarle, por ejemplo, número de compañeros sexuales e infecciones por otros microorganismos. **Objetivo:** Se ha comprobado el perfil de mujeres del municipio de Caruaru, Pernambuco, Brasil, que tenían atipias, lesiones intraepiteliales cervicales y cáncer. **Material y método:** Investigación documental, analítica, retrospectiva, realizada mediante una encuesta en la base de datos del departamento de salud de Pernambuco, a través de TabNet, relativas a los exámenes en el laboratorio del municipio de Caruaru, Pernambuco, Brasil. **Resultados:** En el período del análisis, 18.466 exámenes han sido evaluados. De las muestras analizadas, 735 (4,31%) han sido de atipias escamosas y glandulares; 167 (0,98%) de lesiones intraepiteliales; y una (0,005%) de cáncer. Cocos, Gardnerella vaginalis y lactobacilos han sido los agentes más evidentes en las alteraciones cervicales. **Discusión:** Investigaciones comprueban una relación directa entre agentes infecciosos y el desarrollo de lesiones y cáncer cervical. Gardnerella vaginalis ha sido aquel más frecuente en presencia de anormalidades, pues facilita la invasión por el VPH. **Conclusión:** Mujeres mayores de 30 años infectadas por Gardnerella vaginalis representan una exposición importante al desarrollo de alteraciones. Recomendaciones de prevención y tamizaje deben ser estrategias constantes en el servicio público. Conocer estos factores de riesgo es crucial, porque ellos envuelven el proceso de prevención y etiología de las lesiones y del cáncer de cérvix.

**Palabras clave:** factores de riesgo; neoplasias de cuello de útero; enfermedades de transmisión sexual; infecciones por virus del papiloma humano.

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## INTRODUCTION

Cervical cancer is the third most frequent tumor among women, preceded by breast and colorectal cancer; it is the fourth leading cause of cancer death in Brazil. Cervical cancer reached 5,430 deaths in the year 2013, and for the year 2018, it presents an estimate of 16,370 new cases<sup>(1)</sup>.

The occurrence of cervical cancer has been associated with previous human papillomavirus (HPV) infection. However, there are co-factors that may enhance the risk of developing this cancer, such as early age at sexual initiation, multiplicity of sexual partners, smoking, prolonged use of birth control pills and a history of sexually transmitted diseases (STD) – co-infections with the human immunodeficiency virus (HIV) and *Trichomonas vaginalis* infection<sup>(2)</sup> –, as well as co-infection with causative agents of bacterial vaginosis (BV), characterized by the inversion of the microbiota, with substitution of *Lactobacillus* sp. by the growth of anaerobic bacteria, including *Gardnerella vaginalis*, *Atopobium vaginae* and species of *Mobiluncus* and *Prevotella* spp. Several

studies have observed association of BV with HPV, showing that the prevalence of this combination can reach up to 32%<sup>(3)</sup>. There is a greater complexity in the types of vaginal microbiota from HPV-positive women compared with HPV-negative women<sup>(4)</sup>.

Considering microorganisms as causal factors of STD, it is essential to understand that microorganism entry may occur during sexual intercourse through the pudendal cleft, anatomical region of the female genital system<sup>(5)</sup> that presents a broad and variable microbiota throughout the woman's lifetime<sup>(6)</sup>. However, several factors can influence the incidence of infections, such as socioeconomic status, age, sexual activity, number of sexual partners, menstrual cycle phase, and infections by other microorganisms<sup>(7)</sup>.

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## OBJECTIVE

To verify the profile of women with cervical abnormalities in the cytopathological tests performed at the municipality of Caruaru, Pernambuco, Brazil.

## MATERIAL AND METHOD

This is a documentary, analytical and retrospective study that was carried out through the collection of information obtained from the database of the State Department of Health of Pernambuco [Secretaria Estadual de Saúde de Pernambuco (SESPE)]/TabNet available online.

This work was previously approved by the Research Ethics Committee of the Asces-Unita, under no. CAAE: 44804115.5.0000.5203.

The data collection was carried out from January to March 2015, involving tests carried out in the year 2013 obtained from the database of the SESPE website (<http://portal.saude.pe.gov.br/>), where they are in the public domain and freely accessible, in the field “Informações em Saúde” (Health Information), which has the data from the Information System of Cervical Cancer [Sistemas de Informação do Câncer do Colo do Útero (SISCOLO)], a computerized data input system developed by DATASUS in partnership with the Brazilian National Cancer Institute [Instituto Nacional do Câncer (INCA)], which collects and processes information on patient identification and cytopathological and histopathological reports, providing data for the external monitoring of the quality of the tests and directing the state managers of the programme on quality for the laboratories responsible for reading the tests in the municipality<sup>(8)</sup>.

Results recorded in the system with incorrect identifications, incomplete data (age, last examination, collected material) and results considered unsatisfactory for evaluation (smears obscured by inflammatory exudate, red blood cells, desiccation in more than 75% of the sample, acellular or hypocellular smears with less than 10% of the sample), were excluded from the research.

Statistical analysis was performed using the PRISM software version 6.0. The chi-square test of association was used, considering significance level  $p < 0.05$ .

## RESULTS

During the study period, the results of 18,466 cervical cytopathological tests were evaluated, of which 1,434 tests were considered unsatisfactory and were excluded from the study. Among the included samples, 735 (4.31%) were positive for squamous and glandular atypia; 167 (0.98%) for intraepithelial lesions; one (0.005%) for squamous cell carcinoma; and one (0.005%) for in situ adenocarcinoma (**Table 1**).

**TABLE 1** – Frequency of cervical changes in the cytopathological exams of women from the municipality of Caruaru, Pernambuco, in the year 2013

Cervical changes	n	%
ASC-US	334	36.94
ASC-H	216	23.89
LSIL	102	11.28
HSIL	60	6.63
HSIL – cannot exclude microinvasion	5	0.55
Squamous cell carcinoma	1	0.11
AGC-NOS	156	17.25
AGC-FN	19	2.1
Adenocarcinoma <i>in situ</i>	1	0.11
Adenocarcinoma	0	0
Atypia of undefined origin unlikely to be neoplastic	7	0.77
Atypia of undefined origin (cannot exclude HSIL)	3	0.33
Total	904	100

Source: TabNet of the state of Pernambuco.

ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; AGC-NOS: atypical glandular cells not otherwise specified; AGC-FN: atypical glandular cells favoring neoplasia.

Regarding the age of the patients, they were divided into two groups: under 30 years of age, corresponding to 5,297 women (31.1%), and older than 30 years of age, totaling 11,735 (68.89%). Among the positive exams, patients under the age of 30 years resulted in a total of 337 women (37.27%), while 567 (62.72%) represented those aged older than 30 years.

Regarding the educational level, 610 (3.58%) reported to be illiterate; 3,075 (18.05%) had incomplete elementary education; 1,138 (6.68%), complete elementary education; 1,224 (7.18%), complete high school education; 171 (1%), complete higher school education; and 10,814 (63.49%) presented the schooling field unfilled/ignored. Among the positive exams, 34 (3.76%) were illiterate; 140 (15.48%) had incomplete elementary education; 71 (7.85%), complete elementary education; 64 (7.07%), complete high school education; only six (0.66%) had complete higher school education and 589 (65.15%) presented the schooling field unfilled/ignored.

Regarding the periodicity of the examination, the majority affirmed that they had already taken the test, totaling 14,811 (86.96%); 2,221 (13.04%) stated that they did not have being through it, did not know or did not remember having taking the test previously. Among the tests considered positive, 134 (14.82%) did not have, did not remember or did not know if they had previously taken the test, and 770 (85.18%) said that they had already taken the test (**Table 2**).

**TABLE 2 – Profile of women with cervical changes from the municipality of Caruaru, Pernambuco, 2013**

Variables	Positive cytology	Negative cytology	<i>p</i>	RR	OR
<b>Microorganisms</b>					
<i>Gardnerella vaginalis</i>	82	1,634	0.3026	0.8904	0.8849
<i>Trichomonas vaginalis</i>	11	235	0.5557	0.8405	0.8331
Lactobacillus	265	9,517	0.0001	0.3074	0.2881
Cocci	405	12,136	0.0001	0.2906	0.267
Suggested as <i>Chlamydia</i> sp.	0	1	0.8128	0	5.943
Other Bacillus	5	120	0.5128	0.7523	0.7419
<i>Actinomyces</i> sp.	0	1	0.8128	0	5.943
Herpes virus	0	2	0.7377	0	3.566
Other	9	162	0.9792	0.9915	0.9911
<b>Age</b>					
< 30 years	337	4,960	0.0001	1.317	1.338
≥ 30 years	567	11,168	0.0001	0.7595	0.7472
<b>Education</b>					
Illiterate	34	576	0.0001	2.628	2.724
Incomplete elementary school education	140	2,935	0.0392	0.8317	0.8237
Complete elementary school education	71	1,067	0.1468	1.19	1.203
High school education	64	1,160	0.8983	0.984	0.9831
Higher school education	6	165	0.2916	0.6588	0.6464
Ignored/unfilled	589	10,225	0.286	1.075	1.079
<b>Previous cytology</b>					
Performed	770	14,041	0.1019	0.8617	0.8541
Not performed	134	2,087	0.1019	1.161	1.171

Source: TabNet of the state of Pernambuco.

RR: relative risk; OD: odds ratio.

## DISCUSSION

The persistence of infectious agents is closely linked to the induction of carcinogenesis. In cases where infections are quickly disposed by the immune system, pathological abnormalities are usually not observed, whereas in chronic infections, the risk of developing cancer increases considerably. The literature demonstrates that specific viruses associated with cancer, such as high-risk HPV in the mucous membranes, the persistence of its infection causes damage to deoxyribonucleic acid (DNA), which can trigger the activation of cellular oncogenes or the inactivation of tumor suppressors genes, contributing to the neoplastic transformation of the infected cells<sup>(9)</sup>. The oncogenic subtypes of HPV 16 and 18 are responsible for the origin of about 70% of cases of invasive cervical cancer. Together with the aspects related to HPV infection, the following are considered risk factors for the development of this

disease: early sexual initiation, multiplicity of sexual partners, smoking, simultaneous infection with infectious agents such as early age at sexual initiation, multiplicity of sexual partners, smoking, presence of co-infections of infectious agents, such as the human immunodeficiency virus (HIV) and *Chlamydia trachomatis*, use of birth control pills, multiple births and low intake of vitamin<sup>(10,11)</sup>. Age is intimately associated with the risk of developing any neoplasia throughout life<sup>(12)</sup>.

The lack of prevention programs is another important factor, because by performing the cytopathological test, it is possible to detect the precursor lesion of cervical cancer until fifteen years before the manifestation of the disease. This test is easy to implement, inexpensive and effective<sup>(13)</sup>.

Cervical cancer is also related to a number of epidemiological factors that can be minimized through prevention and the efficient performance of health professionals in an organized way. Another important topic is the women compliance to cytopathological test, which is decisive for the incidence of this neoplasm<sup>(14)</sup>.

In the present study, *Gardnerella vaginalis* was the most frequent agent in the presence of abnormalities. Studies have shown that this bacterium is identified as facilitating the penetration of HPV due to its aggression to tissue, thus increasing the risk of developing cervical cancer<sup>(15)</sup>. However, in the present study, the significant presence of this bacterium in the appearance of lesions was brought to light, corroborating the other studies<sup>(3,4,16)</sup>.

VB can favor HPV infection due to its polymicrobial etiology, which spreads its exotoxins by adhering to the mucosal surfaces, thereby attacking it<sup>(17)</sup>. Effective treatment of this VB condition is essential for the reduction of penetration and exposure to HPV.

It was highlighted that one of the important factors is age, therefore, having as parameters some studies<sup>(18-20)</sup>, two age groups were used: up to 29 years of age and older or equal to 30 years of age. According to the data analyzed, 5,297 patients were younger than 30 years of age, of whom 337 presented positive cytology,  $p = 0.0001$  and relative risk (RR) 1,317; 11,735 patients were aged ≥ 30 years, of which 567 presented positive cytology,  $p = 0.0001$  and RR 0.7595. The significance of the data is clear in relation to the ages presented, but the group ≥ 30 years presented a higher frequency in the development of cervical abnormalities.

In the study by Silva *et al.* (2014)<sup>(21)</sup>, unfilled schooling corresponded to 89.6%. Considering the importance of schooling in combating transmission of HPV, 10,814 patients with unknown schooling were observed, of which 589 presented positive cytology. These data corroborate an associated risk. In the present study, it was observed that the percentage of women with incomplete

elementary education corresponded to 18.05%, followed by those with complete elementary 6.68%, high school 7.18% and higher school education 1%. In the study by Thuler *et al.* (2012)<sup>(22)</sup>, which evaluated cancer patients, the low schooling (incomplete elementary school or less) corresponded to 70%. The schooling variable was shown to be low, although most of the exams presented this item as ignored/unfilled, corresponding to 63.48% among the performed examinations considered satisfactory.

Regarding the periodicity of cytopathological test performance, in the study by Silva *et al.* (2014)<sup>(21)</sup>, most women (92%) who presented altered results had also performed the test in the previous year, data similar to those of the present study, which showed that 85.2% of these women were tested in the previous year. However, a higher percentage of atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesions (ASC-H), and may or may not be associated with incipient lesions.

Despite the low educational level of the patients, the majority with altered tests recognizes the importance of the scrutiny program.

## CONCLUSION

The presence of cocci bacteria and supracytoplasmic bacilli suggestive of *Gardnerella vaginalis* was found in most of the tests with cytological abnormalities. It is important to consider that women older than 30 years of age infected by *Gardnerella vaginalis* should be monitored by cervical cytopathology tests. Even with the low level of education among patients with altered tests, it is worth considering the existence of effective awareness on the relevance of cervical cancer screening. Thus, guidelines related to the prevention of cervical cancer should be a continuous strategy in the public health services, contributing to an effective cervical cancer screening.

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