







Factors associated to the human papillomavirus in women with cervical cancer

Fatores associados ao papilomavírus humano entre mulheres com câncer de colo uterino

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ABSTRACT

Objective: to analyze the factors associated with the human papillomavirus as related to cervical cancer. **Methods:** cross-sectional study carried out using secondary data from 75 medical records. The chi-squared and Fisher's exact tests were used, considering papillomavirus infections as an outcome. Odds ratio were used to measure the effect, and the level of significance adopted was 5%. **Results:** the characteristics associated to the infection by the papillomavirus were: being 24 years old or younger (odds ratio=19.11; p=0.001), having finished high school or higher education (odds ratio=4.06; p=0.031), having multiple sex partners (odds ratio=5.50; p=0.028), and having not gone through menopause (p=0.009). **Conclusion:** sexual behavior and socioeconomic issues are related to cervical cancer as associated with the papillomavirus infection.

Descriptors: Uterine Cervical Neoplasms; Risk Factors; Papillomavirus Infections.

RESUMO

Objetivo: analisar os fatores associados ao papilomavírus humano com o câncer de colo uterino. **Métodos:** estudo transversal, por meio de dados secundários de 75 prontuários. Realizaram-se os testes qui-quadrado e exato de Fisher, considerando a infecção pelo papilomavírus como desfecho, sendo empregado *odds ratio* como medida de efeito, e adotado nível de significância de 5%. **Resultados:** idade até 24 anos (*odds ratio*=19,11; p=0,001), ter concluído o ensino médio ou nível superior (*odds ratio*=4,06; p=0,031), possuir múltiplos parceiros sexuais (*odds ratio*=5,50; p=0,028) e não ter vivenciado a menopausa (p=0,009) foram características associadas com a infecção pelo papilomavírus. **Conclusão:** comportamento sexual e questões socioeconômicas estão relacionadas ao câncer de colo de útero associado à infecção pelo papilomavírus.

Descritores: Neoplasias do Colo do Útero; Fatores de Risco; Infecções por Papillomavirus.

Introduction

Throughout the world, cervical cancer is the fourth most common type of neoplasm in women. There are approximately 530 thousand new cases and 265 thousand deaths a year, meaning it is the fourth cancer with the highest death toll in the female population. As such, it became a relevant public health issue, especially in underdeveloped regions, in which 70.0% of the cases are diagnosed. Data documented by the National Institute of Cancer highlighted the diminution of the incidence of cervical cancer in countries that are going through socioeconomic transitions, due to the implementation of preventive programs⁽¹⁾.

In Brazil, as a final estimate for each year from 2020 to 2022, 16,590 new cases of cervical cancer were expected, with an estimated risk of 15.43 per 100 thousand women, which would make it the third most incident type of cancer estimated for 2020, following breast cancer and nonmelanoma skin cancer. The Southeast region is fifth, with an estimate of 12.01 new cases for every 100 thousand women. In the Espírito Santo state, the incidence is 16.05 new cases per 100 thousand residents, while the incidence in the capital of the same state is 12.05 per 100 thousand residents, leading to an estimate of 300 new cases in the state⁽¹⁾.

The human papillomavirus (HPV) is responsible for 99.0% of cervical cancer and is active in 50.0% of sexually active women⁽²⁻³⁾. The World Health Organization understands that the HPV infection is responsible for cervical cancer, but not for the progression of the disease⁽⁴⁾. As a result, it points to the association it has with other risk factors, such as an early start of sexual activities, high parity, multiple sex partners, in addition to smoking, low socioeconomic conditions, and prolonged use of oral contraceptives^(2-3,5).

The incidence of cervical cancer is at its highest in women from 40 to 60 years old and at its lowest in those below 30, due to the long time the HPV infection takes to progress until the emergence of the cancer⁽⁶⁾. However, a change in this profile has been standing out, as lesions that precede this emergence have been

detected in younger women who started their sex lives earlier, in association with other risk factors⁽⁷⁻⁸⁾.

The disparity in the current economic, social, cultural, and geographic profiles is associated with a diminution in the incidence of new cervical cancer cases, which is the main motivation for this research^(1,4-5). Therefore, although, with regard to regional incidence, the Southeast is the fifth region and Espírito Santo is the fourth state with the highest ones, this study is relevant due to the scarce scientific productions about the epidemiological reality of the state, which can present relations between sociodemographic and clinical variables in cases of cervical cancer from papillomavirus.

As a result, the objective of this investigation is to analyze the factors associated with the human papillomavirus as related to cervical cancer.

Methods

Cross-sectional study based in secondary data on cervical cancer. Data were collected from the database of the Hospital Cancer Records and from the medical records from a hospital that is specialized in the diagnostic, treatment, and monitoring of cervical cancer in the city of Vitória, Espírito Santo, Brazil.

The sample was non-probabilistic, intentional, and made up of 75 patients. Data was collected from the records of patients from 18 to 80 years old, who were diagnosed with cervical cancer from November 2016 to March 2017, in a Single Health System outpatient clinic. Exclusion criteria included: records of patients with more than one primary tumor and of those who were being treated or in follow-up using health insurance but used the institution for hormonal treatment and radiotherapy alone, not being attended by its clinical oncology service. Since the search for data started from the identification of new cervical cancer cases, as informed by the Hospital Cancer Records of this hospital, no record was excluded, as long as it was in accordance to the aforementioned inclusion criteria.

To contribute in the collection of the necessary data for this research, a data collection instrument was used, which was elaborated by the researchers with the objective of the investigation in mind. The variables collected from the records, mediated by the records made by nursing workers, included age, date of the first consultation, race/color of the skin, educational level at the time of enrollment, main occupation, current marital status, family history regarding cancer, alcohol use history, smoking history, origin of the referral for treatment, number of pregnancies, menarche, menopause, coitarche, contraceptive method, level of sexual activity, number of sexual partners, and HPV infection.

Data were organized in the Microsoft Excel 2013 software and analyzed using the Statistical Package for the Social Sciences, 20. At first, socioeconomic and clinical data were analyzed using descriptive statistics, with results being presented in tables, with their respective absolute (n) and relative (%) frequencies. In the second stage, a bivariate analysis was conducted, whose outcome was the HPV infection and whose explanatory variables were socioeconomic and clinical data.

In this stage, the chi-squared and Fisher's exact tests were carried out (when the values expected were lower than five), considering $p < 0.05$ and, finally, the Odds Ratio (OR) was also calculated for each explanatory variable. To do so, the variables age group, race, educational level, marital status, origin of the referral, family history, menarche, coitarche, and contraceptive method were dichotomized to allow for the OR to be calculated. The variables smoking and drinking were redefined, respectively, as currently smokes (yes or no) and currently drinks (yes or no). In the variables number of pregnancies, menopause, and number of sexual relations, the OR was not calculated, since these variables could not be easily dichotomized. As a result, only Fisher's exact test was used.

The research was carried out after it was approved by the Research Ethics Committee, according to legal opinion No. 2,038,599/2017. It received the

Certificate of Submission to Ethical Appreciation No. 66615617.5.0000.5071. All ethical aspects were respected, in accordance to resolution 466/12 from the National Council of Health, through the signing of the Term of Trusteeship.

Results

The analysis of sociodemographic variables showed that the mean age was 44 ± 1.21 years old (with a minimum of 18 and a maximum of 76). Most interviewees were above 35 years old 45 (60.0%); were brown 57 (76.0%); single 36 (48.0%); had a complete high school 57 (76.0%); had a paid job 48 (64.0%); and 42 (56.0%) had a history of HPV infection.

When analyzing the origin of the referrals, 42 (56.0%) women were counter-referred from Primary Health Care Units or Specialized Centers. Regarding their family history of cancer, it was found that 28 (37.3%) women had this factor. It was also found that 21 (28.0%) medical records did not include this information.

When the risk factors were examined, it was found that 44 (58.7%) were not smokers and 48 (65.0%) were alcoholic. Regarding pregnancies, it was found that only five (6.6%) were nulliparous. Most had their menarche between 9 and 10 years old (57.3%), 19 (25.3%) had their coitarche from 17 to 18 years old, and 39 (52.0%) had had a menstrual cycle. Regarding their preferred contraceptive method, it was found that 37 (49.3%) mentioned the contraceptive pill, which was the most prevalent.

Regarding HPV infections, 42 (56.0%) participants had a history of infection by the virus or were currently infected by it. With regard to sexual activity, most 19 (25.4%) had sexual intercourse three times or more per week. Regarding the multiplicity of partners in sexual relations, 26 (34.7%) participants stated to have multiple partners.

A bivariate analysis was carried out to investigate the association of sociodemographic and clinical factors and the HPV infection. Regarding socioeco-

nomic aspects, the variables age group (OR=19.11; p=0.001) and educational level (OR=4.06; p=0.030) were statistically associated to the infection by HPV, meaning that women who were 24 years old or younger were 19 times more likely to manifest the infection, and those with complete high school or higher education were four times more likely. The other socioeconomic variables showed no significant relation with the infection by the virus (Table 1).

Table 1 – Association of sociodemographic factors with infections by the human papillomavirus in patients with cervical cancer, attended in a specialized hospital. Vitória, ES, Brazil, 2017

Relevant outcomes	Not infected n (%)	Infected n (%)	Odds Ratio	95% CI	p-value
Age group (years)					
≤ 24	1(3.8)	25 (96.2)	19.11	2.28 - 160.10	0.001 [†]
>24	13(4.3)	17(56.7)			
Skin color					
White	2(20.0)	8(80.0)			
Not white	12(26.1)	34(73.9)	25.50	4.73 - 137.29	0.680 [‡]
Educational level					
None or up to elementary education	10(38.5)	16(61.5)			
High school or higher education	4 (13.3)	26(86.7)	4.06	1.08 - 15.14	0.031 [†]
Occupation					
Paid work	7(20.6)	27(79.4)			
Unpaid work	7(31.8)	15(68.2)	0.55	0.16 - 1.88	0.340 [†]
Marital status					
Does not have a partner	7(24.1)	22(75.9)			
Has a partner	7(25.9)	20(74.1)	0.90	0.27 - 3.04	0.872 [†]
Referral					
Primary Health Care Unit	7(22.6)	24(77.4)			
Others	1(12.5)	7(87.5)	0.42	0.04 - 4.03	0.53 [‡]
Family history					
No	6(27.3)	16(72.7)			
Yes	8(30.8)	18(69.2)	0.84	0.24 - 2.95	0.789 [†]

*CI: Confidence interval; [†]Chi-squared test; [‡]Fisher's exact test

Regarding clinical variables, the variables associated to the HPV infection were: not having gone through the menopause (p=0.009), and sexual partners (OR=5.50; p=0.028). Those who had sexual intercourse with multiple partners were five times more likely to be infected by HPV (Table 2).

Table 2 – Association of clinical factors with infections by the human papillomavirus in patients attended in a specialized hospital. Vitória, ES, Brazil, 2017

Relevant outcomes	Not infected n (%)	Infected n (%)	Odds Ratio	95% CI	p-value
Currently smokes					
No	12(31.6)	26(68.4)			
Yes	2(15.4)	11(84.6)	7.56	1.46 - 38.96	0.474 [‡]
Currently drinks					
No	12(31.6)	26(68.4)			
Yes	2(15.4)	11(84.6)	7.56	1.46 - 38.96	0.474 [‡]
Number of pregnancies					
Nulliparous	1(20)	4(80)			
1 to 3	8(24.2)	25(75.8)			0.698 [†]
≥4	5(27.8)	13(72.2)	-		
Menarche (years)					
≤11	9(28.1)	23(71.9)			
>11	5(20.8)	19(79.2)	1.49	0.42 - 5.19	0.533 [†]
Coitarche (years)					
≤14	5(27.8)	13(72.2)	0.80	0.22 - 2.88	0.752 [†]
>14	9(23.7)	29(76.3)			
Menopause					
Yes	3(100.0)	0(0)			
No	6(16.2)	31(83.8)	-		0.009 [‡]
Contraceptive methods					
Condom	1(9.1)	10(90.9)			
Others	12(30.8)	27(69.2)	0.23	0.22 - 1.96	0.248 [‡]
No. of sexual relations (per week)					
1	1(33.3)	2(66.7)			
2	2(40.0)	3(60)			
3	2(12.5)	14(87.5)	-		0.050 [†]
≥4	2(100.0)	0(0)			
Sexual partners					
Single partner	6(42.9)	8(57.1)			
Multiple partners	3(12.0)	22(88)	5.50	1.10 - 27.37	0.028 [‡]

*CI: Confidence interval; [†]Chi-squared test; [‡]Fisher's exact test

Discussion

The limitations of this research should be highlighted, since it is an observational study and, as such, it was impossible to show cause-and-effect relations. Also, the data used was obtained from the records of professionals, which can be incompletely filled in. Finally, data was obtained exclusively from women with a cancer diagnostic, meaning that the prevalence could not be estimated, and the data cannot be extrapolated to the general population.

The description of the profile of these patients, associated to other risk factors for cervical cancer, reiterates the need for adequate treatment and follow up, so that the HPV infection does not evolve into a carcinoma, thus affecting public health policies.

Some variables were incomplete. The information collected for this study resulted from data collection instruments, through notes in the medical records of patients. As a result, the nursing consultation shows itself to be an effective tool for research support, with regards to enriching this data⁽⁹⁾. When secondary data scientific research is considered, the precision, maintenance, and register of this information, in accordance to nursing consultations, contribute for the perfecting of statistical analysis, as well as for the reliability of the profiles found⁽¹⁰⁾.

Although literature⁽¹⁰⁻¹³⁾ shows a relation between the use of alcohol and tobacco and HPV infections, these associations had no statistical significance in this study. The size of the sample and likely imprecision of the reports of patients, explained by myths and embarrassment with regard to the use of these substances, may have affected the analysis with regards to this association.

Nearly 15.0% of cases of cancer in humans are caused by viral infections, and 5.0% of them can be attributed to human papillomavirus infections. Consuming tobacco, alcohol, and illegal drugs increases the likelihood of a sexual behavior associated to sexually transmitted infections (early sexual initiation, many sexual partners, not using condoms)⁽¹¹⁾.

Regarding tobacco, it is recognized as a risk fac-

tor for the development of neoplasms, including uterine ones, since the cervical epithelium of women who smoke is more vulnerable to viral infections, contributing for the carcinogenesis process. Estimates indicate that HPV is responsible for 90.0% of cases of cervical cancer⁽¹²⁾. A national research on the prevalence of the human papillomavirus, carried out with 8,562 participants from 26 Brazilian capitals and the Federal District, found that alcohol and illegal drug use were associated to HPV infections; participants who reported these behaviors were twice more likely to be infected by the virus⁽¹³⁾.

Most cases of cervical cancer presented with HPV infections, which reiterates numerous researches and highlights the relevant role of the virus in the development of cervical cancer. Another research found that 55.9% of women presented a positive infection history, confirming the existence of genetic material of the virus in nearly 100.0% of invasive carcinomas⁽¹⁴⁾. Other researches also indicated a higher percentage of HPV-positive women^(5,7,15).

Among associated factors, age group stands out, since women up to 24 years old were more likely to be infected by HPV. This corroborates the findings of a study carried out in Juiz de Fora, Brazil, with women attended by the Family Health Strategy, in which women from 20 to 24 years old were five times more likely to be infected by HPV, when compared to other age groups⁽⁸⁾.

Young women are considered to be more susceptible to HPV infections due to their low level of use of protective methods, systemic immunological immaturity or cervical physiological immaturity, circumstances that favor viral activity⁽¹⁶⁾. Therefore, the findings of this research corroborate literature by pointing out that the relations found are connected to the fact that the incidence of HPV in younger women is due to the increasingly earlier coitarche, the multiple partners, little use of condoms, and unplanned sexual activities⁽¹⁷⁾.

An association of the infection with the educational level was also found to be statistically relevant, since women who had high school or complete higher

education were more exposed to the virus, a result that is in disagreement with other investigations⁽¹⁸⁾, in which most women had incomplete high school, which could be explained by the fact that women with lower educational levels are less present in health promotion and disease prevention services.

There was an association between HPV infections and women who had not gone through the menopause. Corroborating this result, women who are not subject to the clinical signs of menopause can maintain sexual regularity, which, consequently, exposes them to the virus, when the protective element is considered^(3,5-6).

It was also found that women with more varied sexual partners were more likely to contract the human papillomavirus infection, which is in accordance to other researches that found the same association⁽¹⁹⁻²⁰⁾.

The high number of partners lead to more exposure to HPV, increasing the chances of infection, and increasing the odds of contracting cervical cancer. This relationship is observed in clinical practice by the higher number of penis carcinomas in the partners of patients who had cervical carcinoma and tested positive for the virus⁽²⁰⁾.

As a result, the sexual behavior, followed or not by other co-factors, is directly associated to cervical cancer, which leads to reflections on the importance of approaches related to sexually transmissible diseases, aimed at encouraging the use of condoms, at vaccinating against HPV, and at maintaining regular female gynecological examinations. This data could contribute both for preventive actions and for early diagnoses, as it provides important information for the screening of cancer.

Conclusion

It was found that, in the population investigated, age group, educational level, not having gone through menopause, and multiple sex partners were associated to cervical cancer as related to the human papillomavirus. However, the records investigated

presented incomplete information.

Therefore, the findings of this investigation indicate the importance of keeping records of information associated with socioeconomic issues, gynecological history, and sexual behavior, to subsidize individualized plans of care. Furthermore, identifying these factors can contribute to the creation of more effective preventive strategies, both with regards to health education and to public health policies.

Collaborations

Guedes DHS and Santos MVF contributed for the design of the project, data analysis and interpretation, writing of the article, and for the approval of the final version to be published. Fiorin BH, Viana KCG, Portugal FB and Silva RA collaborated with data analysis and interpretation, a relevant critical review of the intellectual content, and in the approval of the final version to be published.

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