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ORIGINAL ARTICLE

SMOKING ASSOCIATED WITH PRECURSOR LESIONS FOR CANCER OF UTERINE CERVIX

TABAGISMO ASSOCIADO ÀS LESÕES PRECURSORAS PARA O CÂNCER DE COLO UTERINO EL TABACO ASOCIADO CON LESIONES PRECURSORAS DE CÁNCER DE CUELLO UTERINO

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ABSTRACT

Objective: to identify the relationship between *smoking* and the *precursors to cervical cancer*. **Method:** transversal documentary study with quantitative approach, performed in the Ambulatory of the lower Genital Tract Pathology and Colposcopy in Cáceres-MT, with 142 records. The collection occurred with questionnaire and analysis in the software EPI INFO 6.04 and SPSS-13.0. The Research Ethics Committee, Protocol n° 2009-141, has approved the research project. **Results:** patients' mean age was 38.8 years, the majority being married (68.3%), white (50.5%) ethnicity, household (57%), and residents in urban area (82.2%). Approximately 44% smoke or are ex-smokers and of these, 69% smoke or smoked more than 10 years. The average daily consumption was 15.8 cigarettes. There was Association of cofactor consumption greater than six years and the risk of cervical cancer. **Conclusion:** the high risk of cervical cancer was associated with women smokers. **Descriptors:** Tobacco; The Cervix; Intra-Cervical Epithelial Neoplastic.

RESUMO

Objetivo: identificar a relação *tabagismo* e *lesões precursoras para o câncer de colo uterino*. **Método:** estudo documental, transversal, com abordagem quantitativa, realizada no Ambulatório de Patologia do Trato Genital Inferior e Colposcopia, em Cáceres-MT, com 142 prontuários. A coleta ocorreu com questionário e análise no software EPI-INFO-6.04 e SPSS-13.0. O projeto de pesquisa foi aprovado pelo Comitê de Ética em Pesquisa, protocolo n° 2009-141. **Resultados:** a média de idade foi 38,8 anos, sendo maioria casadas (68,3%), etnia branca (50,5%), do lar (57%), residentes em área urbana (82,2%). Aproximadamente 44% fumam ou são ex-fumantes e, destas, 69% fumam ou fumaram mais de 10 anos. A média de consumo diário foi 15,8 cigarros. Houve associação do cofator consumo maior que seis anos e o risco de câncer do colo uterino. **Conclusão:** o elevado risco do câncer do colo uterino mostrou-se associado a mulheres tabagistas crônicas. **Descritores:** Tabagismo; Colo do Útero; Neoplasia Intra-epitelial Cervical.

RESUMEN

Objetivo: identificar la relación entre fumar y lesiones precursoras de cáncer del cuello uterino. **Método:** estudio documental transversal con enfoque cuantitativo, realizado en el ambulatorio de menor patología del tracto Genital y colposcopia en Cáceres-MT, con 142 registros. La colección se produjo con el cuestionario y análisis en el software EPI INFO 6.04 y SPSS 13.0. El proyecto de investigación ha sido aprobado por el Comité de ética de la investigación, Protocolo n° 2009-141. **Resultados:** la edad media fue de 38,8 años, siendo más blanco etnia (50,5%), hogar (57%), casado (68,3%), residentes en zona urbana (82,2%). Aproximadamente 44% fuman o son ex fumadores y, de éstos, 69% fuma o fumó más de 10 años. El consumo promedio diario fue de 15,8 cigarrillos. Hubo Asociación del consumo de cofactor de más de seis años y el riesgo de cáncer de cuello uterino. **Conclusión:** el alto riesgo de cáncer de cuello uterino se asoció con las fumadoras. **Descriptores:** Tabaco; El Cuello Uterino; Intracervical Epiteliales Neoplásicas.

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INTRODUCTION

Although theoretical-practical knowledge already exist sufficient to provide high levels of cure, cancer of the cervix has high mortality, that still remains a public health problem in Brazil, even with the existence of various government programs.¹

Whereas these precursor neoplastic lesions with good prognosis if diagnosed and treated early, the way of approach to population control consists of tracing by preventive examination for cancer of the cervix.²⁻³ This is also known as a Pap test, a simple and inexpensive procedure, able to detect changes in premalignant stages, when they are curable with relatively simple measures³⁻⁴ reducing the cumulative risk of cancer of the cervix in 84% for women tracked every five years, and 91% for women who undergo review every three years.³

It is estimated that a reduction of approximately 80% of mortality from this cancer can be achieved through tracking women in the age group of 25 to 65 years with the Pap test and treatment of precursor lesions with high potential for malignancy or carcinoma in situ⁵. After two negative annual analysis, the frequency of Pap smear or cytological colpo examination may be triennial, allowing it to identify the cases in which may have occurred false negative result.⁶

The main factor related to this type of cancer is infection by human papilloma virus (HPV), associated with cofactors such as smoking.⁷⁻⁸ it is noteworthy that the number of smokers, among females, has increased around the world, influenced by numerous economic and socio-cultural factors, especially in developing countries, turning the tobacco in one of the biggest causes of this type of tumor.⁹ Corroborating this fact, a study that addressed the quote changes and pathological risk factors illustrated that 48% of a total of 65 women who had cervical changes were smokers.¹⁰⁻¹¹

Furthermore, tobacco and its derivatives can induce many changes in the immune system, mainly in *natural killer* cells and *Langerhans* cells. In experimental studies, found that tobacco solution applied on the skin of mice triggered the emergence of *Langerhans* cells (LCs) rounded or elongated with few dendrites and development of neoplastic; while the abolition of tobacco presented LCs with numerous dendrites associated with lymphocyte infiltrate and regression of neoplastic cells. *Langerhans* cells are important components in the immune

surveillance system, because they are antigen presenting and specifically activate lymphocytes TCD4. Thus, the changes in these cells, suggest an immunodeficiency in of great significance in carcinogenesis.¹²

Through the exposed, the study aims to identify the relationship between smoking and precursor lesions for cancer of the uterine cervix.

METHOD

Article drawn from the dissertation << epidemiologic study of women with precursor lesions for cancer of the cervix in the region southwest of Mato Grosso in the Central-West >>, presented at Programa de Pós-Graduação em Ciências da Saúde, at the University of Brasilia/UNB. Brasília-DF, Brazil. 2011

Documentary Studydescriptive, transversal. The documentary study is characterized as a source of data collection restricted to documents, written or not, and what is called primary sources, which can be made at the time or after the occurrence of the fact or phenomenon.¹³

In the cross-sectional study, a single group selection, try with criterion to the group meeting time set by the investigator and, only in the analysis of the data it is known who is exposed and who is sick. The descriptive study is intended to inform the distribution of a population in quantitative terms. Reveal various aspects of health services, produces information on the existing situation, reflections and discussions on the subject and points to possible solutions.¹⁴

The municipality of Cáceres, which is 225 km from Cuiabá, in the southwest region of the State of Mato Grosso, configures itself in important regional health center. Has basic health units and 06 10 family health basic units (PSF), 9 in the urban area and one in the countryside. It houses the Regional Health Complex, with attendance of medium complexity.

The PTGIC of Regional Specialty Clinic Dr. Sebastião Batista de Miranda, the Regional Health Complex, was created in May 2001 and meets the users from 22 municipalities in the region, totaling a population of 185,611 users of the unified health system (SUS).¹⁵

Was considered, for the purposes of this study, the Census of the medical records of women met in the PTGIC clinic of Regional Health Complex in the year of 2009, 315 medical records. After application of exclusion criteria remaining 142 records that make up the results of the study.

Were excluded from this study: (1) results of oncologic colpocitologia (CCO) unsatisfactory due to the following factors: wrong ID or absence of identification, identification of the blade was not matched with the form, hemorrhagic, or draining scarce material, thick, purulent smear areas, damaged or missing blade; (2) Pregnant Women, hysterectomies, with the past treatment of cervical cancer and/or its precursor lesions and genital bleeding; (3) Women referred to the service without BCC survey result; (4) Women referred to the service as a result of normal BCC, inflammatory or metaplásico.

Considering directed cervical biopsy gold standard in the diagnosis of cervical intraepithelial lesions, precursors of cancer of the uterine cervix subsequently were deleted: (5) women with Bcc result changed and negative colposcopy exam; (6) women with Bcc result changed, colposcopy, however, without biopsy.

The data were collected in the period from November 2009 to February 2010, with the use of an instrument, data collection form, included 35 topics that discuss information about identification (card number, initials of the name, date of birth); socio-demographic (origin, living area, marital status, ethnicity, occupation, education); reproductive history (menarche, parity, contraceptive methods); sexual behavior (coitarca, total number of partners and in the last year prior, DST); smoking and service-related information in the unified Health System (date of completion of the CCO examination and result, date of submission, date of the first query, result of colposcopy, biopsy and need the biopsy

result). Points out that in this study will be emphasized the information related to the habit of smoking.

The collection of data (typing) was made using the EPI-INFO 6.04 software (version 3.5.1, August 2008). Data base processing was done with Excel ® for Windows ® software. All statistical analyses were done with the software SPSS ® (*Statistic Package for the Social Sciences*, Chicago, IL, USA), version 13 for Windows ®.

Possible associations between variables were evaluated by the Chi-square test (χ^2). The calculation of the odds ratio (*Odds Ratio*, *OR*) was made from 2×2 contingency tables and used the formula reason of cross products. The confidence interval was 95%.

In 2×2 tables, the significance level (p-value) was calculated for the Fisher exact probability test. For all tests, the level of statistical significance was set at p 0.05 (two-tailed). <

The research project was submitted to the Research Ethics Committee (CEP) at the University of Cuiabá-UNIC, in the city of Cuiabá, Mato Grosso State, being approved as Record n° 131 zip/UNIC/2009-Protocol 2009-No. 141.

RESULTS

In the sample of the survey, the average age was 38.8 years most married or in stable (68.3%), with equal or less than the full elementary school (67%), white (50.5%), home (57%) and much reside in urban areas (82.2%).

In table, one and two are found the smoking-related data of the study group and women smoke are smokers.

Table 1. Frequency distribution in relation to the studied women is smoking habit-Ambulatory PTGIC, Cáceres - MT, 2009.

Smoking habit	N	%	% valid
Yes	37	26.1	28.0
Ex-smoker	21	14.8	15.9
Not	74	52.1	56.1
Total valid	132	93.0	100.0
Not informed	10	7.0	

With respect to tobacco use (table 1), it was found that approximately 44% (58) of the women in this study smoke or are ex-smokers and, of these, 69% (40) smoke or smoked for

more than 10 years (table 2). The average daily cigarette consumption was 15.8, with standard deviation of 13.9 and median of 10 cigarettes a day.

Table 2. Frequency Distribution and measures of dispersion and position in relation to the studied women smoke-PTGIC, Cáceres Clinic-MT, 2009.

Smoke time (years) *	In	%	% valid
1 to 3 years	5	8.6	8.6
4 to 10 years	13	22.4	22.4
11 to 15 years	11	19.0	19.0
16 to 30 years	13	22.4	22.4
31 years or more	16	27.6	27.6

*Among the smokers and ex-smokers Tobacco (years) = Average 21.2; Standard deviation = 16.6; Minimum value found = 1; Maximum value found = 60; First quartile = 8; Median = 15.5; Third quartile = 35. No cigarettes/day = 15.8 Average; Standard deviation = 13.9; Minimum value found = 1; Maximum value found = 60; First quartile = 10; Median = 10; Third quartile = 20.

For analysis of odds ratio between the variables of interest *versus* the high and low risk of developing cervical cancer, the result of biopsies was classified into two groups: low risk to develop high grade lesion and cancer, including histopathological result of normal biopsy, chronic cervicitis, HPV and low grade cervical intraepithelial neoplastic (CIN 1); and high risk to develop high grade lesion and cancer, including histopathological result biopsy high grade cervical intraepithelial neoplastic (CIN 2 and CIN 3) and *in*

situcarcinoma, adenocarcinoma *in situ* and invasive carcinoma, micro invasive carcinoma.

The quantitative variables were transformed into ordinal variables using the median as cutting point being: cigarette time (≤ 5 years and ≥ 6 years); number of cigarettes consumed per day (≤ 10 cigarettes/day and ≥ 11 cigarettes/day).

The nominal variable smoking was grouped into two categories: Yes (smokers and ex-smokers) or non-smokers.

Table 3. Odds Ratio of factors linked to smoking associated with Outpatient PTGIC biopsy results, Cáceres - MT, 2009.

Variable	Risk of cancer		Total	OR	IC 95%	x ²	p-value
	High	Low					
Smoker							
Yes	37	21	58	1.62	0.80 -3.29		
Not	38	35	73				
Yes X No						1.820	0.214
Time of smoker							
≥ 6 years	33	15	48	2.20	-4.65 1.04		
≤ 5 years	41	41	82				
≥ 6 years X ≤ 5 years						4.341	0.044
Number of cigarettes/day							
≥ 11 cigarettes	15	10	25	0.87	-2.59 0.29		
≤ 10 cigarettes	19	11	30				
11 cigarettes X ≤ ≥ 10 cigarettes						0.064	1

It is observed in table 3, as to the fact of being a smoker, there was no significant association between the two variables ($x^2= 1.820$, $p = 0.214$). Alternatively, calculation showed that the fact of being a smoker increases in 1.62 times the chance to own precursors to cervical cancer, but did not present a statistically significant value (0.80-3.29).

In relation to the consumption of cigarettes (years) the Chi-square test showed a statistically significant association between the two variables ($x^2= 4.341$, $p = 0.044$). The calculation of OR showed that patients with positive results have 2.20 times higher odds of having used cigarette for over 6 years. (95% CI: 1.04-4.65);

With regard to the number of cigarettes per day Chi-square testwas not statistically significant ($X^2= 1$ and $p = 0.064$). In the calculation of OR, the fact that smoking

cigarettes 11 or more increases in 0.87 times the chance of women present positive result, however there was no significant association between the two variables (OR = 0.87, 95% CI: 0.29 to 2.59).

DISCUSSION

As previously stated 44% of women smoke or are ex-smokers, and of these, 69% smoke more than ten years. Similar results were observed in a study of¹⁶ in which the frequency of women smokers with cervical intraepithelial neoplastic was (59/132) 44.7% and, among these, (41/59) 69.5% smoked more than 10 years.

In a cohort study¹⁷ the authors found frequency (10,070/24,792) 40.6% in 1963 and (11,403/26,381) 43.2% in 1975. A case study¹⁸ control with 684 women, being 171 cases (≥ 1 NIC) and 513 controls have shown that, among women with high-grade lesions for cervical

cancer (≥ 2 NIC), (36/59) 61% of them were passive smokers (9/59) and 15% were active smokers.

Three other studies¹⁹⁻²¹ frequency observed in smokers of intraepithelial lesion (21/64) 32.7% (2026/5485) 35.1% (156/346) 45.1%, respectively and consider such a high percentage, stating that women smokers should be considered as a group at high risk for developing the disease.

The relationship of smoking as an important causal factor for cancer of the cervix is already well known.⁶ study published in 2012 showed that of 15 (19.48%) women interviewed who used cigarettes, seven did so for more than ten years. Research carried out in 2002, in a colposcopy clinic in the United States of America, showed that of the 250 women who had undergone the PAP exams changed or previous diagnosis of uterine cervix cancer, 98 (39%) were smokers, considered a high percentage.⁶

In an analysis of 10 case-control studies of women with carcinoma *in situ* or invasive carcinoma of the uterine cervix, four continents, which assessed the cofactors of risk for cervical cancer, in which were included only women with positive HPV DNA test, it was found that smoking increases the risk of cervical cancer in women with positive HPV DNA test being, OR = 2.17 (IC 95%: 1.46-3.22).²² other authors²³ still described positive association between smoking and cancer of the uterine cervix and demonstrated that the tobacco Association and multiple partners (greater than or equal to two) increase by 2.6 times the risk of cancer, compared to women with a partner and non-smokers (OR = 2.6, 95% CI 2.3 -2.9).

It is worth noting that despite the reported so far, the fact of being a smoker in this study did not show statistically significant difference when compared to the non-smokers. A similar result was found in²⁴ study where the authors did not observe a correlation between smoking and risk of progression to cervical cancer when evaluated in isolation, however, the author reports that smoking, associated with the use of hormonal contraceptives featured a 4.6 times greater risk of developing cervical cancer when compared to other groups of women (only users of oral contraceptive-ACO only smokers, not users of STAINLESS STEEL and non-smokers) (IC 95%: 1.1-18.4).

Study *Langerhans* cells were demonstrated by immunohistochemical method and isometric study, showed that the average density of *Langerhans* cells in the epithelium were 232.41 cells/mm² for smokers and

221.08 cells/mm² for non-smokers. These values did not show statistically significant differences, both in the study of total as histological layered epithelium, confirming comments made by another author⁷ who has studied adolescent smokers and 29 20 non-smokers with cervical Condyloma or cervical intraepithelial neoplastic, noting significant reduction in density of LCs, even between patients with and without NIC.¹²

In the published literature in the year 2010, the authors studied the association between smoking and exam results showed more frequent visual inspection with acetic acid (VAT) positive women non-smokers (47.0%), as well as in cytology with 4.0%, however, in cervicography, there was a higher percentage of exams changed in the Group of smokers (33.0%).²⁵

As can be seen, there are both study showing tobacco Association as a cofactor for cervical cancer, the study added that this Association is not regarded as a cofactor, demonstrating the importance in developing new studies featuring this theme.

One of the analyses described above on the results, to the variable significantly associated with high risk for cervical cancer was the cigarette consumption for a period of more than six years, which, as stated earlier, showed 2.2 times greater chance of women with high-risk cervical changes.

Other than found in this, an author in his study²¹ not observed positive association between HPV positive women and consumption ≥ 6 years (RR = 95% CI 0.61 0.33 - 1.13).

With regard to the number of cigarettes consumed by smokers was¹⁷ noted that consumption of 11 or more cigarettes increases the risk of developing cancer or cancer, as well as prove that passive smoking is also a risk factor for cervical neoplastic.

There was also a dose dependency with the number of cigarettes and the decreased density of *Langerhans* cells. Similar results were observed in another study, in which the sex workers, smokers for more than 5 years or who smoke more than 20 cigarettes/day, presented a high risk of developing cervical intraepithelial neoplastic (CIN) or invasive cancer. Certain authors also confirmed these results, both in ectocervix as in cervical transformation zone of smokers, however, found no correlation with the dose-dependency property.¹²

Evaluation of data from 23 epidemiological studies conducted in the United Kingdom, about cervical cancer, defined with clarity

that the risk of this type of cancer is related to the number of cigarettes per day (intensity) and with the onset of smoking in earlier ages (duration), as well as influence on the survival time of these women, after the occurrence of cervical cancer. High concentrations of cotinina and nicotine cigarette, metabolic, have been detected in the mucus of the cervical canal. It is suggested that these substances are carcinogenic effect and direct co-carcinogenic action yet. In addition, the smoke seems to play role immunosuppressant, modifying so sharp the immune defense mechanisms of changes of concentrations of T4 and T8 lymphocytes.⁶ it is necessary to emphasize that in this study the number of cigarettes did not present significant association, but as has been seen, there are several studies that demonstrate this fact as a cofactor.

The professional should seek educational practices in disease prevention and health promotion of the quality of life of women. Education and health are spaces of production and application of knowledge for human development.²⁶

CONCLUSION

The information obtained in the conduct of this study made it possible to describe some of the features of women smokers with precursor lesions for cancer of the cervix in the region southwest of Mato Grosso. It was found that about 44% of women smoke or are ex-smokers and, of these, 69% smoke or smoked for more than 10 years, and one of the smokers to daily cigarette consumption average was 15.8, and median of 10 cigarettes a day.

The fact of being a smoker and number of cigarettes per day did not present statistically significant association in respect of precursor lesions for cancer of the uterine cervix. It has been shown that the high risk of developing cervical cancer is associated with chronic smokers, women with cigarette consumption by more than 06 years, since the Association of cofactors and the risk of developing cancer of the uterine cervix were positive for cigarette consumption time greater than six years.

Emphasizes the importance of developing new studies conducted with a larger number of cases for the results as to the effect of smoking as a cofactor of the appearance of precursor lesions for cancer of the uterine cervix.

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